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Wednesday, September 21

10:00-10:30

Transdisciplinary project: Medicine & Life Sciences

Chair: Ruedi Haller / Swiss National Park, President Club da Hockey Engiadina

Immune-inflammatory proteome of elite ice hockey players before and after SARS-CoV-2 infection

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Coronavirus disease 19 (COVID-19) is an infectious disease transmitted mainly through aerosol spread of severe acute respiratory syndrome coronavirus-2 (SARSCoV-2) and in most cases leads mild to moderate respiratory illness, which usually resolves within 5-7 days. Regular moderate-to-vigorous exercise has been associated with a strong and timely immune response against infections, thus reducing susceptibility to acute respiratory illness, and also protecting from severe COVID-19 outcomes. Frequent high intensity training has also been proposed to enhance vaccine-induced cellular and humoral immunity. However, long-term high-intensity physical activity and stressors associated with elite sports might cause hyperinflammation in some individuals and increase the risk of respiratory illness, and ice hockey players are among those winter sport athletes, who have the highest incidence in that context. Proteomic profiling of COVID-19 patients has proven valuable in the discovery of novel biomarkers associated with disease susceptibility, course, complications and severity, but so far there are no reports of COVID-19 proteomic studies in athletes. Herein, we examined the immune-inflammatory proteome of elite ice hockey players before and after a team-wide COVID-19 outbreak with the omicron BA.1 variant in December 2021.

Serum blood samples and questionnaire data were obtained from 24 players of a Swiss National League ice hockey team 3 months prior to COVID-19 and from the same players within 1-2 weeks after nasal swab PCR-confirmed SARS-CoV-2 infection, and of 20 controls, that are non-ice hockey players after recent recovery from COVID-19. Proximity extension assay (PEA) technology by OLINK was used for targeted proteomic serum analyses of 180 proteins measured in the OLINK immune response and inflammation panels (92 proteins each, 4 overlaps).

Immune-inflammatory profiles of ice hockey players were compared at two time points (preand post-COVID-19). Additionally, post-COVID-19 profiles of ice hockey players were compared to the post-COVID-19 control group for reference. Ice hockey players and control subjects reported comparable rates of previous SARSCoV-2 infections, atopic comorbidities (asthma, allergic rhinitis), regularly occurring upper respiratory tract infections (URTI), fever and recurrent herpes labialis. COVID-19 vaccination history did not differ between athletes and controls. Control subjects reported a higher prevalence of symptoms in general, and respiratory symptoms specifically. Clinical laboratory serum analyses showed no difference between ice hockey players and controls. PEA-based proteomic analyses of serum samples from elite ice hockey players identified 28 differentially expressed proteins involved in immune response and inflammation with a rather distinct representation of biological process networks. While similar process networks were found to be present at both sampling time points, specifically, lymphocyte proliferation (CXCL12, CD40, PRKCQ, TNFSF14pre-COVID19 and TRAF2, IRAK4, CASP-8 post-COVID-19) and innate inflammatory response (PRKCQ, IRAK1 pre-COVID-19 and of TRAF2, IRAK4 post-COVID-19), the post-COVID-19 profile was uniquely marked by an increase in proteins involved in innate immune response to viral infection, neutrophil activation, IL-12/-15/- 18 and IFNy-signaling. This last finding therefore may reflect how the immune system responds efficiently to COVID-19, where a timely release of antiviral interferons seems to be essential. While we could clearly separate athletes pre- and post-infection, post-COVID-19 comparison of ice hockey players with post-COVID-19 samples of the control non-ice hockey players group revealed similar proteomic patterns, with only CCL11 showing a significantly higher expression in the control group. Of note, levels of CCL11 have recently been found to be elevated in patients experiencing cognitive symptoms ("brain fog") after mild COVID-19 compared to those without such symptoms. 6 However, we did not assess incidence of post- or long-COVID-19 symptoms in our cohorts. It could be hypothesized that the higher reported incidence of COVID-19 symptoms in the control group might be linked with a weaker immunological response to either the virus, the vaccination or both, or even due to the fact that more ice hockey players had received a booster shot by the time they got infected (33% vs. 15% of controls).

To conclude, we found that immune-inflammatory proteomic profiles in serum of elite ice hockey players differ significantly pre- and post-COVID-19. The cause for this observation might be multifactorial, e.g., direct impact of the recent SARS-CoV-2 infection, seasonal changes, or training-related influences on sampling timepoints. Although proteomic profiles generally did not differ between athletes and control subjects post-COVID-19, the higher incidence of symptomatic disease in the control group warrants follow-up studies to investigate the potential impact of athletic workloads on (SARS-CoV-2) infection susceptibility, disease course and vaccination response, as well as to identify associated biomarkers.

Wednesday, September 21

10:45-12:00

Session 1 Medicine & Life Sciences

Chairs: Tiziano Serra / AO Research Institute Davos, Michael Villiger / Swiss Research Institute for Sports Medicine (SRISM), Spital Davos

Combination of the collagen membranes within the LEGO[®] inspired interlocking system, a new therapeutic alternative for bone regeneration in maxillary defects

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The regeneration of bone defects in the lower jaw is an important topic, but with few therapeutic alternatives.

Planning the future restoration of the lower jaw area, a correct diagnosis of the defect and adequate case planning are essential.

There are several causes of bone defects, although a simple tooth extraction and periodontopathies are the main diseases that cause this clinical problem. Additionally, on a smaller scale, other conditions such as infections, trauma, tumors, cysts and even the use of dental prostheses can increase bone resorption leading to great deformities.

When teeth are extracted, the bone that supports them tends to shrink over time. This process is called resorption and is a natural consequence of the lack of stimulation to the bone by the forces exerted on the teeth. Resorption of the alveolar bone (the bone that supports the teeth) begins almost as soon as the tooth is extracted and continues over time. The bone loses both height and width through resorption. When multiple teeth are lost, with or without dentures to replace them, there can be significant bone loss in the jaw, and this can lead to difficulty in subsequent rehabilitation.

Guided Bone Regeneration (GBR) is currently considered a therapy of great importance in Implantology, to promote bone regeneration in bone defects of the jaw. The purpose is to create a suitable area for subsequent rehabilitation with implants or conventional prostheses. GBR is based on the use of resorbable and non-resorbable membranes in combination with filler biomaterials such as bone from various sources or alloplastic materials with mechanical barrier functions, tending to exclude epithelial and conjunctival cells from the repair area, allowing the invasion of osteoprogenitor cells.

Scientific evidence shows that resorbable (biocompatible plastics) membranes can be successfully used for GBR.

However, in certain clinical situations, these membranes do not resist the pressure exerted by the tissues during healing, therefore, their use is advised in combination with different types of grafts, with the intention of maintaining these structural spaces.

3d printer scaffolds are fundamental components for tissue engineering. but since there are still challenges to overcome, such as the correct combination of their mechanical properties, degradation speed, porosity, biocompatibility and functional integration with the bone, these must be combined with other materials.

Due to the printing porosity and low attachment properties of the scaffold cells that are seeded on top fall through and cannot be retained as previous studies have showed.

To provide different alternative to existing treatments, the present work aims to find a suitable collagen membrane capable of retaining the cells within the scaffold structure previously designed with a configurable layer composition based on the LEGO[®] principle to achieve the promotion of cell viability and response.

The LEGO[®]-like structures are virtually designed using CAD software (Autodesk Fusion 360[®]) and printed into layered scaffolds composed of polycaprolactone (PCL) Using a RegenHu 3D Discovery[®] bioprinter. The collagen membranes that we used were: 1. Lyostypt (B. Braun) and 2. Collagen Cell Carrier (CCC) (Viscofan Bio Engineering). These membranes are placed in between layers of the 3D-printed scaffolds layers that interlock with each other via the LEGO[®] system. We seeded mesenchymal stromal cells (hBM-MSCs) on top of the assembled scaffold. In a 7-day retention experiment we examined the viability of hBM-MSCs within the scaffold with and without collagen membranes at two-time points Day 1 and Day 7. We performed DNA and LIVE/DEAD assays and we were able to observe a good cell survival showing 1. that membranes can retain cells, which was not possible testing the scaffold only 2. that hBM-MSCs on CCC membranes showed increased spreading compared to the Lyostypt membrane.

We can show that hBM-MSCs can be retained by the combination of the collagen membranes and the LEGO[®] inspired interlocking system and opens a wide possibility of achievements in reconstructive medicine. We propose it as a new therapeutic alternative in the tissue engineering approach for reconstruction of jawbone defects. Ongoing tests aim to demonstrate the osteogenic capabilities of collagen membranes placed inside 3D printed scaffolds.

Building a data analysis pipeline for long-read, amplicon-based, raw DNA-sequence data generated by Oxford Nanopore Technology

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Introduction:

Modern DNA sequencing techniques are capable of generating so-called "long reads" of single-stranded DNA. Such "long reads" enable a haplotype-specific analysis of the two parental allele variants. This is particularly important when (at least) two single nucleotide variants (SNVs) are several hundred base pairs apart, making it difficult to determine their relationship to each other using conventional methods. Oxford Nanopore Technology (ONT) currently allows the longest read lengths of up to four mega base pairs.

However, using this promising technology poses a major challenge due to downstream data analysis. Currently, there is no clearly established software pipeline for processing and analyzing the raw sequencing data to obtain haplotype-specific results. Rather, several publicly available software tools must be combined. These individual elements are often poorly documented and require a high level of bioinformatics knowledge to use efficiently.

We have therefore developed a data analysis pipeline that allows the automated processing of amplicon-specific long-read ONT sequencing data.

Materials and Methods:

We designed long range PCR reactions for the partly homologous *FUT1*, *FUT2* and *FUT3* genes. These genes encode the human blood group systems "Lewis" and "H". 32 DNA samples were amplified and processed according to the ONT protocol for amplicon barcoding with native barcoding expansion 96 (EXP-NBD196, and SQK-LSK109) then analyzed on MinION using an R10.3 flow cell.

Basecalling was performed in high accuracy mode using Guppy Basecalling Software ((C) Oxford Nanopore Technologies plc. Version 6.1.3+cc1d765d3) and separated by barcode ID. An initial quality check was performed with NanoPlot (version 1.40.0).

Reads were subsequently filtered for quality score and expected amplicon length using NanoFilt (version 2.8.0).

Alignment to the reference sequence was done with minimap2 (version 2.24-r1122). The resulting SAM (sequence alignment map) file was then converted to its binary counterpart using samtools (version 1.15, htslib 1.15). Bcftools (version 1.15) was used for calling variants and filtering according to quality score.

Phasing of haplotypes was performed by whatshap (version 1.4) and ONToHap (ONToHapv1.0.0) respectively. Whatshap statistics yielded an overview of phasing data including variant characteristics for each gene. Haplotype specific sequences in FASTA format were generated by bcftools (version 1.15).

Finally, this analysis sequence was automated using Linux bash script.

Results:

For each gene, this data analysis pipeline generated phased haplotypes of approximately 11 kilo base pairs. Processing the raw data was performed simultaneously for all 32 DNA samples.

Conclusion:

The described data analysis pipeline allows for simple and time efficient processing of long read, amplicon-based sequencing data generated by Oxford Nanopore Technology.

Characterization of single allergen-specific IgE+ B cell from cow's milk allergic children during the oral immunotherapy

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Background:

The prevalence of allergic patients suffering from IgE-mediated food allergies has been increasing in recent decades. The immunological mechanisms causing IgE-mediated food allergy have been comprehensively investigated. In this context, B cells are the main source of allergen-specific IgE antibody production and markedly contribute to the development of IgE-mediated food allergy. Therefore, the aim of this study is to characterize the role of single allergen-specific IgE+ B cells in children with cow's milk allergy during oral immunotherapy (OIT).

Methods:

Peripheral blood mononuclear cells (PBMC) from cow's milk allergic children participating in clinical OIT were isolated and immortalized with a retroviral vector containing GFP, BCL6, and Bcl-xL. Cells were enriched by culturing with CD40L and IL-21. Total and specific IgE, IgG, and IgG subclass antibodies (IgG1, IgG2, IgG3, and IgG4) from the culture supernatants of immortalized B cells were measured by ELISA. Subsequently, the single IgE+ B cells were identified and sorted in flow cytometry with the combination of different surface markers such as IgM, IgD, IgG1, IgG2, IgG3, IgG4, and IgA. Next generation single cell RNA sequencing was performed for quantitative transcriptomics using state-of-art 10X genomics technology.

Results:

The production of specific IgE, IgG1, and IgG4 from the culture supernatants of the immortalized allergen-specific B cells pools from 7 patients before and 18-35 after OIT was significantly increased when compared with the non-specific population. Using the candidates immortalized B cell pools with the highest specific IgE production, we sorted the single allergen-specific IgE+ B cell along with their other immunoglobulin subclasses (IgG1, IgG2, IgG3, IgG4, and IgA) B cells and further processed them using 10X genomics' single-cell RNA sequencing technology.

Conclusions:

This study mainly focuses on the characterization of single allergen-specific IgE+ B cells from allergic individuals. Interestingly, allergen-specific immortalized B cells secreted an increased amount of specific IgE, IgG1 and IgG4. The differentially expressed genes of single allergen-specific IgE+, IgG1+, IgG2+, IgG3+, IgG4+, and IgA+ B cells need to be further investigated to uncover the immunological mechanisms that cause IgE-mediated food allergy.

Keywords:

Single IgE+ B cells, food allergy, oral immunotherapy (OIT), immunoglobulin subclasses, differentially expressed genes (DEGs)

Natural bone inspired 3D printed composite biomaterial-ink composed of hyaluronan, collagen and calcium phosphate particles to promote bone regeneration

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Introduction: Bone has the intrinsic capacity to regenerate after injury. However, in large bone defects caused by trauma, tumor resection, skeletal abnormalities or infections, the self-healing capacity of bone is insufficient and leads in 10-20% of the cases to non-union. The clinical gold standard treatment autologous bone grafting, where bone is harvested from a donor site in the same patient, has limitations, since to harvest the bone another injury is created and the amount of bone that can be harvested is limited. Besides, current tissue engineered constructs lack spatial control over scaffold architecture to anatomically match complicated bone defect sites. This represents an extensive clinical challenge and a need to develop new treatment options for large bone defects. 3D printing can overcome the above-mentioned limitations, by enabling the fabrication of patient specific bone graft substitutes that are customized to fit the bone defect site. This technology also facilitates control over the microarchitecture of scaffolds, including the pore size, porosity, and shape. Additionally, 3D printing facilitates the fabrication of materials composed of multiple components to resemble the heterogenous composition of bone. Therefore, this study aims to develop a 3D-printable composite biomaterial-ink to fabricate patient-specific bone graft substitutes that provide control over shape, architecture, and composition to promote bone regeneration. Inspired by the natural composition of bone, the biomaterial-ink consists of inorganic osteoinductive calcium phosphate particles (CaP) in a biopolymer matrix made of tyramine modified hyaluronic acid mixed with Collagen (THA-Col) of tailorable printability properties.

<u>Methods:</u> Biomaterial-ink was composed of CaP that were incorporated in THA or THA-Col, supplemented with horseradish peroxidase (HRP) and Eosin Y, for crosslinking. Precrosslinking, by addition of H_2O_2 and NaOH, was carried out to form a gel that can be extruded using 3D-printing and keeps its shape after extrusion. After the desired 3D structure was printed, scaffolds were further cured with green light (505 nm) for 30 minutes. Biomaterial-ink formulations were characterized by printability (continuous strut, line spacing, lattice, and an overhanging strut on a pillar structure), cohesion, swelling, *in vitro* degradability, and compressive modulus. Compositions were assessed *in vitro* using a metabolic activity assay. Additionally, human mesenchymal stem cells (hMSCs) will be cultured on different scaffold compositions to evaluate for new bone formation potential by differentiating hMSCs into osteoblasts assessing mineralization, alkaline phosphatase (ALP) production, and gene expression.

<u>Results:</u> Both THA alone and THA-Col are 3D printable, it is possible to extrude via a nozzle and when extruded it forms a continuous strut without waviness and hold its shape. Swelling of the formulations reached a plateau after 24 hours. The increasing addition of CaP into the organic matrix resulted in increasing compressive modulus and decreasing *in vitro* degradation rate. *In vitro* evaluation, without the addition of CaP, revealed that THA-Col showed both higher metabolic activity of hMSCs and higher ALP content after 14 days of osteogenic differentiation, compared to THA alone. <u>Conclusion</u>: Here, a 3D printable composite biomaterial-ink of THA-Col with CaP was biofabricated. This biomaterial-ink overcomes current treatment limitations and holds great potential as bone graft substitute to promote regeneration in large bone defects. This work, inspired by the natural composition of bone, is significant since it can aid in the treatment of bone defects without the necessity to harvest bone from a donor site.

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Gut epithelial barrier damage by commonly used emulsifiers polysorbate-20 and polysorbate-80

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Environmental exposures such as emulsifiers introduced to our lives with modernization and industrialization can alter the structure of the gut microbiome and influence the development of diseases. Polysorbate emulsifiers are a class of food additives used in food processing commonly used in pastry, bread, ice creams etc. We investigated the effects of polysorbate-20 (P20) and polysorbate-80 (P80) on cytotoxicity, barrier function, transcriptome and protein expression in gastrointestinal epithelial cells.

Enterocytic liquid-liquid interfaces were established by culturing Caco-2 cells on permeable supports, emulsifiers were added to the apical compartment individually or together, and then cytotoxicity, transepithelial-electirical-resistance (TER), paracellular flux and immunofluorescence staining of tight junctions were measured. Moreover, RNA-seq transcriptome and targeted proteomics were analyzed. Starting from the 0.1% concentration, cells showed lysis in response to P20 and P80 exposure. A disrupted epithelial barrier was found with decreased TEER, increased paracellular flux and irregular TJ immunostaining in liquid-liquid interfaces of Caco-2 cells. We also used gut-on-a-chip model that is a 3D approach and observed nearly same results with 2D model.

The RNA-seq analysis showed that P20, P80 and P20+P80 together upregulated biological processes including developmental process, response to starvation and response to organic substances. Apoptotic process was significantly upregulated in response to both P20 and P80, whereas cell differentiation, cell-cell adhesion and response to wounding pathways were upregulated only in response to P80. The RNA-seq analysis also showed regulation of genes encoding tight junction and adherence junction in response to P20, P80 and P20+P80 together. The targeted proteomics analysis revealed significantly change in 33 proteins in response to P80, and 23 proteins in response to P20+P80 related with immune and inflammation response.

Overall, this study provided that P20 and P80 directly impair barrier integrity of gastrointestinal epithelial cells and are potent at doses of daily usage.

Wednesday, September 21

10:45-12:00

Session 2 Natural Sciences

Chairs: Ana Petrus / University of Applied Sciences of the Grisons, Nadine Salzmann / WSL Institute for Snow and Avalanche Research SLF

Differences in vegetation composition, bacterial community and soil properties after restoration of construction sites on alpine grasslands

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Alpine and subalpine areas in the mountainous region of Switzerland have long been inhabited by humans and used for grazing by cows or sheep and represent a living cultural landscape. Abandonment and forestation are leading to a decline in these alpine meadows and pastures, which represent a third of all agricultural land in Switzerland. In addition, the brisk construction activity of recent years is exerting additional pressure on the agricultural land, especially in areas used for recreation and tourism. Since the 1990s, the number of transport infrastructure (in particular drag lifts, number of cable cars remained stable) in the mountains has decreased slightly (status 2020: 2,433 installations), but the extent of snow making infrastructure has increased substantially. Of the 22,500 ha of pistes in Switzerland, 11,975 ha now have artificial snow (in 2020: 53 %). Typically, these structural interventions (e.g. pipe trenches) and anthropogenic soil movements affect easily accessible subalpine and alpine nutrient-poor grassland, which have very slow regeneration times due to temperature and the short vegetation period. Today, the high-altitude revegetation shows a pleasing success with regard to the important erosion protection and the achieved coverage of the vascular plants. From a phytosociological perspective however, it represents insufficient restoration, which contradicts the conservation of alpine biodiversity in Switzerland. Therefore, several success controls of high-altitude revegetation have already been carried out in recent years. However, with the advent of genetic analyses for species identification, revegetation can now be evaluated not only on the surface, but statements can be made about the entire biocenosis. The present work on the differences in disturbed and undisturbed alpine pastures is a start by applying these same methods on a small geographical scale to the well-studied species group of soil bacteria, combined with phytosociological surveys and soil chemical analyses.

Vegetation surveys and soil samples were taken within two former construction sites and near them in undisturbed areas at 2500 m a. s. l., above the tree line in circular 10 m2 plots at the Curtinella ski lift on the Corvatsch mountain range (Canton Graubünden, Switzerland) in 2021. The construction sites were re-vegetated in 2017 (seeding and turf) and 2020 (turf). The areas from 2017 are used as ski slopes with artificial snow. The vegetation cover of the species was recorded, the soil cover (stones, gravel, fine soil) estimated and the soil depth, pH and electrical conductivity measured. The nutrient content (C, H, N) as well as the content of active microorganisms of the soil samples were analysed. In addition, the bacterial community was analysed via 16S rRNA-sequencing. The Shannon index was used as a measure of Biodiversity of species community, which was compared in pairs between the different types of sites investigated.

The plots of the sown construction site from 2017 show a decrease in the number of species and Shannon index compared to the undisturbed plots, the plots of the construction site with turf from 2020 show a decrease in the vegetation cover and Shannon index. Soil chemical and biological parameters correlated strongly with soil depth and the proportion of gravel fraction of the topsoil as well as the cover of the herb layer. Both former construction sites show a significant decrease in soil depth and nutrients and an increase of pH. In addition, a significant decrease in soil microbial activity could be detected, as well as a general decrease in bacterial abundance. The Shannon index of the bacterial communities, however, was higher in the disturbed areas. In general, the composition of the bacteria differed and the undisturbed areas could be clearly distinguished. This resulted in eight common taxa of bacteria at the genus level, which in turn will serve as indicators for undisturbed alpine soils in the study area.

Despite the rather successful revegetation for this altitude, the results of this small-scale study in construction sites after one to four years, show a considerable loss of plant species diversity and topsoil quantity, which has a direct impact on the nutrients available in the soil as well as on the bacterial abundance and its composition. With the claim of maintaining biodiversity in high elevation revegetation, this methodology can be applied in a larger scale study to include additional species groups and describe a more holistic biocenosis. Given the slow regeneration time of soils and habitats at this altitude as well as the current high soil losses worldwide, the results speak also for a considerate approach to future construction sites in alpine regions.

Keywords:

Restoration, alpine, vegetation, soils, microorganisms, bacteria

Analysing the migration patterns of red deer

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The red deer *(Cervus elaphus)* is a common ungulate in Switzerland, Austria and Italy. The different characteristics like a high climatic variability and various anthropogenic influences of these areas make it difficult to predict the movement of red deer. The aim of this thesis is to analyze red deer migratory behavior with respect to propensity and distance in eight different study areas. Furthermore, the timing of migration in spring and autumn is investigated in relation to environmental covariates.

First, the migration pattern of 346 red deer were analyzed using MigrO, a QGIS plug-in based on the SeqScan algorithm. Defined criteria were applied to classify the red deer trajectories into migratory, resident, and disperser individuals. For the following analysis the focus lied on the migratory and resident red deer. Next, the home range size (HRS), altitude, distance and timing were analyzed for all populations. These parameters are all outputs of MigrO. The results for all parameters of the eight study areas were then compared. Furthermore, intersexual differences were looked at. Influences of environmental factors such as snow, vegetation and temperature on migration timing were then investigated with the Cox Proportional Hazard Model. For snow, the Normalized Difference Snow Index (NDSI) was used, provided by MODIS Aqua. Vegetation was predicted by the Normalized Difference Vegetation Index (NDVI) supplied by MODIS Terra and for temperature data the Land Surface Temperature (LST) by MODIS Aqua was used.

The different results for the migration probability per study site showed that red deer behavior is dependent on various environmental factors (i.e. weather conditions and topology) and anthropogenic influences like hunting, supplementary forage and human made barriers. In addition, only moderate intersexual differences were observed for the behavior. Moreover, few red deer individuals (females and males) traveled to rutting grounds outside of their seasonal home ranges.

Resident animals show a larger covered HRS than migratory individuals. Consequently, resident individuals likely roam larger areas within one larger annual range, while migratory animals fulfill their needs in two spatially separated smaller ranges. Stags cover a larger HRS than hinds and generally also have their home ranges at lower altitudes than female red deer. Generally, all migratory individuals traveled to lower elevations during winter and migrated to higher altitudes in summer. The traveled distances between the home ranges were evenly distributed between hinds and stags. Only on the study site in Tyrol, where supplementary feeding has a long tradition in winter, the traveled distances are significantly lower than compared to the other study sites, suggesting effects of supplementary feeding in altering migration behavior. The spring migration starts earlier for stags than hinds, whereas in autumn the stags migrate all at once in a short time. This is assumed to be in relation to an event like for example the end of hunting or changing weather conditions.

The results of the Cox Proportional Hazard Model shows that the timing of spring migration is assumed to be determined by changes in vegetation and temperature, while the determinant driver for the autumn migration is snow.

Overall the results show plastic responses of red deer to environmental and anthropogenic drivers. Differences in the studied populations show that various factors influence the

migration behavior of red deer which need still more research to fully understand the mechanism.

The historical ozone trends simulated with the SOCOLv4 chemistry-climate model

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There is evidence that the ozone layer has begun to recover due to the ban on the production of halogenated ozone-depleting substances by the Montreal Protocol and its amendments. However, despite overcoming the decline in global total column ozone, there has been no sustained recovery in near-global [55°N-55°S] total ozone. Although recent studies report increases in tropospheric ozone and confirm upper stratosphere ozone recovery, they also indicate that lower stratosphere ozone recovery in the tropics and mid-latitudes is slower than expected. In addition, some studies have reported signs of a continuous decline in near-global ozone in the lower stratosphere. Moreover, it has been shown only by observations but current global chemistry-climate models (CCMs) do not reproduce them, demonstrating either positive or near-zero trends in lower stratospheric ozone. This makes it difficult to reliably determine ozone recovery and raises debate about the ability of modern CCMs to model future ozone trends.

We applied the new advanced earth system model SOCOLv4 to evaluate its ability to model ozone trends extracted from observations and reanalysis. We used dynamic linear modeling (DLM) to estimate long-term trends in ozone over the historical period 1985-2018 in the SOCOLv4 reference experiment and compared them with a homogenized BAyeSian Integrated and Consolidated (BASIC) ozone composite, as well as reanalysis data for different atmospheric layers. The analysis is carried out separately for periods of ozone depletion [1985–1997] and ozone recovery [1998–2018]. The recovery of ozone in the mesosphere, upper and middle stratosphere, the absence of a robust depletion of ozone in the extrapolar lower stratosphere, and the steady increase in tropospheric ozone are obtained and explained.

The modeled ozone trends are generally consistent with the observations and reanalysis, but the statistical significance in the lower stratospheric ozone is lower. Yet, we claim that current chemistry-climate models are generally capable of modeling observed ozone changes, justifying their use to predict future ozone behavior. However, further efforts are needed to study the observed near-global ozone decline in the lower stratosphere and the reasons why it has not yet been adequately reproduced in climate models.

How large-scale bark beetle infestations influence the protective effects of forest stands against avalanches: A case study in the Swiss Alps

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The increase of large-scale bark beetle infestations in spruce dominated mountain forests has already had major effects on forest structure and ecosystem services in the past, and this trend is likely to intensify further with climate change. However, it is unclear how forests recover from bark beetle infestations over the long term, and how well different recovery stages fulfil the capacity of forests to protect infrastructures and human lives from natural hazards such as snow avalanches.

The aim of this study was to investigate how the structure and protective function of an uncleared bark beetle forest changed over time. The study area is located at the Gandberg in the Canton of Glarus in Switzerland, where the storm Vivian (1990) and subsequent bark beetle infestations (1992-1997, peaking in 1993) affected large parts of the forest. We resurveyed the species composition and height of the tree regeneration, as well as the height and degree of decay of deadwood, in plots along transects that were already surveyed 20 years earlier. Eleven of our 24 sample plots were in the montane zone (1200-1450 m a.s.l.) and 13 in the subalpine zone (1450-1600 m a.s.l.). We used remote sensing data and avalanche simulations (RAMMS) to assess the protective effect of the forest against avalanches before the disturbances (1985) and afterwards (1997, 2007, 2014, and 2019) for frequent (30-year return period) and extreme (300-year return period) avalanche scenarios.

Post-disturbance regeneration led to a young forest that was again dominated by spruce, but still retained large amounts of deadwood, 27 years after the peak of the infestation. In 2020, the average height of the saplings (trees >1.3 m) reached 3 m in the subalpine zone and 4 m in the montane zone and crown cover was 10% and 30%, respectively. Although both elevational zones were dominated by spruce, the montane zone had a higher share of broadleaved species. Deadwood covered 20-25% of the forest floor. Most of the deadwood was in an early or intermediate decay stage and more seedlings were found on higher decay stages. More decomposed deadwood also had smaller heights than fresher deadwood. Less than 5% of the deadwood was taller than 10 m, which is a significant decrease compared to the value in 2001, where it was 50%. Remote sensing data and avalanche simulations showed that the forest prior to Vivian provided protection from both frequent and extreme avalanches. The storm Vivian caused new potential avalanche release areas within the forest, which were visible in the 1997 satellite image. During this time, the simulations showed a potential risk regarding extreme avalanche events. The protective capacity reached an overall minimum in 2007 because of the forest openings caused by the bark beetle infestation. The protective capacity partially recovered by 2014 and further increased by 2019, thanks to the establishment of new trees.

Our simulations and the fact that no avalanche events have been observed within the study area since the bark beetle infestation indicate that the protective effect of bark beetle

stands may often be underestimated and that it may be sufficient, at least for frequent events. Furthermore, it is likely that subalpine forests take longer to recover their protective function due to harsher growing conditions. Forest structures with potentially insufficient provision of avalanche protection occur around 10-15 years after the infestation due to deadwood decomposition. Thanks to gradually establishing tree regeneration – first on soil and later on decomposing logs - the protective function increases again after this minimum. Nonetheless, careful planning of silvicultural, technical, and organizational measures is necessary to keep the risks from natural hazards following bark beetle infestations at an acceptable level, while allowing natural processes to develop towards more heterogenous and therefore more resilient forest structures.

Non-native species in the Swiss National Park: current state and future challenges

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Introduction:

Non-native species, so-called neobiota, are spreading world wide. Global changes such as climate warming and increasing human mobility cause neobiota to invade areas beyond their native occurence. The impact on ecosystems is severe and may result in the extinction of native species as well as reduced ecosystem functioning and services. Neobiota which affect ecosystem or human well-being are referred to as invasive alien species. Invasion biology became a major research topic in recent years and neobiota are part of any political agenda by now.

So far, mountain regions are less affected by non-native invaders than the lowlands. However, on-going climate warming moves species range limits upwards and neobiota will spread to higher elevations.

Here, we focus on neobiota in the Swiss National Park (SNP), a protected area in the Central Alps. In 1914, human management was stopped in order to restore the disturbed ecosystems to wilderness. Thus, our study area offers the unique opportunity to examine invasion processes in nearly untouched environments. By now, non-native species within the SNP are rare, but are expected to become more frequent and possibly problematic. We explore for the first time in a comprehensive study the current state of neobiota in the SNP, urgent for long-term monitoring. Additionally, we incorporate historic and recent neobiota observations around the park area to anticipate potential future invasions.

Location:

Swiss National Park SNP in Graubünden, Switzerland. Area: 170 km². Elevation: 1400-3174 m asl.

Study organisms:

Non-native plant, animal and fungi species, referred to as neobiota. All species introduced within the last 500 years are considered as non-native.

Methods:

Database query, field survey and expert knowledge are combined to identify all neobiota species occuring within the SNP as well as in closest proximity. Historic and recent data allow to follow invasion processes and to test the hypotheses whether neobiota track climate warming and invade higher elevations, and whether neobiota emerge more often in the area than migrating native species. Based on our analyses, species which might become invasive within the park area and eradication methods to prevent the invasion will be discussed.

<u>Results:</u>

The project started in June 2022, results will be presented at the conference.

Concluding remarks:

Our study not only provides insights in invasion processes, but also serves as baseline for an indispensable discourse: How to deal with invasive alien species in a national park? Should management strategies be arranged to "remain wilderness"? A question belowing both to conservation biology as well as politics and philosophy.



Swiss National Park SNP (green area) and a selection of neobiota which may become invasive in the future within the park area: Bunias orientalis (Brassicaceae), Lupinus polyphyllus (Fabaceae), Harmonia axyridis (Coccinellidae). Sources: map.geo.admin.ch (map), infoflora.ch (plants), neozoen.ch (beetle)

Wednesday, September 21

13:30-14:45

Session 3 Natural Sciences

Chairs: Peter Bebi / WSL Institute for Snow and Avalanche Research SLF, Lucas Lombriser / University of Geneva

Energy dissipation of anticrack propagation in a weak snowpack layer

Bastian Bergfeld, Alec van Herwijnen

WSL Institute for Snow and Avalanche Research SLF, Davos, Switzerland

For a slab avalanche to release, a weak layer buried below a cohesive snow slab is required, and the system of weak layer and slab must facilitate crack propagation over large distances. This process, called dynamic crack propagation, is still rather poorly understood even though it is highly relevant for avalanche release. While models are nowadays able to simulate crack propagation over increasingly larger distances, validation data from field experiments are not yet available.

We therefore performed a series of flat field Propagation Saw Test (PST) experiments, up to ten meters long, over a period of 10 weeks on the same weak layer. Within this period, PST results evolved from crack arrest to full propagation and back to crack arrest. All PST experiments were analyzed using digital image correlation to derive high-resolution displacement fields. From these we determined the static specific fracture energy at the onset of crack propagation. In addition, we computed a dynamic fracture energy of the weak layer. To do so, we separated the work done in the weak layer during dynamic crack propagation in two parts. One part is the energy required to advance the crack ahead of the crack tip, namely the dissipation of dynamic fracture, the second part is used for weak layer compaction, the elastic-plastic compaction part.

Results showed that in our leveled propagation saw tests, the dissipation due to compaction was around 30 times higher than the dissipation of dynamic fracture. The latter was in the range of 5 mJ m-2 to 0.43 J m-2 and therefore somewhat lower than the static specific fracture energy prior to crack propagation that ranged from 0.1 to 1.5 J m-2. The dissipation of dynamic fracture alone is insufficient for self-sustained crack propagation in leveled terrain. The separation of the two energy dissipations can help distinguish between stable (small whumpfs) and unstable crack growth (remote triggering of avalanches) occurring in layered snowpacks.

Overall, our dataset provides new insight into the dynamics of crack propagation and provides valuable data to validate models used to study this process.

Aerosol Optical Depth observations: Evaluation of the SKYNET Network Improved Langley Plot method through calibration transfer from the GAW-PFR network

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Aerosols are an important atmospheric component regarding the study of atmospheric processes, which affects the Earth's energy budget and distribution by scattering and absorbing solar and terrestrial radiation. They also play a crucial role in cloud formation and properties [Fan et al. 2016]. Their effect on solar radiation is a main driver of surface solar radiation variations for several decades [Wild 2012] hence a significant forcing of the climate [IPCC 2021]. Surface solar radiation is important for its biological effects (mainly in the Ultra Violet (UV) region) and for solar energy applications [Horneck 1995, Hou et al. 2021]. Interactions between aerosols and clouds are also important for radiative forcing attribution, climate modeling and weather forecasts [Rosenfeld et al. 2014, Glotfelty et al. 2019, Huang & Ding 2021]. Finally, aerosols are one of the most important air pollutants with various health effects [WHO 2013].

One of the most important parameters regarding aerosols is the Aerosol Optical Depth (AOD). It is the parameter that describes the aerosol column direct effect on solar radiation and the most important aerosol-related parameter for studies related to the Earth energy budget [WMO 2003], which is critical for climate studies. The AOD is observed through Sun photometers. Sun photometers are instruments that measure the direct solar irradiance reaching the ground at specific wavelengths. To retrieve the AOD through the solar irradiance on the ground, the solar irradiance at the top of the Earth's atmosphere is required (calibration constant of a Sun photometer). Several networks of different Sun photometers have been developed worldwide in order to measure the AOD. One difference between networks aside the technical characteristics of their instrument, is calibration method (the method to estimate the solar irradiance that the instrument would measure at the top of the atmosphere).

This study aims to compare the calibration methods, for the estimation of the solar calibration constant, between the networks: Global Atmospheric Watch-Precision Filter Radiometer (GAW-PFR) (<u>https://www.pmodwrc.ch/en/world-radiation-center-2/worcc/gaw-pfr/</u>) and Sky Radiometer Network (SKYNET) (<u>https://www.skynet-</u>

<u>isdc.org/aboutSKYNET.php</u>). The GAW-PFR instruments (Precision Filter Radiometers-PFR) are calibrated by comparison with the AOD reference triad

(https://www.pmodwrc.ch/en/world-radiation-center-2/worcc/triad/) linked with the Langley Plot method (LP) in high altitude locations [Kazadzis et al. 2018]. The SKYNET instruments (Prede POM sky radiometers) are calibrated 'on site' with the Improved Langley Plot method (ILP) [Nakajima et al. 2020]. Intercomparisons between instruments from both networks have been conducted at Sapienza University in Rome and PMOD/WRC in Davos during the campaigns QUAlity and TRaceabiliy of Atmospheric aerosol Measurements campaign (QUATRAM) (1,2 and 3) and Filter Radiometer Comparison (FRC) (IV and V).

'On site' calibrations can be conducted more often, increase the instruments' operational period, and protect the instrument from potential damages during the shipment towards and from the calibration location, but their accuracy may be reduced. Because the ILP method's results can be affected by atmospheric conditions and therefore be dependent on the location and the time period in which the calibrations are performed. Also, the AOD is calculated from different algorithms and its intercomparison may not be sufficient to assess the performance of the method. Therefore, we compare the raw signals of PREDE-POMs and PFRs to retrieve new calibration constants for PREDE-POMs based on the PFRs' calibration constants and use it to retrieve the AOD. The AOD retrieved using the GAW-PFR calibration transfer is compared with the AOD retrieved by the ILP for both locations in order to identify the effect of the calibration method on AOD observations. We also aim to assess the uncertainties of both methods on AOD retrieval and examine their common or different sources. Our goal is to contribute on improving the accuracy and possibly on reducing the gaps of AOD observation. Aerosols remain an important source of uncertainties in climate science [IPCC 2021] and weather forecasting [Huang & Ding 2021]. An improved aerosol monitoring can be beneficial to these scientific fields.

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Slope stability research in alpine environment based in soil characterisation and monitoring

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The mountains in the Swiss Alps are frequently subjected to extreme weather conditions, with periods of freezing temperatures, snow-melting, intense rainfall and temperature variations. These dynamic processes result in mass movements, such as rockfalls and landslides which endanger settlements and infrastructure.

In a research paper during the author's doctoral thesis at ETH Zürich, the mass movements, in a scree slope at the Meretschibach catchment, canton Valais, south of Switzerland at an elevation between 1840-1910 m.a.s.l. were monitored and characterised, the objective was to provide information for the prediction of potential landslides jeopardising the village of Agarn located at 637 m.a.s.l. and their 720 inhabitants.

The events of mass movements in the Meretschibach reported in the area since the year 2000, were mostly debris flow type: 2 events in October 2000, 31 July 2002, 21 May 2003, 19 August 2003, 29 July 2008, 20 July 2014, 28-29 July, 2014. Additionally, in 2012 data provided of movements recorded by satellite InSAR were of 0.5 m/year at some places in the slope, which was of concern for the community, due to the vicinity to an active channel that is known for having led to extensive debris flows reaching the valley below in the past.

The research question was assessed by means of a long-term soil instrumentation and monitoring, subsequent site characterisation including field and laboratory testing, and the numerical and physical modelling testing program. The project in alpine location represented several challenges for instrumentation and data collection techniques. The site was monitored through a three years field campaign, providing information of soil volumetric water content and soil temperature. A geophysical survey was performed alongside the monitoring to define bedrock depth. Additionally, the data were complimented by precipitation data from two meteostations.

Next to the information collected from the long-term field monitoring and soil characterisation, a schematic ground model was developed and modelled in physical and preliminary numerical simulations of surficial landslides induced by rainfall infiltration. The slope stability analysis was conducted in terms of soil depth to the bedrock, slope geometry and intensity of rainfall infiltration.

The study concludes from the hazard point of view, that the scree slope studied is unlikely to experience a significant slope failure that could endangered the village of Agarn, this due to the well drained conditions, shear strength of the gravel and the limited soil thickness (1-3 m). However, a surficial landslide could be triggered in locations where the bedrock is shallow, or at steps in the bedrock. A combination of local erosion and soil saturation under a critical rainfall intensity would lead to slope failure and mass movement due to loss of effective stress of the gravelly soil. An important aspect is the data collected during the monitoring, und their use as an input for future studies and early warning systems development. Furthermore, this information can help to understand the seasonal response of scree slopes in other locations, under similar seasonal conditions in Graubünden.

IBAR is also currently conducting studies on natural hazard protection and infrastructure with sustainable building materials that can help make slopes and infrastructure structures

safe in the canton of Graubünden. These include: "Slope stabilization with wood wool fascines" and "Special anchors for avalanche and rockfall protection." The latter is suitable for use on higher steep slopes, where damage and erosion from rockfall or avalanches are to be expected.

The knowledge gained at the Meretschibach in terms of alpine slope stability, plus the motivation and competences at IBAR can be applied to solve similar problematics in alpine slope stability in Graubünden.

The solar active regions, flares, coronal mass ejections and their space weather consequences

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The Sun is the main source of energy for our planet, and it is a star that has a higher impact on our lives. The Sun is a dynamic body, a source of strong gravity force, continuously emits radiation and energetic particles. The continuous stream of particles generated by the Sun is called the solar wind. The solar wind determines the condition of the space between the Sun and Earth and even beyond, so-called space weather. The huge impact on the space weather has rapid and highly energetic processes in the solar atmosphere, such as flares or coronal mass ejection. The flare is a high increase of intensity in the solar atmosphere connected with the emission of the particles. The coronal mass ejection (CME) is a huge release of energy and mass from the solar atmosphere into space. The strong flares or CMEs can be a source of the beautiful aurora and can be a danger for astronauts, satellites, and generate geomagnetic storms that can damage our electric systems, pipelines, and radiocommunication.

To understand the processes responsible for solar wind creation and predict them, we must first link how the activity in the outer part of the Sun, called the solar atmosphere, influences the solar wind and space weather. To this aim, we focus on the solar atmosphere. The solar atmosphere is divided into three layers based on the temperature and density changes. They are the photosphere, chromosphere, and solar corona. The photosphere has a temperature of around 6000°C. The photosphere is the deepest layer we can observe; hence it is defined as the solar surface. Then, the temperature slightly increases in the layer called the chromosphere. Finally, the temperature riches more than a million degrees Celsius in the solar corona. The solar corona is the outer part of the solar atmosphere. According to the dynamics, we can distinguish three main groups of regions in the solar corona. (1) The coronal hole is the relatively cold and is build from less dense plasma then other regions in the solar corona. (2) Hotter and higher dynamic region with numerous small-scale structures (usually up to 10 000km) is called the quiet Sun. (3) The active region is the most dynamic, full-filled with large structures (e.g., hot coronal loops). The active regions are the source of the flares and the CMEs.

Satellite observations allow us to investigate the evolution of the solar atmosphere. We use simultaneous multi-satellite observation of active regions. The continuous monitoring of the solar atmosphere from photosphere to the solar corona provides the Solar Dynamics Observatory. The more detail information about the photosphere and chromosphere is obtained by Interface Region Imaging Spectrograph (IRIS). Satellite Hinode observe the solar corona. However, the most details data are provided by the Solar Orbiter. Launched in the 2020 mission, the Solar Orbiter provides the images of the solar atmosphere with unprecedented spatial (~100km/pixel) and temporal (~1.5 sec) resolution as well as in-situ measurements of the solar active regions, flares and CMEs. We analyse the plasma velocity, density, temperature and magnetic field. This data allows us to understand the processes and physics of the solar atmosphere. Then, the solar disk observations are linked with changes of the solar wind properties. The solar wind properties are measured in-situ.

Finally, we show how the evolution of the solar disk structure influences solar wind and space weather.

The environmental impact of a higher education institution in the context of SARS-CoV-2 – the case of the University of Applied Sciences of the Grisons in Switzerland

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This study examines the environmental impact of a small Swiss University of Applied Sciences in a regular year of operation (2019) against that generated in 2020, which includes the periods of the governmentally ordered lockdown. The direct emissions of owned facilities, indirect energy emissions of purchased electricity as well as other indirect emissions which are the outcomes of the university's activities but controlled by third parties are considered for 2019 and 2020 through a consumption-based methodology. The data is modelled with specific background data from ecoinvent v3.7.1 applying life cycle assessment (LCA). The results of 2019 show that student commuting, employee commuting and business travel, with 86% (2'204 t CO_2 -eq) contributed the most to the total global warming potential of 2'572 t CO₂-eq. In 2020, a decrease of 60% to the total (total 1'075 t CO₂-eq), was recorded. Home-office opportunities and desk-sharing could facilitate improved environmental performance in a post-pandemic era because they reduce mobility and floor space. Interestingly, the environmental impact due to energy consumption remained almost on the same level, irrespective of the absence of students and employees on-site for more than half of the year in 2020. This study has brought transparency and a much-needed baseline against which future mitigation efforts could be compared.

Wednesday, September 21

13:30-14:45

Session 4 Medicine & Life Sciences

Chairs: Mübeccel Akdis / Swiss Institute of Allergy and Asthma Research (SIAF), Marie-Charlotte Brüggen / Christine Kühne – Center for Allergy Research and Education

A new strategy for the treatment of *staphylococcus aureus* fracture-related infections using bacteriophage-derived enzymes and antibiotics

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Bacterial infections are normally treated with antibiotic chemotherapy. A growing number of infections, however, are becoming more difficult to treat as the antibiotics commonly prescribed are becoming less effective due to antibiotic resistance. Biofilm formation represents another strategy that allows bacteria to survive antibiotic treatment. Moreover, bacteria such as *Staphylococcus aureus* can polymerize host fibrinogen into a mesh of fibrin, forming a physical barrier to host immune cells. Strategies that disrupt the fibrin protecting the bacteria could support the resolution of the infection. In general, infections associated with medical implants can be extremely difficult to eradicate and can negatively affect patient's health. To counteract the bacterial threat, alternative approaches need to be considered and examined.

In this study we tested the activity of a staphylokinase phage-derived enzyme with / without support of antibiotic treatment on *S. aureus* cells. Staphylokinase is an enzyme that converts human plasminogen into plasmin with ultimate action of digesting fibrin. Bacteria were grown between 2 layers of collagen gel in presence of human plasma for a total of 16 hrs to form fully developed microcolonies surrounded by fibrin. After microscopic confirmation of the formation of the fibrin protective layer, staphylokinase ($10 - 5 - 2 - 0.5\mu$ M) was applied to the cells for 120 min, followed by 4 hours gentamicin or vancomycin treatment (10xMIC). To determine the activity of each treatment, microscope images were taken to assess the fibrin degradation followed by quantification of bacteria count after antibiotic administration.

Microscopy evaluation showed that the fibrin protective structure was degraded by the activity of the staphylokinase with the strongest effect observed at the highest concentration. The activity of the enzyme alone resulted in a slightly reduction of the CFU count when compared to the untreated sample. A combination of 10 μ g/ml gentamicin with 10 μ M staphylokinase showed a 2-log fold reduction on the CFU count indicating a strong synergism of the paired antimicrobials, compared with gentamicin alone which did not affect the viability of the cells. Highest concentration of staphylokinase associated with 20 μ g/ml vancomycin presented a moderate reduction of the CFU count, however not as efficient as observed for the gentamicin.

Our data suggest the importance of the staphylokinase treatment in disrupting the protective fibrine layer for maximizing the antibiotic action. Combination of specific enzymes and antibiotics could improve the resolution of difficult infections and prevent bacteria from developing antimicrobial resistance.
Characterization of enzymatic electrochemical glucose and lactate sensors for liver cell monitoring in a "Plug & Play" microfluidics system

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Liver fibrosis affects up to 9 percent of the adult European population with no effective drug therapies currently available for patients. New drug development is time consuming and costly, but strategies in predictive toxicology utilizing adverse outcome pathways (AOP) have the potential to bridge this gap. AOPs are structured representations of biological events that lead to harmful effects and can be used for various risk assessments. Although detailed AOPs for liver fibrosis are available, quantitative data on the driving cellular events are lacking. The BRIDGE Discovery project "AOP Plug & Play" aims to offer a quantitative solution for *in vitro* AOP analysis, through an easy-to-use state-of-the-art microfluidic platform. Here, we present a characterization of enzymatic electrochemical sensor candidates that will be integrated into the multi-sensor microfluidic platform.

To mimic sequential events in an AOP, the microfluidic platform will use fluidic control systems to regulate fluid exchange between the cellular components and the sensor modules (Figure 1). Glucose, lactate, pH and reactive oxygen species sensors will all be integrated into the final platform. The sensor module will monitor cell health and metabolic status by measuring analytes in the cell culture medium, such as glucose and lactate. Initial characterization of a lactate sensor demonstrates a dynamic range from 0.1-10 mM while operating at 37°C in phosphate buffer for 2 hours (Figure 2). Characterization of electrochemical enzymatic glucose and lactate sensors will be presented with target ranges of 1-20 mM glucose and 0.5-10 mM lactate with a minimum 8 hour sensor lifetime.

Data gathered by these sensors will be used to develop predictive *in vitro* models to assess cell health and response. Upon successful model development, *in vitro*-to-*in vivo* extrapolation (IVIVE) will be the next step to quantitatively support new therapies that may result in streamlining drug development based on AOPs.



Figure 1: Concept of the AOP "Plug & Play" fluid manipulation strategy leveraging pumps and valves to control exposure to different modules of the platform.



Figure 2: Calibration curves of a second generation lactate sensor design (n=7) operating at 37 °C in phosphate buffer with a dynamic range of up to 10 mM.

Mass spectrometry-based identification of allergen proteins involved in seafood related allergic reactions

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Shellfish are one of the most common causes of food allergies and a major cause of foodinduced anaphylaxis. Approximately 2.5% of the world's population has experienced an adverse reaction to seafood and the prevalence of seafood allergy is higher in populations residing in coastal geographic areas where seafood is an integral part of their diet. Sensitization and subsequent reactions occur most frequently upon food ingestion. However, they can also occur because of skin contact. Shrimps are, among all, the most consumed type of seafood worldwide and for that it is important to identify and characterize all possible allergens. Tropomyosin has been thought to be the most important allergen in shellfish, but also novel minor allergens have been discovered and characterized, and advances in component resolved diagnostics have provided insights into the prevalence of sensitization and their clinical importance in shellfish allergy.

As proteins consist of amino acid sequences, we will identify tropomyosin allergen proteins from peptides specific to seafood allergens. These peptide sequences can be only identified in seafood organism which share a high percentage of sequence identity and not in other organisms. As control we will also look for peptides from conserved protein regions. In our mass spectrometry-based experimental design, shrimp tissue is disrupted and homogenized, proteins are extracted, enzymatically digested, and subjected to Liquid Chromatography (LC) prior to Mass Spectrometry (MS). In this bottom-up proteomics approach the experimental mass spectra are then matched to peptides for protein identification, and these proteins are validated using a targeted MS-based proteomics approach called Parallel Reaction Monitoring (PRM), which is used to acquire high-resolution full MS/MS spectra for each target allergen peptide. In PRM a target precursor peptide is isolated in a quadrupole mass analyzer, fragmented in a collision cell and fragments are detected in an Orbitrap. Data analysis it then performed using conventional tools and as result we will obtain a chromatogram at each retention time point which consist of different transitions for all fragment ions, of one peptide precursor, displayed as colored lines identified in the legend.

Total protein extracts from shrimp (*Penaeus monodon* and *Penaeus vannamei*) are isolated and processed through in-gel tryptic digestion of SDS-PAGE gel fractions or using PreOmics columns with or without fractionation. Resulting peptides are then collected and purified prior to LC-MS/MS analysis and the MS raw files are processed by the SEQUEST algorithm within the protein database for decapods (TaxID = 6683). Tropomyosin proteins specific for shrimp, prawns, lobster, and crab are identified in our discovery workflow sharing a sequence identity between 89% and 100%. To support our findings, the PRM analysis is then performed looking for all shrimp unique tropomyosin peptides. A transition list for each peptide, from in silico digestion, is generated and analyzed within the Skyline open-source software. The same is performed for all other novel minor allergens identified within our MS analysis.

In all shrimp samples we accurately identified our proteins of interest. We established a MSbased proteomics workflow for the identification of proteins involved in seafood related allergic reactions. We were able to detect peptides from conserved protein region, e.g., shrimp actin (P60706), as well as peptides from protein regions specific to seafood allergens, e.g., shrimp tropomyosin (Q3Y8M6). It was possible to confirm the presence of the tropomyosin allergen as well as other minor allergens (arginine kinase, glyceraldehyde-3phosphate dehydrogenase, sarcoplasmic Ca²⁺-binding protein, hemocyanin, troponin, etc.) with high confidence. The results obtained suggest the reproducibility of this proteomics workflow, so as to be used not only in the identification of other important allergens in seafood related allergic reactions, but also of allergens involved in other types of allergic diseases.

Developing materials for cartilage regeneration under mechanical load

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Introduction: Osteoarthritis (OA) is one of the most common causes of disability in older adults, with increasing prevalence due to population ageing. It is a degeneration of the cartilage tissue in the joints, especially the knee, and it leads to increased pain during movement and a reduced range of motion. The main problem is that cartilage, unlike other tissues such as skin, does not regenerate easily. The current solutions for OA are antiinflammatory drugs but, in the worst cases, the joint must be replaced with an artificial one by surgery. Thus, research on cartilage regeneration is increasing. Animal models are most accurate when developing cartilage therapies as they consider the three-dimensionality of the joints and their complexity closely resembles the complexity of the human body. On the other hand, the 3Rs principle encourages the reduction in the use of animals. Classical invitro models would then be an alternative: they are easier to reproduce and analyse. Their main drawback is that they are often too simplistic to describe the problem in a representative way. In between the previously mentioned models, the use of dynamically loaded in-vitro models offers the desired solution. In this model, a bioreactor that mimics the knee joint movement and a 3D scaffold, are used to study the cartilage regeneration mechanisms. The bioreactor is composed of three main units: a ceramic ball, a holder, and a motor. The scaffold is placed in the holder, against which the ceramic ball is pressed. The motor rotates the ball and moves it up and down to apply load, mimicking the motion of the joint. The scaffold can be made of various biomaterials that should mimic the properties of the joint cartilage. The gold standard for this model is using a polyurethane (PU) foam scaffold: PU is a polymer that presents the proper characteristics to mimic cartilage. The main drawback is its low reproducibility. The aim of this research is to design a scaffold whose properties mimic cartilage without sacrificing reproducibility. To address this issue, two approaches are being attempted: soft gels called interpenetrating polymer networks (IPNs) and 3D printed scaffolds, exploring new biomaterials use and new architectures.

<u>Methods</u>: IPNs are prepared as reported elsewhere [1]. Different formulations are tested, to check for their gelation time. Samples are tested for swelling up to 7 days, for unconfined compression and for bioreactor loading in the absence of cells. The bioreactor loads in compression and shear for 6 hours. For the swelling test, the samples are covered evenly with PBS, incubated at 37°C and checked at different time points (24 hours, 5 days, 7 days).

<u>Results</u>: Not all the formulations of the IPNs gelled in the expected time. Once gelled, they were too brittle to load in the bioreactor. These differences influenced the mechanical properties of the samples. All the samples showed brittle-like behaviour. The samples did not show a significant degree of swelling over the 7 days test and they retained their brittle-like behaviour over that period of time. Tests on the mechanical properties and the bioreactor loading are still ongoing, as well as production and tests on 3D printed scaffolds.

<u>Conclusions:</u> IPNs need to be further tested to gain more data about their properties. Current and future experiments using the 3D printed technology could be the solution to obtain a reproducible scaffold which shows cartilage-like properties. Materials to be tested are PU [2] and polycaprolactone (PCL) [3]. Different architectures are also to be tested, in order to tune the mechanical properties of the scaffold to match the ones of interest.

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The effectiveness of Alpine Altitude Climate Treatment on tapering oral corticosteroids in patients with severe asthma

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<u>Introduction:</u> For many years Alpine Altitude Climate Treatment (AACT) is used in the treatment of severe asthma patients. The alpine climate is characterized by dry, clean air with decreased levels of allergens (e.g. house dust mites). Some studies already demonstrated the beneficial effects of AACT. Many patients with severe asthma need to use oral corticosteroids (OCS) to control asthma symptoms, with serious adverse effects as a consequence. Therefore, a treatment goal of AACT is often to taper OCS use. However, evidence on tapering OCS is limited.

<u>Study aim</u>: To investigate the effect of AACT on the tapering of OCS use in patients with severe asthma. Furthermore we aim to characterize patients who were able to successfully taper OCS use.

<u>Methods</u>: In this retrospective observational study 156 patients with severe asthma were included. These patients were under treatment in the Dutch Asthma Centre in Davos (1600 metres above sea-level) for 8-12 weeks, between 2019-2021. All patients were tested on admission and on discharge. Data was extracted from the digital patient file. Patients were evaluated on asthma phenotype (allergic, eosinophil, late/early onset), OCS use, asthma-related quality of life (Asthma-related Quality of Life Questionnaire, AQLQ), asthma control (Asthma Control Questionnaire, ACQ), sino-nasal symptoms (Sino-Nasal Outcome test, SNOT-22), lung function (Forced Expiratory Volume in one second, FEV1), exercise capacity (shuttle walk test), allergic sensitization (serum IgE levels) and inflammation (fraction of exhaled nitric oxide, serum eosinophil levels).

Results:

We included 156 patients (67% female, 64% early onset, 76% allergic, 49% eosinophil phenotype). The mean age was 49 years. At baseline 69 of the 156 patients (44%) needed OCS chronically. After treatment, 33 out of 69 patients (48%) could completely discontinue OCS use (p<0.001). Additionally, the maintenance doses OCS of the remaining patients were significantly reduced (14.3 mg to 7.25 mg, p<0.001).

Discussion/conclusion:

Maintenance OCS use is associated with several side effects. Therefore the reduction of OCS use is important for patients with severe asthma. Almost half of the patients (48%) were able to completely discontinue OCS after AACT. The remaining patients were able to significantly reduce the required OCS dose. Tapering OCS is especially relevant for patients with high OCS dose. AACT contributes to the treatment goal of severe asthma patients to discontinue or taper OCS use.

Wednesday, September 21

15:00-15:30

Transdisciplinary project: Natural Sciences

Chair: Britta Allgöwer / Academia Raetica

Risk management and self-responsibility when practising mountain sports in the Alps

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Enthusiasm for nature is bringing more and more people to the mountains. Although this trend is very welcome, it also leads to an increase in alpine accidents. Complex questions of criminal liability arise, mainly due to the unpredictability of nature and the tendency of people to overestimate their ability to keep risk under control. For these reasons, the research project "Natural hazards in mountain environments: Risk management and Responsibility" (led by the University of Innsbruck and funded by the call for tender *Research Südtirol 2019*) focuses on the legal assessment of these liability issues.

Specifically, the project aims to explore how the inherent residual risk and the lack of legally binding precautionary rules can be better addressed. Indeed. In order to analyze these issues, we have used an interdisciplinary empirical research design. In particular, we thought to construct a questionnaire aimed at analysing risk perception and awareness in general and, in particular, perceptions, preparation, equipment and information methods while practicing seven different sports activities, both summer and winter ones. To do so, we first consulted some technical stakeholders, who have been also supporting us in triangulating the results obtained from the empirical research. Due to the covid19 emergency and the impossibility to reach people while doing winter sport activities, we then decided to administered two different questionnaires: a face-to-face questionnaire addressed to tourists in a hotspot area, the area of Sesto Pusteria (in South Tyrol, Italy), one of the most tourist areas with the highest number of accidents among hikers; in summer 2021 we reached 300 hikers while they were hiking at different levels of difficulty. The main guestionnaire was instead administered online, mainly to members of the main mountain sports associations in Trentino, South Tyrol (Italy) and Tyrol (Austria). In autumn 2021 we reached 3841 sportsmen and women living in the three areas.

The results of the two surveys show a complex picture. First of all, among the interviewees, a good general preparation, transversal between disciplines and very good use of weather reports. With regard to risk awareness, namely with reference to the causes of mountain rescue operations, the respondents put more blame on inadequate equipment and bad weather than on reality. The risk of experiencing an accident while mountain biking seems to be somewhat underestimated in relation to the number of rescue interventions. Furthermore, in terms of perceived responsibility within a group, the majority of the respondents attribute transversal responsibility to the most experienced member of the group, who should check that the route is suitable for everyone (but also the weather and the equipment of everyone - less so in mountain biking).

To give some more examples, among the winter disciplines, a big distinction emerges between snowshoers and ski mountaineers, especially in the use of ARTVA, in having skills to prevent avalanches and in the impact of accidents. In the summer disciplines, for example, the practice of climbing routes is usually learned through personal experience.

Regarding residual risk perception, a clear difference between tourists and sportsmen emerges: among sportsmen, unlike tourists, there is a perception that zero risk does not

exist. Furthermore, the level of experience in sports, age, fear of something going wrong, and experience of past accidents seem to have a significant influence on the risk perception of having an accident.

The empirical research thus provided crucial findings for a criminal law analysis of mountain accidents. Several components need to be considered in this regard. First, a residual risk can never be totally excluded in the mountains. Second, the victim's own behaviour can play an important role, too: it is often the victim that actually brought him-/herself into a dangerous situation. Therefore, the role of self-responsibility should play a pivotal role in criminal law.

However, not all European States recognise self-responsibility as an important component of criminal law. Consequently, the project currently aims to analyse the role of self-responsibility in Austria and Italy. Several questions have arisen in this context. For instance, when can we refer to a 'self-responsible' behaviour? Does the victim have to perfectly know the risk s/he is exposing her-/himself? What kind of risk do hikers and mountaineers perceive? The empirical research provided important insights to answer these questions. On a more juridical level, at what point can self-responsibility play a role in the analysis of criminal law carried out by the courts? Being culturally influenced, this question is answered differently in the two countries

By linking empirical research and comparative criminal law, this project try to offer crucial insights into the behaviour of people in the mountains. It analyses the different European legal systems and argues for giving the victim's self-responsibility a more central role in criminal law. The ultimate goal is also to promote an appropriate risk culture among the population, improving everyone's awareness and safety in the mountains.

Wednesday, September 21

15:45-17:00

Session 5 Medicine & Life Sciences

Chairs: Silvia Generelli / Centre Suisse d'Electronique et de Microtechnique SA, Ron Clijsen / University of Applied Sciences and Arts of Southern Switzerland

Development of bioprinted osteochondral tissue: an *in-vitro* model for drug discovery

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<u>Introduction:</u> Osteochondral (OC) disorders like osteoarthritis (OA) and rheumatoid arthritis (RA) damage the joint's cartilage and subchondral bone. Their treatment remains a significant challenge for both researchers and orthopedics. *In vitro* models of OC tissue have become an essential tool to help investigate pathogenesis, develop drug screening, and test potential therapeutic approaches. This study aims to create a bio-printed OC construct recapitulating the bone and cartilage compartment as drugs testing platforms.

<u>Methodology</u>: Two different hydrogels including a blend composed of gelatin methacrylate (GelMA) with nanosized hydroxyapatite (nHA) and tyramine-modified hyaluronic acid (THA) were selected for the bioprinting of bone and cartilage tissue mimics. The composition of GelMA hydrogel (10% w/v) with different concentrations of nHA (1-10% w/v) and THA with concentrations of 2.5-5% w/v were characterized by rheology and their cytotoxicity was assessed via live-dead assay. Later, the pre-differentiated osteoblast and endothelial cells were encapsulated into GelMA-nHA and micropellet chondrocytes into THA hydrogels for bioprinting osteochondral construct. After 2 weeks of culturing, the successful generation of OC tissue was confirmed by real-time RT-PCR and histology.

<u>Results:</u> The storage modulus (G') of all GelMA/nHA hydrogels was significantly higher than GelMA, however, there was no significant difference in G' values for the GelMA/nHA as a function of added nHA. Due to the know temperature sensitivity of GelMA, a rheological temperature sweep and series of printing tests were performed to establish a suitable printing temperature, which was confirmed to be 20°C, independent of the addition of nHA. Calcein-AM (Ca-AM) and Ethidium Homodimer-1 (EthD-1) staining for GelMA (10% w/v) with three concentrations of nHA (1, 3, and 5% w/v) at 2, 24, 72, and 168 h after printing showed the percentage of living cells after 72h in GelMA containing 3 and 5% (w/v) nHA was less than 50%, while in GelMA with 1% (w/v) nHA it remained high (>95%) even after 168h. Therefore, this formulation was chosen for the subsequent generation of bone tissue mimic.

Shear flow curves of THA hydrogels showed an increase in viscosity as a function of THA concentration. The damping factor, which is a ratio between the loss modulus G'' and the storage modulus G', has been shown to be directly related to the extrudability¹. The calculated damping factors for each concentration of THA (%w/v) (THA 2.5%= 0.4947 \pm 0.038, THA3.5%= 0.5935 \pm 0.012, and THA5%= 0.7391 \pm 0.039), indicated that THA3.5%(w/v) was in the printable range. Cell viability assays for THA hydrogels showed a high percentage of living cells for THA 3.5% (w/v) compared to THA 5% (w/v) after 168 h. Based on cell

¹ Petta et.al, 2018, ACS Biomater. Sci. Eng, DOI: 10.1021/acsbiomaterials.8b00416.

viability assay, viscosity, and printability, a 3.5%(w/v) concentration of THA was selected for generating cartilage tissue mimic part.

<u>Conclusion</u>: We developed GelMA-nHA and THA hydrogels for bone and cartilage parts respectively. We also optimized printing parameters based on printability and shape fidelity and cell density according to cell viability for bioprinting OC constructs.

Keywords: Osteochondral tissue, Bioprinting, Hydrogels, Rheology, Drug discovery

In depth analyses of non-lesional and lesional atopic dermatitis skin by spatial and single cell sequencing technologies

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<u>Background</u>: Atopic dermatitis (AD) is a chronic inflammatory skin disorder affecting more than 10% of infants and 4% of adults. Because of its huge public health burden, there is a current need to investigate the complex pathogenesis of AD. We and others have performed next-generation RNA sequencing (seq) transcriptome analyses of skin biopsies from AD patients and reported the findings on the immunopathogenesis of AD in the whole RNA. The single-cell analysis of AD lesions showed the details of the molecular and cellular characterization of AD, however the detailed information on spatial and neighboring cells is still not fully understood.

<u>Method:</u> Skin tissues examined for spatial gene expression were derived from the upper arm of 6 healthy control (HC) donors and 7 AD patients (lesion and non-lesion). We performed Visium spatial transcriptomics sequencing (10x Genomics) to characterize the cellular infiltrate in lesional skin. For single-cell analysis, we analyzed the previously published singlecell data from suction blister material from AD lesions and HC skin at the antecubital fossa skin (4 ADs and 5 HCs) and full-thickness skin biopsies (4 ADs and 2 HCs). Both of them were collected and CD45+ cells were enriched by FACS. The multiple proximity extension assays were performed in the serum samples from 29 AD patients and 20 HCs.

<u>Specific aim</u>: This project aims to investigate the complex pathogenesis of AD with a singlecell and a spatial level to identify molecular mechanisms of skin lesion formation.

<u>Result:</u> The single-cell analysis identified unique clusters of fibroblasts, dendritic cells, macrophages and T cells in the lesional AD skin. Spatial transcriptomics analysis showed the upregulation of COL6A5, COL4A1, TNC, and CCL19 in COL18A1-expressing fibroblasts in the leukocyte-infiltrated areas in AD skin. CCR7-expressing dendritic cells (DCs) were also identified in the lesions. Additionally, M2 macrophages expressed CCL13 and CCL18 in the same localization. Ligand–receptor interaction analysis of the spatial transcriptome identified neighboring infiltration and interaction between activated COL18A1-expressing fibroblasts, activated CCL13- ad CCL18-expressing M2 macrophages, CCR7- and LAMP3expressing DCs, and T cells. As observed in skin lesions, serum levels of TNC and CCL18 were significantly elevated in AD, and correlated with clinical disease severity.

Conclusion and Impact of this study:

Our results will have a major impact on the dermatologic disease and other allergic diseases because AD initiates the allergic march, such as bronchial asthma, allergic rhinitis, and food allergy. In this study, we report that the leukocyte-infiltrated area in lesional AD skin is characterized by unique inflammatory fibroblasts, M2 macrophages, activated DCs, and T cells interacting with each other and shaping the molecular and cellular characteristics of AD.

Identifying novel mechanisms that play a role in maintaining skin homeostasis and lesion formation can progress in various ways. First, a better understanding of the mechanisms of exacerbations. Second is the demonstration of novel targets for prevention and drug development. Our findings will substantially contribute to decreasing the socioeconomic burden of these devastating diseases.

A portable and modular readout solution for electrochemical measurements

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The need for fully integrated and automated diagnostics solutions for human health is increasing, fueled by the widespread tendency of the industry to offer portable approaches enabled by the latest technological improvements in many medical sectors. CSEM has been working towards a highly versatile, easily customizable, and intuitively usable solution that allows non-invasive, point-of-care body fluid testing even for non-medically skilled users. Assays sensitive to pH, glucose and sodium have been developed and validated, with the possibility to expand measurements to several other biomarkers.

To circumvent the use of error prone measuring methods such as color-changing dipsticks, CSEM has developed electrochemical sensor solutions that directly acquire measurements through industry standard analog front-ends, leaving no space for human misinterpretation of the data. The now quantitative and digital measurements are accessible by the user through several means of communication for analysis and diagnosis. For example, with a Bluetooth connection and a smartphone application, the data analysis possibilities are highly improved with respect to what simple embedded processors can offer. This also allows to obtain a cost effective, rugged, and low-to-no maintenance design of the electronics side, since the data visualization is detached from the measuring device, allowing a considerable degree of flexibility for the different possible use cases.

The modularity of the system derives from the stacking strategy used throughout the design phase. A main board, housing the microcontroller, memory, Bluetooth chip and battery, is acting like a central computer and a board-to-board connector allows this main board to communicate with other peripheral boards, including the analog front-end board that carries out the electrochemical measurements.

The electrochemical reader measures electrical signals generated by the analytes on a turnkey designed sensor array. It interfaces with a cartridge, the disposable part of the system, which houses the electrochemical sensor array. Within several development projects, CSEM refined the cartridge assembly design and has reached, following multiple revisions, a very promising stage of evolution for the electrochemical sensor itself, fabricated through low-cost printing and deposition techniques. The sensors show very good reproducibility and outstanding agreement with laboratory measurement instruments. In addition, the cartridge assembly allows calibration solutions, buffers, analytes and rinsing solutions to be applied sequentially on the sensor array. Currently, this is still done manually; A fluidic actuation board capable of automating all liquid handling procedures is now in development to improve the readout solution and eliminate one more possible source of error from the system.

The result is therefore a versatile, high-performance electro-chemical reader, pocket sized but just as capable as other commercially available but much more bulky and expensive solutions. This reader along with a microfluidic cartridge integrating a range of different sensor assays and coupled to a smartphone, allows users to perform automated electrochemical measurements far away from a laboratory and at a far lower cost and footprint. Future developments will focus further on miniaturizing and integrating the solution into everyday use items, making non-invasive electrochemical monitoring accessible in everyday life.

Development of electrochemical nitric oxide microsensors for the real time monitoring of inflammation in chondrocytes

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<u>Introduction</u>: During inflammation, cells produce and release nitric oxide (NO), a metabolite which can be used as a biomarker to monitor the progression of inflammatory diseases¹. Common methods imply the use of Griess method or paramagnetic electron resonance (EPR) for indirect NO measurement in a solution. However, all these methods cannot provide real time monitoring, limiting the investigation of drug response and the clinical translation. The use of electrochemical sensors can overcome this issue; however, the selectivity of this sensing tool could be critical if not specifically designed for the biological use².

<u>Methods</u>: As sensor's working electrodes, platinum wires were used bare or modified with polymers and/or Carbon Black nanomaterial³. Two different modifications were performed: an electropolymerization with poly-o-phenylenediammine (p-OPD/PPD), applying +700 mV vs an Ag/AgCl reference electrode and a physical adsorption on the wire surface with CB dispersion in NafionTM by drop casting and oven drying (200°C for 2 minutes). The sensors were calibrated with known concentration (0 to 100 μ M) of a NO donor molecule, the SNAP (s-nitroso-n-acetylpenicillamine), by applying a potential of +865 mV. As common biological interferences, Ascorbic acid (AA), L-glutammine (Glu) and hydrogen peroxide H₂O₂ were tested. Nitric oxide was measured in real time in 2D chondrocyte culture for 48h in presence and absence of 10 ng/ml IL1 β , by applying the same potential vs Ag/AgCl RE directly in cell culture plate.

Results: p-OPD and CB were homogenously distributed on sensor surface. The coating with p-OPD showed lower background noise for AA and none for Glu but considerable for H₂O₂. Contrarily, the coating with CB-Nafion strongly decreased all the interferences. The real time monitoring of NO in chondrocytes showed significant difference in signal between the groups. The use of CB coating increased the analytical performance in terms of selectivity and reproducibility during real time monitoring in inflamed biological system (Figure 1).



Figure 1: (A) Sensor stability and modification, (B) Calibration curve with SNAP, (C) interference analysis with AA and H202, (D) real time monitoring with PPD and CB sensors in 2D chondrocytes culture during inflammation.

<u>Discussion and conclusions</u>: Real time monitoring of NO release by electrochemical sensor during the inflammation in vitro and eventually in vivo could help to determine the progression/status of widespread pathologies or infections from pathogens in biological

fluids and cell culture medium. However, we provide evidence that in a complex system such as cell culture medium, it is of paramount importance to properly modify the active surface of the sensor to avoid the interference with analytes not of interested, such as the large production of hydrogen peroxide. Herein, we prove how the modification with CB-Nafion does not limit the sensor performance while increasing the selectivity for the NO.

Acknowledgements: AO Foundation, Innosuisse funding scheme.

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Association between atopic dermatitis and cardiovascular diseases

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<u>Background</u>: There is contradictory evidence on the association between atopic dermatitis (AD) and cardiovascular diseases (CVD). The aim of this study was thus to further explore this connection and how it relates to the presence of atopic comorbidities.

<u>Methods:</u> This observational multicenter study included cross-sectional data of 705 adult patients suffering from AD and 80 control participants (without history of AD, allergic rhinitis, food allergy, asthma, or psoriasis) of the ProRaD cohort (Zürich, Davos, Bonn, Augsburg). EASI, body surface area (BSA), SCORAD and objective SCORAD were used to grade AD severity. The presence of atopic, cardiovascular, and metabolic conditions was assessed by a dermatologist. Cardiovascular risk factors (age, sex, smoking habits, physical activity, body mass index) as well as other clinical and epidemiological data were asked in a standardized questionnaire. The main outcome variable for statistical analysis was the presence of CVD, the main dependent variables being the presence of AD and the severity of AD respectively. In the minimally adjusted model, we controlled for age and sex, in the fully adjusted model for all the above-mentioned cardiovascular risk factors.

<u>Results:</u> Our analysis did not show an overall association between AD and cardiovascular outcomes. However, patients with severe AD were significantly more often suffering from CVD than control participants (24.4% [29/119] vs. 10.0% [8/80]). Furthermore, AD patients without atopic comorbidities (pure AD) had a significantly higher prevalence of CVD compared to AD patients with atopic comorbidities (29.7% [41/138] vs. 14.3% [81/567]). Yet, both associations could not be confirmed in the adjusted models. In patients with pure AD, there was a statistically significant relation between the severity of AD (EASI and BSA) and the presence of cardiovascular comorbidities, which could be confirmed in multivariate analyses.

<u>Conclusions</u>: Our study does not suggest an overall association between AD and cardiovascular comorbidities but suggests a more complex relation between the two conditions: A higher BSA involvement may be indicative of a stronger pro-inflammatory type 1 reaction in pure AD and represent a risk factor for CVD. Conversely, a more prominent

type 2 response (clinically evidenced by atopic comorbidities) might counterbalance this tendency.

Wednesday, September 21

15:45-17:00

Session 6 Medicine & Life Sciences

Chairs: Sibylle Grad / AO Research Institute Davos, Milena Sokolowska / Swiss Institute of Allergy and Asthma Research (SIAF)

Hyaluronan-collagen bioink for the printing of intervertebral disc models

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<u>Introduction</u>: The intervertebral disc (IVD) is a vital structure of our spine, essential for movement. Aging and trauma eventually lead to its degeneration, which results in debilitating pain for the patient and loss of mobility. Despite the high prevalence of this condition and its burden on the population and healthcare system, disc degeneration is still poorly understood and treated. This is in part due to the lack of suitable models, which could be used for further research and development of novel treatments. Current models are either oversimplistic, failing to adequately represent the disc's heterogeneous composition, structure, and mechanical function, or based on animal tissue, which is often poorly representative of humans. Continuous advances in 3D bioprinting over the past years have given rise to a technique which allows fabrication of complex structures with precise and reproducible control over the cell microenvironment. As a first step towards developing a better, reproducible, and representative model of the intervertebral disc, we have formulated a material suitable for the 3D bioprinting of structures resembling the gel-like nucleus pulposus (NP) of the IVD.

<u>Methods:</u> Type I collagen and hyaluronan, both essential components of our tissues, have been combined at concentrations approaching those of the NP. Due to inherent properties of collagen and a chemical modification of hyaluronan with tyramine, the resulting composite material can form an elastic gel via changes in pH, enzymatically induced crosslinking in the presence of horseradish peroxidase (HRP) and hydrogen peroxide (H₂O₂), or exposure to green light. By initially employing pH increase together with enzymatic crosslinking, the composite is turned into a soft gel which can be extruded through a printer's nozzle. The printed structures can then be further strengthened via exposure to green light. We studied the material rheologically by monitoring its gelation and transitions between liquid and elastic state during extrusion-like conditions, evaluated its response to compressive loads, seeded the material with bovine NP cells to demonstrate its biocompatibility, and printed simple lattice-based 3D structures.

<u>Results:</u> We observed good material extrudability. Under high strains (such as those in the printer nozzle) the material flowed, followed by a recovery of its shape and elasticity when the strains were decreased (as they would after printing). Shear storage modulus after exposure to light reached 4.6 kPa, whereas under compression the light crosslinked gels exhibited a 5.3 kPa equilibrium modulus. Both the shear and compressive properties are in the range of those previously reported for healthy human NP. Embedded NP cells demonstrated good viability and proliferation after 5 days of culture.

<u>Conclusions:</u> We present a bioink with rheological and compressive properties within the range of healthy human NP. To our knowledge, this is also the first bioink simultaneously composed of biochemically suitable components representative of native NP, and approaching the high concentrations observed in tissue. This work brings us a step closer to better, reproducible, and representative 3D printed IVD models, and the promise of new insights into the treatment of disc degeneration.

<u>Acknowledgements:</u> Funded by the Swiss National Science Foundation (189310) and the French National Research Agency (ANR-19-CE06-0028) as part of the INDEED project.

Determining the presence of food-antigen specific total IgG and IgG4 antibodies in the plasma of eosinophilic esophagitis patients.

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<u>Background:</u> Eosinophilic esophagitis (EoE) is a chronic immune-mediated inflammatory condition that showed increased prevalence during the past decades. Although the mechanisms underlying EoE are not completely understood, several studies suggested the involvement of Th2 cytokines and antibody production. Also, food ingestion may play a role in EoE triggering, however it appears not to be a typical IgE-mediated food allergy. Rather, recent observations showed that EoE patients have high levels of IgG4 in esophageal biopsies and of circulating food antigen-specific IgG4. This preliminary analysis aimed to differentiate EoE patients according to the levels of food antigen-specific antibodies.

<u>Methods</u>: Blood samples from 142 EoE patients were collected at the Swiss EoE Clinics at the University Hospital Zurich. The patients were categorized in active (>15 eos/hpf) and inactive (<15 eos/hpf) state of the disease, based on peak eosinophil counts in the esophagus. After processing blood samples, we used the plasma to measure food allergen-specific antibodies. Specifically, we measured total IgG and IgG4 against casein, whey, wheat and egg extracts, and the cow's milk individual allergens alpha s1 casein, A1 beta casein, A2 beta casein and I beta casein by enzyme-linked immunosorbent assay (ELISA).

<u>Results:</u> Among 142 samples, we could identify patients with highly positive, intermediate, and low levels of IgG and IgG4 antibodies specific for casein, whey, wheat, egg and cow's milk individual allergens.

<u>Summary and outlook:</u> This analysis will allow us to identify patients with high levels of food antigen-specific antibodies, which will be employed for a deeper analysis. In particular, we will isolate antigen-specific B cells and perform single-cell transcriptomics. Moreover, we will correlate this data with serum biomarkers identification, in order to ease the monitoring methodologies.

Post-exercise systemic heat therapy decreases the inflammation process during recovery: a systematic review and meta-analysis

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Introduction:

Systemic heat therapies are often used in the general population for pleasure and relaxation [1]. Forms such as hot water immersion, sauna bathing, steam bathing, and infrared bathing are defined as systemic heat therapies [2]. The effects of these treatments can vary widely including a decrease in mean arterial pressure, systolic pressure, diastolic pressure [3] and an increase in glucose metabolism [4] and insulin sensitivity [5]. Also, an increase in muscle and tendon flexibility [6] and a reduction of subacute and chronic musculoskeletal pain were observed [7]. In sports, systemic heat therapies are regularly used after activities and are recommended as a recovery method [8]. Recovery is linked to a lower injury rate and increased competition performance. To the best of our knowledge, no evidence-based recommendations exist about post-exercise systemic heat therapies. Therefore, our aim was i) to generate an overview of the currently available literature and ii) to establish the results of post-exercise systemic heat therapies.

Methods:

The following review and meta-analysis were performed according to the current guidelines "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA) [9]. A systematic literature search was conducted using the four medicinal online databases Pubmed, Ovid, EBSCO, and Cochrane. The following criteria were considered: (1) the participants had to be healthy; (2) the study contained an intervention and control group; (3) the intervention group performed a systemic heat therapy after exercise; (4) the heat intervention was a systemic external application above 36°C; (5) the control group underwent passive rest, sham-heat therapy, or a placebo intervention without heat; (6) the results were reported before and after the intervention; and (7) the article was written in English, Dutch, or German. Two researchers identified independently relevant articles. The methodological quality of the included studies was assessed with the help of the reliable and applicable rating tool Cochrane risk of bias tool 2 (RoB 2). The results were found, the intensity level of the pre-performed exercise, the heating modality, and the temperature were analysed.

Results:

A total of n=17 studies met the inclusion criteria. The results of the meta-analysis revealed that participants of the intervention group had significantly lower inflammation blood levels (p = 0.008) within one hour after application compared to the control group. There is evidence, that systemic heat therapies after exercises with higher intensities benefit more than after medium or low-intensity exercises. Studies using hot water immersion and

interventions with higher temperatures showed better effects on inflammation blood levels than those using air-heating or lower temperatures. After 72 hours, endurance performance was significantly higher in the intervention group compared to the control group (p = 0.008). Again, a higher benefit was achieved in studies with exercises of higher intensities compared to medium or low intensive exercises. In contrast to these results, the subjective estimation of the muscle soreness showed significantly better results in the control group (p = 0.004) within one hour after the control intervention compared to the heating group. No significant results were found between the groups for the muscle force, jump performance, maximum oxygen capacity, and blood lactate levels at any time point.

Conclusion:

Post-exercise systemic heat therapy can lead to significantly lower blood inflammation markers compared to passive recovery within the first hour after application in a healthy population. The best effects were achieved when higher temperatures and the heating modality water were involved. These findings indicate a short-term anti-inflammatory effect of post-exercise systemic heat applications and give the needed evidence-based recommendations for trainers, therapists, athletes, and the general active population. It remains unclear if studies assessing the effectiveness of post-exercise heat therapy in patients will correspond to the present results. A special interest might be in patients with inflammatory diseases.

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Investigation of allergen specific B-cells in allergy concordant and discordant twins

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Background:

Food allergies are defined as a type 2 IgE-mediated immune response against certain food proteins. The balance between effector and regulatory B cells determines if an individual has an allergic or tolerant response to ingested food. This means there should be significant differences in B cell subsets and, therefore B cell regulation between healthy and allergic individuals. Therefore, an investigation into the B cell regulation in IgE production and the development of food tolerance vs food allergy is a promising trail to understand the causal pathways for food allergy. This project aims to characterize allergen-specific B cells on a transcriptomic level and investigate the differences in their B cell subsets in allergic to comparison to healthy twins.

Methods:

We used bio-banked PBMCs from mono- and dizygotic twins that are either food allergy concordant or discordant. The corresponding allergens were biotinylated and then coupled with a streptavidin linked to a fluorophore and an oligonucleotide barcode. This enabled us to sort for the allergen specific cells B cells and identify their allergen specificity during gene expression analysis. Additional hashtag antibodies allowed for sample multiplexing to avoid batch effects between twins. The PBMCs were sorted by FACS for cell type and allergen specificity. Using the 10x genomics Chromium Next GEM single cell sequencing technology the we generated gene expression and V(D)J libraries from the RNA of the sorted cells. These libraries were sequenced for the RNA transcriptome and also for the BCR repertoire. We analysed the sequencing data to gain insight on the abundance, clonotype and gene expression of allergen specific B cells. Comparing the cells between healthy and allergic twins will enable us to gauge the impact of V(D)J variances in allergies.

Physico-chemical characterization of polyelectrolyte coatings composed of a bacterial exopolysaccharide and chitosan

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Introduction:

Normal tissue repair, and integration of implanted medical devices, involves a controlled immune response. The recruitment of cells to remove damaged tissue occurs in the early phase, before switching to a later healing phase where cells such as M2 macrophages support tissue regeneration. In case of excessive or chronic inflammation at the injury site (e.g. due to infection or underlying systemic inflammation), this process is disturbed, slowing down tissue repair.

Immunomodulatory treatments aim at lowering inflammation for these difficult cases, however orally administered or intravenously injected anti-inflammatory drugs may have off-target effects due to systemic administration. Local application could overcome these drawbacks by targeting the injured site directly. In this project, we produced and characterized a bacterial exopolysaccharide, a type of sugar produced by bacteria, from a *Bifibobacterium* (BIEPS) as a potential coating for implanted devices.

Methods:

The BIEPS used for all experiments was isolated from. *Bifidobacterium Longum subsp Longum*. The production process consisted of bacterial growth on agar plates, collection of the bacterial biomass with a cell scrapper, resuspension and centrifugation of the bacterial biomass in PBS, filtration and precipitation of the supernatant with ethanol, dialysis and finally reverse phase column filtering of the precipitate. Polyelectrolyte multilayers were created from alternating layers of negatively charged BIEPS and positively charged chitosan on glass disks substrates. The process consisted of dipping the disks in baths containing 1mg/mL BIEPS at pH 5 or 1 mg/mL chitosan at pH5. Dipping was done for 5 minutes, with 2 rinsing baths in between each coating in a bath composed of MilliQ water at pH 5 for 2 minutes. A negative control replaced the BIEPS bath with an alginate bath, at concentration 1mg/mL and pH 3, with the rinsing baths also at pH3.

A zeta-sizer was used to measure zeta potential and hydrodynamic radius was measured by dynamic light scattering for the BIEPS, chitosan and alginate. Surface topography measurements through atomic force microscopy were used to characterize the coatings thicknesses and surface properties. Human Interleukin-10, an immunoregulatory cytokine secreted by cells such as T helper cells, macrophages, monocyte and dendritic cells, was quantified through ELISA to evaluate the immunoregulatory effect of coatings. Coated disks were exposed in vitro for 24h to human peripheral blood mononuclear cells.

Results:

The thickness of the coatings was found to be proportional to the number of layers deposited, with very thin coatings in the nanometer range. Zeta potential, quantifying polymer particle charges in solution, was measured for the BIEPS, chitosan and alginate at

concentrations ranging from 0.01 mg/mL to 10 mg/mL. For all groups the absolute zeta potential value increased with polymer concentration. Dynamic light scattering was used to measure the hydrodynamic radius, a measure of the size of polymer particles in solution, for the BIEPS, chitosan and alginate at concentrations ranging from 0.01 mg/mL to 10 mg/mL.

When dissolving the BIEPS in media, an increase in IL-10 expression in hPBMCs was observed in a dose dependent manner. The control [$6.27 \pm 2.67 \text{ pg/mL}$] and 1µg/mL group [$7.20 \pm 2.17 \text{ pg/mL}$] had a similar expression, while a large increase was observed for 10µg/mL [$79.68 \pm 9.23 \text{ pg/mL}$] and 100µg/mL [$105.66 \pm 0.14 \text{ pg/mL}$]. Compared to the uncoated glass disk control [$9.04 \pm 1.12 \text{ pg/mL}$] IL-10 expression increased for all polyelectrolytes groups as the number of layer increased from 1 layer [$41.35 \pm 5.74 \text{ pg/mL}$], to 5 layers [$90.93 \pm 24.65 \text{ pg/mL}$], to 10 layers [$116.57 \pm 15.92 \text{ pg/mL}$]. For the 10 layers group, the IL-10 expression dropped to [$18.17 \pm 4.83 \text{ pg/mL}$] when the BIEPS was replaced by alginate, another negatively charged polymer, confirming the specific immunoregulatory action from the BIEPS.

Conclusion:

Our study could confirm the immunoregulatory property of BIEPS in vitro when incorporated in polyelectrolyte BIEPS/chitosan coatings. Future steps include further characterization of additional inflammatory cytokines to better understand the overall immune response to the BIEPS, ellipsometry measurements to determine the thicknesses of individual chitosan/BIEPS layers and size exclusion chromatography to determine the molecular weight and polydispersity of the polymers. These polyelectrolytes coatings could have potential for dampening inflammation and facilitating tissue healing.

Thursday, September 22

10:30-12:00

Session 7 Humanities & Social Sciences

Chairs: Patric Arn / University of Applied Sciences of the Grisons, Barbara Haller-Rupf / Academia Raetica

Police communication in the digital era - The police use of social media in the area of tension ranging between information obligation and independent information

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The police, as part of the executive power and thus part of the public administration, is obliged to inform the population in an appropriate manner. However, digitization poses a challenge here that requires the constant adaptation of communication channels in police work. Police organizations as part of government communications "need to change in order to remain relevant and to continue to effectively fulfill their constitutional mandate" (Raupp, Kocks, Murphy 2018: 1). However, the police are still uncertain about how to deal with the digital space, especially with communication in social media (Rüdiger 2019: 23). Above all, there is a lack of an overarching strategy that regulates the structure and content of communication in the digital space (Rüdiger 2019: 23).

The fundamental difficulty that the use of social media brings with it in public administration is based on legal restrictions on the publication of content (Breyer-Mayländer, Zerres 2021: 142). Because everything that has to do with state affairs can quickly trigger a social or legal discourse, which is why there are limits to both state public relations and administrative communication (Raupp, Kocks, Murphy 2018; Kocks, Knorre, Kocks 2020). For this reason, it will be examined what is permitted in terms of police communication in social media in Switzerland, i.e., how free the police are in their decisions, what is part of the information obligation and whether there is perhaps talk of persuasive communication by the state (Neuroni, Trappel 2006; Prier 2017; Persily, Tucker 2020). In addition to the legal and political aspects, it must be examined to which personnel and organizational adjustments must be made to be able to clarify responsibilities for the use of social media in police work (Bruhn 2019: 73; Breyer-Mayländer, Zerres 2021: 148), who produces the content, what is produced in what form, and on which channels this content is published. This is an important part of the work, because to master the "field of tension between official organizational logic and the functional logic of social media" (Kocks, Knorre, Kocks 2020: 3), competencies must be specifically developed (Breyer-Mayländer, Zerres 2021: 150).

This tension between the increasing need for digital forms of communication and legal restrictions raises the following research question: How do the police in Switzerland use social media, what regulatory framework conditions exist, who produces the content and how is it produced?

Consequently, this work consists of three levels of investigation:

- 1. Legal and political level: objectives, tasks and obligations of the police, interaction of the state levels
- 2. Structural level: Who produces the content and how? How is police communication organized? In particular, police influencers and persuasive communicators are examined in more detail here.
- 3. Content level: What, how and on which channels do the police / police influencers communicate?

The planned research is based on theoretical approaches to public administration and administrative communication (Kocks, Knorre, Kocks 2020). In addition, theoretical aspects of political communication (Jarren, Donges 2002) and public relations (Raupp, Kocks, Murphy 2018: 1) are discussed.

In general, the review of the existing work makes clear the need for an own analysis, which will be covered with the help of a multi-method research design with the combination of qualitative and quantitative procedures. In a first step, a multimodal analysis of the Instagram and TikTok content of the cantonal police (both personal and official accounts as well as some accounts of city police) will be carried out to be able to identify characteristics and create a typology for Switzerland, which will then be quantified, i.e., checked for frequency. These typologies also serve to examine the strategies behind them in the expert interviews with Swiss police organizations and state actors. Another qualitative method is the focus group with population groups, in which their associations with the typologies (content) and their expectations of police communication are analyzed. The participants are selected from cantons with different communicative strategies. To then be able to develop recommendations for action for Swiss police organizations, the results of the expert interviews (intentions, strategies) are compared with the results of the focus groups (associations, expectations).



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Same same but different? Swiss Schools' Challenges and Strategies after two years of COVID-19 pandemic

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In spring 2020, the outbreak of the COVID-19 pandemic presented major challenges to all areas of society. In most cases, no tried-and-tested strategies for action were available and this particularly holds true for educational settings (UNESCO, 2020). Core tenets of school and teaching such as the transfer of knowledge and the promotion of the domain-specific and cross-curricular competencies of all pupils were suddenly at stake and a number of studies report of learning losses due to the pandemic (e.g., Tomasik et al., 2021). In no time alternatives to "regular" forms of teaching were required that would both allow for reaching out to students at a distance and to teaching remotely (Hodges et al., 2020). Even after the abrupt start of the pandemic, schools had to continuously adapt to new pandemic-related regulations and challenges and the need for agility in conditions of high uncertainty has ever since never waned. This may have a long-term impact on learning, teaching, collaboration and organization in and among schools.

The first results of the trinational S-CLEVER study in the German-speaking part of Switzerland, Germany and Austria (2020-2022) in which school principals (N = 802-1449 principals) participated through three online-questionnaires, suggest that since the outbreak of the pandemic (1) the use of digital learning have grown, (2) students have been more required to take responsibility of their own learning and (3) collaboration among teaching staff and with parents has enhanced (Feldhoff et al., 2022). Additionally, a first longitudinal analysis suggests that pre-pandemic experience in digital learning and a culture of knowledge sharing among colleagues before the pandemic had positive effects on schools' capacities to deal with the pandemic and the professionalization of teachers a year later, in summer 2021 (Suter et al., 2022). However, studies with data from 2017 show that schools in the French- und Italian-speaking parts of Switzerland tend to have less digital equipment than schools in the German-speaking parts (educa, 2021). The COVID-19 pandemic might have, hence, led to further educational inequalities. In order to better assess the situation and to work out future requirements, nationwide studies are needed that take all language regions into account. This is the goal of S-CLEVER+, which is a followup study to S- CLEVER. The following research questions will be at the core:

- 1. *Challenges and strategies*: What challenges do schools face two years after the COVID-19 pandemic and how do they handle them?
- 2. *Effects and changes*: What effects have been perceived by school principals in terms of teaching, individual support for pupils and schools as a whole? What further changes do school principals anticipate?
- 3. *Regional differences*: In relation to RQ 1–2, to what extent are there differences between language regions?

In order to address these questions, a survey of school principals has been carried out in summer 2021 in various Swiss cantons (AG, BE fr., GR, JU, LU, NE, SG, TG, TI, ZH) and in

Germany.

Data collection will be finished by September 2022. We will be able to present preliminary results from descriptive and multivariate analyses concerning the Swiss sample at the conference.

The study results will allow us to better understand Swiss schools' moments of crises, such as the COVID-19 pandemic, by comparing the different regional contexts. Furthermore, they will inform school authorities regarding factors that are important for positively navigating through a long-lasting crisis. Moreover, the results can help to identify equity and inequality issues in the Swiss educational system, which in turn can be the basis to develop strategies in order to reduce educational inequalities.

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Social networks as the basis to strengthen agri+touristic value creation in Alpine regions

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In large areas of the Alps, agriculture and tourism have great economic and social importance. Due to their comparatively low value added both sectors face major challenges, which have to be met with new offers and organizational-structural innovation. This requires both improved framework conditions and economic support as well as a more comprehensive understanding of "agritourism" that includes on-farm activities. It also means developing synergy and cooperation potentials between all involved sectors in the regional system of value chains. We refer to this as "agri+tourism" (Hediger et al., 2019), which is essentially built upon social networks. Those can have different characteristics and structures in different regions and constitute an essential basis for the development and functioning of business relationships within industries and regions.

Social network analysis is a method that is particularly suited to capturing and analyzing connections between individual actors in a network and their interactions from an overall perspective. It enables to measure the strength of a network and to derive recommendations for further development. They constitute an essential basis for the development and functioning of business relationships within industries and regions. Based on different forms of relationships, such as kinship, friendship, membership in associations and other organizations, they connect individual actors with each other and create a foundation of trust that is the most important factor in building new relationships. The analysis of the networks (Jansen, 2003; de Nooy, 2010) is primarily used to identify individual actors and their roles in the agri+touristic value chains, and to determine the connections between these actors in regional organizations.

The purpose of this paper is to illustrate the importance of stakeholder networks for the development of regional systems of value chains at the interface of agriculture and tourism ("agri+tourism") and the possibilities offered by the method of social network analysis in this context. For this purpose, the actors of agricultural business (collared in green), food processors (orange) and hotel/gastronomy businesses (blue) were examined to see how they cooperate with each other. For illustrative purposes, we analyze three study regions in the canton of Grisons, Switzerland (Hediger et al., 2019; Ospelt et al. 2020): a nature park region (Parc Ela), a rural-tourism region (Lenzerheide) and a region with a successfully launched agri+touristic initiative (Valposchiavo).

Results: The agri+touristic network of the Valposchiavo region consists of three main clusters, as illustrated in Fig. 1. On the outside, there two clusters of farms from each of the municipalities of Poschiavo (left) and Brusio (right), respectively. In the middle is a cluster mainly consisting of food processors and hotel and restaurant businesses. Their central position in the network is explained by the relatively large number of connections to other actors. From this and the graphical representation with the thicker connection lines and point sizes (number of connections mentioned), it can be concluded that the food Figure 1. Network Valposchiavo



processors, together with the hotel and gastronomy businesses, drive the network in Valposchiavo. The farmers play a less central role.

The agri+touristic network of the Parc Ela Fig. 2. region shows a collection of farmers that are very centrally positioned. One reason for this is probably the distinct agricultural structure of the region. The food processors and the hotel and restaurant businesses have a lower centrality and are therefore arranged with a certain distance around the central cluster. However, some food processors act as brokers and connect hotel and restaurant businesses to the central agricultural cluster through business relationships. In addition, some small separate networks ("satellites") can be identified, which have no or hardly any contacts with the main network.

The agri+touristic network of the Lenzerheide Fig. 3. region has a very different structure than those of the previously considered regions. The key players in this network are mainly food processors and hotel/restaurant businesses, with one strong food processor standing out as having ties to all three industries. This is the "Puracenter," which takes on a central gatekeeper role and serves as a strategic contact for other actors in the network. Farmers, on the other hand, tend to be positioned on the periphery of the network. This might be a



Figure 2. Network Parc Ela



consequence of the strong touristic character of the Figure 3. Network Lenzerheide region.

Analyzing social networks

Social network analysis has proved to be a useful tool in the context of this project, which aimed to illustrate the purpose of stakeholder networks for the development of regional of value chains. The graphical presentation of the regional networks enables the development and presentation of a differentiated analysis. This can also be communicated to a wider audience with interested actors in a simple and comprehensible manner. The visualization helps to identify the structural characteristics of the networks. This is an essential prerequisite for recognizing regional development potentials and strengthening agri+tourism in the individual regions.

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Educational aspirations in school transitions from lower secondary to tertiary education

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What is the significance of students' educational aspirations in the course of their educational careers, to what extent are they influenced, and how does this manifest itself, especially during school transitions?

If one takes a look at the structure and organization of the Swiss education system, one could assume that every child living in Switzerland can fulfill his or her educational aspirations - provided that the will and the willingness to perform are available for the path to the dream job. The Swiss education system is characterized, among other things, by its permeability. The Federal Constitution states: "The Confederation and the cantons shall jointly ensure, within the scope of their competence, a high quality and permeability of the Swiss education system." (Swiss Federal Constitution, Art. 61a, para.1). This permeability makes it possible to obtain the same diploma via different educational paths (EDK, 2021). Another feature that distinguishes the Swiss education system is its openness. Anyone can complete the desired education, provided he or she meets the relevant requirements (EDK, 2021). There are exceptions where only a limited number of training companies exist for basic vocational training and in a few fields of study where a numerus clausus regulates the number of students (ibid.).

This contrasts with the fact that inequalities in access to education still exist in Switzerland despite the permeable and open education system and regardless of performance. School transitions are particularly "prone" to the occurrence of such inequalities (Becker & Zangger, C., 2013). At the same time, however, it is precisely these transitions in which educational aspirations manifest themselves, because it is at these points in time that educational decisions are made for the further course of education (Hermes, 2017).

In Switzerland, there are studies on educational aspirations at individual school transitions, most of them on the transition from elementary school to lower secondary school. Most studies focus on the influence of parental aspirations on the assignment to lower secondary school or they shed light on differences in educational aspirations of adolescents with and without a migration background as well as on correlations between parental aspirations and school careers (Stamm, 2005; Neuenschwander et al., 2013). A study by Becker & Glauser (2017) was able to prove that educational aspirations of adolescents and regional opportunity structures are related. However, there is a lack of studies examining learners' educational aspirations over time at multiple school transitions, shedding light on the extent to which these aspirations depend on influencing factors at different levels (from individual to institutional and societal conditions). In particular, interesting research gaps exist in the school transition from lower to upper secondary education in connection with the use of bridging offers.

The dissertation investigates the extent to which young people's educational aspirations change during school transitions from lower secondary level to tertiary level in Switzerland and on which influencing factors this depends. The dissertation examines selected influencing factors at the individual, institutional, and regional levels and draws on existing longitudinal survey and register data from the TREE2 cohort of the University of Bern and the

LABB study of the Swiss Federal Statistical Office. Data linkages are used to determine the contribution of educational aspirations to explaining educational careers in Switzerland.

Koordination – Konflikt – Kompromiss. Das Projekt Lehrplan 21 unter konventionssoziologischer Perspektive

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In den 21 deutsch- und mehrsprachigen Kantonen der Schweiz ist der Lehrplan 21 mittlerweile in Kraft. Er definiert für die Volksschule 363 Kompetenzen, die in 2304 Kompetenzstufen gegliedert sind. Die Entwicklung des sprachregionalen Lehrplans dauerte insgesamt elf Jahre und kostete rund neun Millionen Franken. Um die 340 Personen waren in verschiedenen Gremien direkt ins Projekt involviert (D-EDK, 2015). Der Entwicklungsprozess zeigte sich sehr dynamisch, was darauf zurückzuführen ist, dass die Akteure auf ein prinzipiell offenes Ergebnis hinarbeiteten und ständig mit der Unberechenbarkeit des weiteren Projektverlaufs konfrontiert waren. Die Folge war ein fortlaufendes Bemühen, Ordnung in der Situation herzustellen. Hier setzt die Frage dieses Beitrages an: Wie schafften es die Akteure, den Prozess zu stabilisieren und ihre Handlungen zu koordinieren? Um das zu klären, wird der Entwicklungsprozess im Folgenden aus einem bildungshistorischen, einem erziehungswissenschaftlichen und einem soziologischen Blickwinkel betrachtet.

Aus bildungshistorischer Sicht war die Ausgangslage des Lehrplanprojekts zu Beginn der 2000er-Jahre geprägt durch eine bildungspolitische Aufmerksamkeitsverschiebung von Instrumenten des Inputs hin zu Wirksamkeitsfragen (Criblez et al., 2009). Mittels der Einführung von Bildungsstandards auf nationaler Ebene sollten die kantonalen Schulsysteme harmonisiert und über Leistungsvorgaben gesteuert werden (EDK, 2004). Das Standard-Konzept basierte auf der Idee der autonomen Einzelschule, welche im Rahmen eines so genannten Kerncurriculums inhaltlichen Gestaltungfreiraum erhalten, im Gegenzug aber mittels Schulleistungstests extern überprüft werden sollte (Klieme et al., 2003). Bereits am Anfang des Lehrplanprojekts wurde jedoch entschieden, kein Kerncurriculum, sondern einen direkt einführbaren Lehrplan zu entwickeln, der keiner Konkretisierung durch die Schulen bedarf (AG Lehrplanarbeit, 2005). Für diese «nächste Lehrplangeneration» (D-EDK, 2006) bestanden die Hauptherausforderungen darin, die Entwicklungsarbeit sprachregional zu koordinieren und das Verhältnis zu den im laufenden HarmoS-Projekts entwickelten Bildungsstandards zu klären.

Die erziehungswissenschaftliche Lehrplanforschung erlebte in den 1970-Jahren mit dem Versuch der Verwissenschaftlichung der Lehrplanarbeit und der theoretischen Bestimmung von Lernzielhierarchien ihre Blütezeit. Aufgrund der Kritik an ihrer technologischen Ausrichtung und dem schwindenden Interesse der Politik verringerten sich die Forschungsanstrengungen Anfang der 1980er-Jahre rapide (Buhren, Meier & Ruin, 2016). Die bis in die 1990er-Jahre fortgeführten Forschungsprojekte machten deutlich, dass zwar die meisten Aspekte der Lehrplanarbeit bekannt und empirisch untersucht waren, der Überschuss an Struktur- und Planungsproblemen und die Dynamik des Entwicklungsprozesses jedoch nicht theoretisierbar ist (Hopmann & Künzli, 1998). Mit der veränderten Steuerungsintention in der Bildungspolitik verschob sich Anfang der 2000er-Jahre auch die Forschungsperspektive weg von den Lehrplänen hin zu allgemeinen Fragen der Steuerung von Schulsystemen. Die Educational Governance Forschung identifizierte die Handlungskoordination als komplexes, interdependentes Wirkungsgeflecht im verschachtelten Mehrebenensystem der Schule (Maag Merki, Langer & Altrichter, 2014). Allerdings zeigte sich dabei das für die Sozialwissenschaften typische Problem, dass die Akteure selber die Struktur bilden, nach der sie wiederum handeln (Langer & Brüsemeister,

2019). Gefragt ist also eine theoretische Perspektive, welche dem Dualismus von Handeln und Struktur entgeht.

Die Soziologie der Konventionen (EC) bietet eine alternative Konzeption der Verbindung zwischen situativer Handlung und struktureller Wirklichkeit (Barthe et al., 2016). Soziale Strukturen wie z. B. Institutionen stellen nicht im Vorhinein den Analyserahmen dar, sondern gelten als sozial konstruierte Regeln. Ausgehend von den Akteuren werden Strukturen nur dann relevant, wenn sie zur Handlungskoordination herangezogen werden (Diaz-Bone, 2018). Analyseeinheit der EC bilden komplexe, durch Unsicherheit charakterisierte soziale Situationen. Die involvierten Akteure sind kompetent, in diesen Situationen unterschiedliche, historisch geformte Ordnungskonzepte ins Spiel zu bringen, um gemeinsam handlungsfähig zu bleiben (Boltanski & Thévenot, 2014). Für den Bildungsbereich wurden solche Ordnungskonzepte unter dem Begriff der «Schulwelten» von Derouet (1992) vorgelegt und von Leemann und Imdorf (2019) weiterentwickelt. Schulwelten bilden die Ressourcen, mit denen Akteure die Pluralität, Widersprüchlichkeit und Komplexität situativ flexibel bewältigen. Allerdings beinhalten sie auch widersprüchliche Handlungsrationalitäten, was zu Aushandlungen um gültige Ordnungsprinzipien führt.

Auf die Ausgangslage des Projekts Lehrplan 21 bezogen ergibt sich nun die Frage, wie die Akteure in den komplexen Aushandlungs- und Entscheidungssituationen kooperierten und welche Rolle dabei die Bezüge auf bestimmte Schulwelten spielten. Zur Beantwortung wird auf ein heterogenes Quellenkorpus aus öffentlichen und internen Lehrplandokumenten zurückgegriffen, die interpretativ-rekonstruktiv vor dem erkenntnistheoretischen Hintergrund der EC ausgewertet werden. Die Analyse fokussiert konfliktive Aspekte der Aushandlungsprozesse. Dazu wurden Themenkomplexe identifiziert, deren Bearbeitung sich über mehrere Projektphasen und Projektgremien hinweg als problematisch erwiesen, darunter das Stufenproblem der vertikalen Gliederung und Hierarchisierung der Lehrplaninhalte.

Die bisherigen Analysen zeigen, dass Handlungskoordination mehr einen interpretativen denn einen strategischen, auf ein definiertes Ziel hin ausgerichteten Prozess darstellt (Grass & Alke, 2019). Als bedeutsam für die Koordination erweist sich unter anderem der Kompetenzbegriff, dessen Unbestimmtheit und Vieldeutigkeit es den Akteuren erlaubt, sich in den Aushandlungsprozessen auf die unterschiedlichen, auch widersprüchlichen Logiken der Schulwelten zu beziehen. Kennzeichnend für das Projekt Lehrplan 21 ist, dass mithilfe der Kompetenzmodelle ein Kompromiss zwischen der effizienten Schulwelt, wie sie die Bildungsstandards verkörpern, und der gemeinschaftsförmigen Schulwelt der individuellen Förderung geschlossen wird. Darin kann der Versuch gesehen werden, die Differenz zwischen dem normativen Programm der Schule und den individuellen Lernprozessen zu überwinden. Entwicklung und Produkt des Lehrplans können demnach als umfangreiche Investitionen in die soziale, räumliche und zeitliche Gültigkeit eines Kompromisses betrachtet werden.

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The regulation of Airbnb and its impact on hotel performance

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The rise of players of the sharing economy revolutionized the accommodation sector. Academic research considers the hospitality industry as one of the industries which is impacted the most by the sharing economy with Airbnb being its most popular representative. Airbnb and other sharing economy-based platforms have been viewed as serious threat to traditional accommodation formats and are accused to unfairly compete in an unregulated environment. Many cities have already implemented short-term rental (STR) regulations. Since both economies, the traditional hotel industry and the sharing economy, offer the same core product, they can be considered at least partly as substitutes. That implies, that stricter regulation may lead to a decrease in STR supply, a rise in STR accommodation prices and consequently, an increase in demand for the traditional accommodation sector. Even though a plethora of academic literature deals with different aspects of the sharing economy and Airbnb, up to today only very limited research can be found that examines the financial impacts of STR regulation on the traditional accommodation industry.

In view of this major knowledge gap, this master thesis contributes to the debate by quantifying the impact of STR regulation on hotel performance metrics revenue per available room (RevPAR), average daily rate (ADR) and occupancy rate (OCC) in five European cities running a panel data regression model with fixed effects. The model combines two approaches found in academic literature: On the one hand, the approved model of Dogru et al. (2019, 2020) to investigate the impact of Airbnb supply on hotel performance metrics RevPAR, ADR and OCC, on the other hand the approach of Furukawa & Onuki (2019) to create a score specifically determined to quantify STR regulation, which is integrated as an additional covariate into the model provided by Dogru et al. (2019, 2020).

The findings show that strengthening the STR regulation increases the occupancy rates but decreases hotel room prices. The significant positive impact between a stricter STR regulation and the occupancy rates confirms the assumption that the two products hotel and Airbnb overnights are substitutes. A stricter STR regulation leads to a reduction in Airbnb supply and a rise in Airbnb accommodation prices and therefore, a shift in demand from Airbnb to the hotel industry. This also confirms the effectiveness of STR regulation from the perspective of the traditional accommodation sector. Contrary, the results show that hotels lower their room rates as an answer to stricter STR regulation. A possible explanation is that hotels utilize aggressive pricing strategies to mitigate the adverse effects of Airbnb. The process of introducing and tightening regulations is likely to be accompanied by increased public attention and thus might intensify the perception of Airbnb as a competitor to the traditional hotel industry, leading hotels to react to the competition by lowering their prices.

These findings have important implications not only for the traditional accommodation industry but also for public authorities who must respond accordingly to the disruptive potential of Airbnb and other representatives of the sharing economy. First of all, it is essential for hotels to recognize Airbnb as a direct competitor which threatens the traditional accommodation sector by acting as a substitute and causing financial damages. The understanding of the threat potential must be accompanied by a reflection on how and which values are created for customers. Hotels have key attributes that cannot be met entirely by Airbnb. In order to retain and reattract customers, the focus must lie on strengthening and promoting these attributes. When regulating STRs, the authorities have to weight different interests, and the hotel industry is only one of many players involved in the issue. From the perspective of policymakers, the findings show the disruptive potential of Airbnb for the hotel industry, but they also suggest that STR regulation is effective and strengthens the hotel sector. There exists no single right solution for STR regulation. It is important to deepen the understanding on the issue: A mandatory registration obligation and or the issuance a license for STRs helps to understand and value the economic and social interactions of Airbnb, and possibly could be combined with an agreement with Airbnb to automatically collect taxes helping to solve the problem of lost tax revenues. As several researchers have outlined, cities should adopt their regulation approach according to the impact of Airbnb and the degree of problems cities are facing. This makes it all the more important for authorities to have reliable assessments on the impact of Airbnb. This master thesis contributes significantly to the limited understanding body of work regarding Airbnb, its regulation and the relationship with the traditional hotel industry. Yet future research must improve and expand the academic understanding of the topic, not only but also to enable the authorities to base future decisions on scientific findings.

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Thursday, September 22

10:30-11:45

Session 8 Medicine & Life Sciences

Chairs: Pierre-Yves Mantel / Christine Kühne – Center for Allergy Research and Education, Michael Pfaff / Clinica Holistica Engiadina

Anti-inflammatory and regenerative effects of liraglutide on inflammatory human osteoarthritic chondrocytes in vitro

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Osteoarthritis (OA) is the most common degenerative joint disease and a leading cause of disability worldwide, affecting >40 million people in Europe. With the aging population, OA is predicted to affect 170 million people globally by 2030. Current treatments only relieve OA symptoms. Liraglutide is well known as an anti-diabetic medication that is used to treat type 2 diabetes, and obesity, and to support chronic overweight management. Liraglutide has shown a unique triple effect (anti-inflammation, pain relief, and cartilage regeneration) in inflammatory and post-traumatic OA animal models¹. The goal of this study is to determine and validate the anti-inflammatory and regenerative effect of liraglutide on human OA cartilage cells (chondrocytes).

In this study, we examined the anti-inflammatory and regenerative effects of liraglutide in a human OA cartilage cell aggregate (pellet) culture model in vitro. Chondrocytes were isolated after informed consent from femoral head cartilage of patients undergoing hip arthroplasty. Firstly, the non-toxic dose range of liraglutide (between 0.05-10 μ M) on 2D cultured human OA chondrocytes was determined using a cytotoxicity assay. After that, 2 concentrations of liraglutide (0.5 μ M and 10 μ M) were selected for testing in the pellet study. Hereby, human OA chondrocytes were plated in a V-bottom 96 well cell culture plate and cultured as pellets for one week in the medium that promotes cartilage tissue formation before the liraglutide treatment. After that, the cartilage pellets were divided into 4 groups: the control group, OA group, OA group + 0.5 μ M liraglutide, and OA group + 10 μ M liraglutide. The control group was cultured in a basic medium. The OA groups were stimulated with pro-inflammatory factors. The culture medium was refreshed and collected 3 times per week. Pellets were collected at 3-time points (day 0, 7, and 14) for analysis. RNA isolation was performed for gene expression analysis of anabolic, catabolic, and inflammatory proteins. The content of cells and extracellular matrix in the cartilage pellets were also measured. Snap-frozen pellets were sectioned for histological analysis and immunohistochemical staining of important cartilage matrix proteins such as collagen type II. The ongoing analysis will demonstrate if liraglutide has anti-inflammatory and/or regenerative effects on human OA chondrocytes. The results of this study provide further insight into the mechanism of action of this drug and its feasibility for the treatment of OA.

Acknowledgment:

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¹ Meurot, C., Martin, C., Sudre, L. et al. Liraglutide, a glucagon-like peptide 1 receptor agonist, exerts analgesic, antiinflammatory and anti-degradative actions in osteoarthritis. Sci Rep 12, 1567 (2022). https://doi.org/10.1038/s41598-022-05323-7

Association between heart rate variability and physical activity in the treatment of exhaustion as a component of stress-related disorders: study protocol

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<u>Background:</u> Chronic stress may cause an imbalance of the autonomic nervous system, thereby affecting cardiovascular as well as mental health and causing stress-related disorders. Exhaustion is a common symptom in this regard, closely associated with conditions such as burnout and depression. Physical activity plays an important role in the treatment of stress-related disorders, as it may have a positive effect on the autonomic nervous system. In addition, patients with stress-related disorders often have decreased cardiorespiratory fitness. Heart rate variability (HRV) is a non-invasive marker of autonomic nervous system. Several studies reported lower HRV in stress-related disorders compared to healthy controls and exhaustion has already been linked to reduced HRV in stress-related disorders. However, to date, research has mainly focused on comparing HRV in healthy controls and patients with stress-related disorders. Limited research exists on the relationship between exhaustion severity, physical activity and HRV, with partly conflicting results. Moreover, the effect of inpatient treatment on this relationship is largely unknown. In particular, the appropriate intensity of physical activity to ameliorate symptoms, which takes into account exhaustion severity, remains unclear.

<u>Objective</u>: This study aims to explore cross-sectional and longitudinal association of exhaustion severity, physical activity and HRV in the treatment of stress-related disorder.

Methods: Participants, aged 18-64 years, with an ICD-10 depressive episode (F32 or F33) and burnout syndrome (Z73), undergoing multimodal treatment in a rehabilitation clinic, specialized in the treatment of stress-related disorders, will be recruited. Exclusion criteria include (according to medical history) severe cardiovascular, metabolic and renal diseases, tricyclic medication, beta-blockers, presence of factors precluding exercise testing, BMI <17,5 / >35, known pregnancy, comorbid psychiatric disorders as well as severe drug or alcohol abuse. The Mini-International Neuropsychiatric Interview will be used to determine comorbid psychiatric disorders. The following parameters will be assessed at baseline and in the last week of treatment: Shirom-Melamed Burnout Measure to rate exhaustion severity and Beck Depression Inventory-II to measure depression severity. HRV will be assessed under laboratory (resting short-term recording), real-life (24-hour recording) and stress conditions (orthostatic test and submaximal exercise test). Cardiorespiratory fitness will be tested with the Åstrand-Rhyming test and cardiovascular health will be evaluated through blood pressure as well as pulse wave velocity. Cognitive function will be appraised with the THINC-Integrated Tool. Continues data (up to six weeks) will be collected with Garmin smart watch and includes physical activity (accelerometry), sleep, heart rate and HRV. Results will be analyzed with series of hierarchical regression models including control variables.

<u>Social relevance</u>: This study can yield crucial objective insights into exhaustion severity of individuals suffering from stress-related disorders and parameters of physical and mental functioning. Monitoring physical activity and HRV can give important feedback to patients having issues with self-awareness and stress management. Results will highlight feasibility of HRV recording methods and physical activity monitoring in a rehabilitation clinic and aim to optimize treatment of exhaustion in stress-related disorders.

<u>Keywords</u>: Stress-related disorders, physical activity, heart rate variability, exhaustion, rehabilitation clinic, study protocol

Novel biomarkers of disrupted gut permeability in severe COVID-19 patients

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Although coronavirus disease 2019 (COVID-19) is primarily a respiratory infection, mounting evidence suggests that the gastrointestinal tract is involved in the disease, with gut barrier dysfunction and gut microbiota alterations related to disease severity. Increased gut barrier permeability can cause a local inflammation and change circulating inflammatory thresholds leading an enhanced leakage of bacterial products to the circulation.

We designed this study to examine whether severe COVID-19 is associated with novel biomarkers of gut barrier dysfunction. Serum samples were collected from 327 COVID-19 patients (52 mild, 178 moderate and 98 severe) and 49 healthy controls at the time of admission. Levels of zonulin family peptides (ZFP) and bacterial DNA were determined in serum. Additionally, 180 circulating biomarkers were assessed by using proximity extension assay (OLINK) targeted proteomics.

Compared with healthy controls, all COVID-19 patient groups including mild (P < 0.001), moderate (P < 0.001) and severe (P < 0.001) had significantly increased levels of circulating ZFP. We also detected that levels of circulating bacterial DNA were significantly elevated in severe COVID-19 patients compared with healthy controls (P < 0.001), with mild COVID-19 patients (P < 0.001) and with moderate COVID-19 patients (P < 0.001). Interestingly, there was no correlation between the levels of circulating bacterial DNA and ZFP in COVID-19 patients. Compared to healthy controls, we defined 39 proteins as potential biomarkers in COVID-19 severity. When we analyzed patients with lymphopenia, it was found that severe COVID-19 is associated with higher levels of bacterial DNA and markers of inflammation and immune response including IL-10, MCP-3 and AREG in the circulation.

Our results demonstrate that changes in blood proteins associated with disease severity and levels of ZFP and bacterial DNA can potentially be used as early biomarkers to predict severe COVID-19 patients.

A new one-step functionalization based on a UV crosslinking polymer for the electrochemical detection of C-reactive protein

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Nowadays, diagnostics tests are usually made by the analysis of one or more biomarkers at the hospital. It typically takes more than one day to obtain the results. Moreover, specialized personnel and bulky, expensive instrumentation is required to perform the test. An alternative to this procedure involves the use of point-of-care (POC) analysis devices, that allow to achieve an accurate and specific analyte detection in the most convenient and rapid way for the patient. The present work describes the development of a novel POC platform for the quantification of biomarkers, based on an electrochemical immunoassay. This platform is based on screen-printed electrodes (SPEs) which can be miniaturized for integration in a compact and cost-effective POC device. This technology can achieve sensitivity and specificity that match the specifications of the standard methods.

One of the main challenges with the immobilization of antibodies on a sensor surface involve the number of steps necessary, which directly impacts the time required for the functionalization and the reproducibility of the processes in view of mass production. In order to bring a solution to such challenges, we propose a photoreactive polymer, which is capable to crosslink various categories of biomolecules onto the sensor surface, e.g. antibodies, enzymes, and receptors, by one-step UV activation.

As a model system, we developed a C-reactive protein (CRP) sensor based on a sandwich immunoassay with a LOD<1 ng/mL. First, the polymer (Fig.1a) was drop-casted on the working electrode and immobilized by partial UV crosslink, then the capture antibody (cAb) was applied on the surface and covalently bound to the polymer backbone by UV crosslinking. Successively the entire sensor was incubated with bovine serum albumin, to block any sites that may be still available for unspecific binding.

For comparison, another sensor was prepared by immobilization of the antibody by EDC/NHS functionalization. The sensor (EDC/NHS) was prepared as illustrated in Fig.1b. The number of steps involved in this process is significantly higher than for the polymer-based sensor (Fig 1a), which we believe being the source of the decreased reproducibility of the sensor.

A biotinylated mouse anti-CRP IgG was used as the detection antibody (dAb₁-biotin), then horseradish peroxidase-labelled streptavidin (HRP-strept) was bound as electrochemical tracer. The electrochemical reaction occurs by adding the 3,3',5,5'-tetramethylbenzidine (TMB) substrate after the immunoassay and the current is measured by chronoamperometry, by the reduction of the product (Fig. 3).

To characterize the antibiofouling effect, the biotinylated goat anti-mouse IgG (dAb₂-biotin) was directly bound to the immobilized capture antibody (Fig. 2a). To measure the signal-to-noise ratio and characterize the anti-fouling properties, a fixed concentration of cAb was crosslinked on the electrode and the blank was prepared by crosslinking the same concentration of BSA. The results (Fig.2b) showed the antifouling effect of the polymer, the blank signal is equal to $0.12\pm0.06 \mu$ A even at higher concentrations of HRP-strep, since the non-specific binding is supressed by the polymer.

The immunoassay demonstrated that the immunoactivity of the cAb immobilized on the polymer is preserved and by consequent so is the capability of the system to detect CRP in

buffer. The calibration curve gives a LOD of 0.30±0.03 ng/mL, while the IC50 is 16±4 ng/mL (Fig. 3). In comparison, the EDC/NHS sensor gained a higher dynamic range but presented a higher LOD 1.8±0.3 ng/mL. The comparison of the reproducibility shows that the relative standard deviation (RSD) of the polymer-based sensor is comprised between 5 and 9%, which is lower than the EDC/NHS sensor, ranging from 6 to 30%. The higher RSD is probably due to the higher number of steps for the preparation of the sensor.

In summary, the proposed polymer showed the capability of crosslinking biological sensing material to the sensor surface in one step by UV radiation, and an efficient antifouling behaviour. The comparison with EDC/NHS immobilization technique proved, a reduced time of functionalization a reduced number of processing steps, an increase of reproducibility and a decrease of the LOD. The next development steps will be to optimize the sensing for detection in human serum and the integration of the sensors into a multi-biomarker assay platform.



Figure 1. Sensor preparation: (a) the sensor surface functionalization with the photoactive polymer, and (b) with EDC/NHS chemistry.



Figure 1. (a) Schematics of the immunoreaction and chronoamperometric detection used in the antifouling tests. (b) The antifouling property of the polymer is tested by incubation with

different dilutions of HRP-Streptavidin. The blank signal (blue) is almost constant with increasing concentrations of HRP-Streptavidin, while the analyte signal (teal) increases. The experiment was conducted in buffer. N=3



Figure 3. Schematic view of the CRP immunoassay and respective calibration curves, obtained by the polymer sensor (teal) and with the EDC/NHS sensor (black). The polymer sensor shows a lower LOD and an enhanced reproducibility. The experiment was conducted in buffer. N=3

Rhinovirus-induced epithelial RIG-I inflammasome activation suppresses antiviral immunity and promotes inflammatory responses in virus-induced asthma exacerbations and COVID-19

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Rhinoviruses (RV) and inhaled allergens, such as house dust mite (HDM) are the major agents responsible for life-threatening asthma exacerbations. The mechanisms of this virusallergen interactions in airway epithelium in asthma are largely unknown. To address this, we compared molecular mechanisms of HDM and RV interactions in experimental RV infection in patients with asthma and healthy individuals. RV infection was sensed via retinoic acid-inducible gene I (RIG-I) helicase, but not via NLR family pyrin domain containing 3 (NLRP3), which led to subsequent apoptosis-associated speck like protein containing a caspase recruitment domain (ASC) recruitment, oligomerization and RIG-I inflammasome activation.

This phenomenon was augmented in bronchial epithelium in patients with asthma, especially upon pre-exposure to HDM, which itself induced pro-IL-1 β release and early inhibition of RIG-I/TANK binding kinase 1/I κ B kinase ϵ /type I/III interferons (RIG-I/TBK1/IKK ϵ /IFN-I/III) responses. Excessive activation of RIG-I inflammasomes was partially responsible for alteration and persistence of type I/III IFN responses, prolonged viral clearance and unresolved inflammation in asthma. Finally, we investigated the role of severe acute respiratory syndrome coronavirus (SARS-CoV-2) in exacerbations of asthma or the influence of preexisting viral or allergic airway inflammation on the development of coronavirus disease 2019 (COVID-19).

We found, that RV/HDM-induced sustained IFN I/III responses initially restricted SARS-CoV-2 replication in epithelium of patients with asthma, but even this limited infection with SARS-CoV-2 augmented RIG-I inflammasome activation. In summary, timely inhibition of the epithelial IL-1 β signaling may lead to more efficient viral clearance and lower the burden of RV and SARS-CoV-2 infection.

Thursday, September 22

13:30-14:00

Transdisciplinary project: Communication Science

Chair: N.N.

Innovations in local communication in Switzerland and the case of the Grisons

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Digitalization has shaped the media landscape quickly and drastically in the past years: It has weakened existing business models to fund journalism and it has changed processes to produce content. At the same time, it enabled new formats, new revenue models etc. due to changed media consumption behavior. This process is highly challenging for all legacy media, and it is even more precarious for local media since "[...] most [local news organizations] have fewer opportunities to pursue scale and more limited resources to invest in digital media" (Jenkins & Nielsen, 2018, p. 5). This is particularly problematic in countries with a decentralized political system, such as Switzerland, where citizens make political decisions even at the municipal level and participate in the government. Hence, citizens ideally need to be fully informed about local issues to make informed decisions (Park, Fisher & Lee, 2021, pp. 1-2).

Whilst this transformation is a challenge for local media organizations, it is a challenge for the municipality administrations as well (Möser, 2020, p. 202). Local communication is shifting on several plains. Media organizations and municipalities are not only adapting to these circumstances, but some are also developing innovative ways of local communication: certain municipalities have already implemented online participation tools ("digital village square") while some legacy media and rather new online-media have successfully adapted to the changing system and developed innovative strategies to create economically sustainable local journalism in the digitalized world. These media often introduce new journalistic formats like citizen journalism or pursue partially different content strategies but do also look for new ways to fund journalism (as crowdfunding, funding by foundations, new forms of advertising like native ads). According to the structure-conduct-performance-model it is to be expected that their (organizational) structure (including work processes) and particularly their performance for local polity and policy differs from those of legacy media (Mierzejewska, 2018).

Thus, this paper aims at analyzing the transformation of local communication. Thereby, the paper is a reference to and a continuation of existing research (e.g. Jangdal, 2019; Jenkins & Nielsen, 2020; Brückner, 2021; Fawzi, Baugut & Reinemann, 2018; Klinger, Rösli & Jarren, 2015) whilst placing the focus somewhat differently from similar previous research: The main focus is not on the weakening local communication as the negative consequences of the media crisis and the connection with political participation (e.g. Oberholzer-Gee & Waldfogel, 2006; Nielsen, 2015; Kübler & Goodman, 2019), but on the current innovation-driven developments in Swiss local communication and its further potentials. How are municipalities all over Switzerland currently communicating? How are legacy and new local media structured (including journalistic concepts, business models etc.)? Can – and do – they contribute to sustain a local public sphere?

To answer these research questions, we present new data from a transdisciplinary research project about local communication in Switzerland which has never been realized to this extend. On the one hand, the data are based on a typology of local media we build upon a survey of all local media (print, radio, TV and online). On the other hand, this research is

based on a survey of all Swiss municipalities conducted in 2021 and 2022. As the conference will take place in Davos, we plan to put our attention on results from the Grisons (with answers from 37 municipalities and 18 local media organizations in our dataset).

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Thursday, September 22

14:15-15:30

Session 9 Gemischte Themen DEUTSCH

Chairs: Cordula Seger / Institut für Kulturforschung Graubünden, N.N.

Cascading impacts of combined climate extreme events: A case study to evaluate the altered protective function of forests against gravitational natural hazards

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Combined climate extreme events are expected to occur more frequently under climate change. Impacts of such events can propagate through natural and socio-economic systems and further interact with other non-climatological risks (e.g. infrastructure failure, earth quakes, conflicts). Resulting process cascades may have unprecedented physical, ecological and societal impacts. Adaptation to future climate requires estimations of the likelihood and possible impacts triggered and enhanced by combined climate extreme events. Most available methods only simulate individual elements of possible process chains. It is therefore necessary to couple several processes for a given scenario.

Mountain forests are a key element in impact cascades caused and/or amplified by climate change. The protection against gravitational hazards including avalanches, rockfall and landslides is an important ecosystem service provided by such forests in populated mountain regions. Climate change, by altering tree species composition and distribution, will most likely affect the protection function of mountain forests. Furthermore, climate extreme events make mountain forests more susceptible to forest disturbances such as windthrow events, forest fires or bark beetle outbreaks. Interactions between different disturbances are likely. Forest disturbances may strongly affect the protection function against natural hazards. However, recent studies and long-term data suggest that the protective effect of deadwood against rockfall and avalanches has often been underestimated.

Based on a case study for the Dischma valley near Davos, we aim at assessing how combined climate extreme events alter the protective function of forests against gravitational hazards. We will apply the mass movement model RAMMS to simulate rockfall trajectories and avalanche deposition zones for different forest scenarios obtained from previous work. The goal is to couple climate extreme scenarios, ecological models and avalanche/rockfall impact models to ultimately allow for an enhanced process understanding and a 'translation' into practice. Here, we present first results and report on the progress and challenges of extending existing approaches to evaluate cascading impacts of combined climate extreme events.

Keywords: Combined climate extremes, Ecosystem services, Avalanches, Rockfall, Protection forests

Die Mehrsprachigkeitsdidaktik: eine junge Disziplin auf der Suche nach Forschungsansätzen und Forschenden

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In den letzten Jahren haben verschiedene Massnahmen auf unterschiedlichen Ebenen zur Förderung und Entwicklung der Fachdidaktiken als eigenständige wissenschaftliche Disziplinen in der Schweiz beigetragen (swissuniversities, 2022). Die Perspektiven für deren Konsolidierung in der schweizerischen Hochschullandschaft richten sich u.a. auf die Netzwerkbildung, die Laufbahnförderung, die Annährung der Institutionen und die Förderung des doppelten Kompetenzprofils in den unterschiedlichen Fachbereichen (Bader et al., 2022). Letzteres meint eine Verschränkung von Wissenschaftsfundierung und Praxisorientierung in einem bestimmten Gebiet und ist an Pädagogischen Hochschulen (PH) eine zunehmend gestellte Anforderung an Dozierenden (Biedermann et al., 2020).

Was die wissenschaftliche Weiterentwicklung dieser relativ jungen Disziplinen anbelangt, sind insbesondere die Förderung der Nachwuchsforschenden sowie die Orientierung an bestimmten Forschungsansätzen von grundlegender Bedeutung (swissuniversities, 2022). PHs als Ausbildungsorte für Lehrpersonen gelten in der Schweiz als institutionelle Heimat der Fachdidaktiken. Da es sich dabei um professionsorientierte Hochschulen mit einem klaren Berufsbezug handelt, sind PHs auf anwendungsorientierte Forschung angewiesen (Prenzel, 2020). Es liegt nahe, dass fachdidaktische Forschung sich vordergründig an einen anwendungsorientierten Ansatz orientieren muss. Anwendungsorientierte Forschung an PHs hat ebenfalls, wie die Hochschullehre, nicht nur Wissenschaftsfundierung, sondern auch Praxisorientierung nötig. Dementsprechend soll das Profil der künftigen PH-Forschenden, wie auch dasjenige von PH-Dozierenden, beide Bereiche abdecken. Es bleibt aber zu klären, welche methodischen Vorgehensweisen bei den einzelnen Fachdidaktiken zielführend sind. Weiter ist auch unklar, wie sich bei Nachwuchsforschenden das doppelte Kompentenzprofil in ihrem jeweiligen Forschungsgebiet fördern lässt.

Der dreisprachige Kanton Graubünden mit seiner vielfältigen Schullandschaft ist schweizweit ein hervorragendes Forschungsfeld für die unterschiedlichen Fremdsprachendidaktiken. Hier findet die Mehrsprachigkeitsdidaktik einen reichhaltigen Nährboden für deren Konsolidierung und wissenschaftlichen Weiterentwicklung (vgl. Cathomas et al., 2022). 2022 ist an der PH Graubünden das innovative Forschungs- und Entwicklungsprojekt QUATTRO gestartet, welches im Zentrum des vorliegenden Beitrags steht. QUATTRO bezeichnet ein Netzwerk bestehend aus vier Akteur:innen: Primarlehrpersonen, PH-Studierende, PH-Dozierende und PH-Forschende. Das Hauptziel des Projekts besteht in der Entwicklung von Fördermodellen, welche zu einer Stärkung des doppelten Kompetenzprofils aller vier Akteur:innen im Bereich der Mehrsprachigkeitsdidaktik führen, um letztendlich neue PH-Nachwuchskräfte in diesem Gebiet zu gewinnen. Gleichzeitig wird durch das Zusammenführen der Akteur:innen auch eine Annäherung zwischen zwei Bündner Institutionen hergestellt, nämlich zwischen der PH Graubünden und der Bündner Volksschule. Somit trägt das QUATTRO-Projekt den einleitend erläuterten Zielsetzungen von swissuniversities (2022) Rechnung (Krompák & Todisco, 2022).

QUATTRO gliedert sich in zwei Teilprojekte. Eins davon ist im Bereich der mehrsprachigkeitsdidaktischen Forschung untergebracht und in einem bestimmten Sprachfach eingebettet. Mehrsprachigkeit kann nämlich in der Schule in Bezug zu jeder Sprache gefördert werden. Im Bündner Kontext stellen Mehrsprachigkeit und deren Schulpraxis aber nicht nur ein Forschungsgegenstand dar. Um die Verständigung und den Austausch zwischen den Bündner Sprachgemeinschaften zu fördern, sollen verfassungsmässig die zwei kantonalen Minderheitssprachen Romanisch und Italienisch mit den erforderlichen Massnahmen unterstützt werden (Verfassung des Kantons Graubünden, 2021/13.06.2021, Art. 3). Diese Vorgabe betrifft auch den Bildungskontext. Das Teilprojekt (wie auch das Gesamtprojekt) berücksichtigt dieses bildungspolitische Ziel und richtet den Fokus auf das Schulfach Italienisch als Fremdsprache. Den Forschungskontext stellen Deutschbündner Primarschulen dar, an denen Italienisch ab der 3. Primarschulklasse unterrichtet wird. Ziel des Teilprojekts ist, mehrsprachigkeitsdidaktische Unterrichtspraxen und -materialien für das Schulfach Italienisch als Fremdsprache zu entwickeln, wobei gleichzeitig die theoretischen Grundlagen der Mehrsprachigkeitsdidaktik auf empirischer Basis präzisiert werden.

Auf der Suche nach einer passenden methodischen Vorgehensweise ist die Wahl auf partizipative Ansätze gefallen. Diese ermöglichen, PH-Forschende als Wissenschaftexpert:innen und Primarlehrpersonen als Praxisexpert:innen zusammenzubringen und dadurch methodisch eine Brücke zwischen Wissenschaftsfundierung und Praxisorientierung zu schlagen (vgl. doppeltes Kompetenzprofil). Ausgehend von den Erfahrungen im Rahmen eines Vorprojekts (Crameri, 2021) hat man sich in QUATTRO für den Design-Based-Research-Ansatz (DBR; Peters & Roviro, 2017) entschieden (Crameri, 2022). Der Beitrag richtet den Fokus auf diesen neu eingeschlagenen Weg und zeigt, wie DBR der Weiterentwicklung der Mehrsprachigkeitsdidaktik dient. Ausserdem wird erklärt, wie durch DBR das doppelte Kompetenzprofil der am Forschungsprozess beteiligten PH-Forschenden, aber auch der Primarlehrpersonen, gefördert werden kann. Dies geschieht, indem PH-Forschende als Wissenschaftexpert:innen von der Expertise der Primarlehrpersonen als Praktiker:innen profitierten und umgekehrt. Empirische Daten werden erst nach Projektabschluss (voraussichtlich in Dezember 2024) zeigen, ob DBR als Fördermodell zur Stärkung des doppelten Kompetenzprofils im Bereich der mehrsprachigkeitsdidaktischen Forschung taugt.

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Upflows in the quiet Sun – a highly active place

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The solar corona is the outermost layer of the Sun, which extends far into the open space. It is characterised by temperatures of up to several million degrees Celsius, but extremely low densities. Those contradictory conditions are still not fully understood and are known as the "Coronal heating problem". The solar corona itself can be separated into three different regions: first the active regions, which are big bright and dynamic features; second the quiet Sun, which are regions with only small and weak features and third the coronal holes, which are colder and nearly featureless regions. Furthermore, the solar corona is known as being the source of the solar wind, which is an omnipresent stream of highly energetical particles and electromagnetic fields. Leaving the Sun, the solar wind travels towards the Earth, where it can have strong impacts. The beautiful effects on Earth can be observed as polar lights, but in a modernised world the negative effects dominate. Those can be malfunctions in satellites, disturbances in communication systems and blackouts in electricity systems.

Energetic events in active regions like solar flares and coronal mass ejections are usually seen with a big outflow of plasma. In our previous work, we have used spectroscopic data to show that strong upflows of plasma can be observed even from small-scale features in the quiet Sun and coronal holes. Those small features were previously not considered as sources of strong upflows since they were barely visible in the previous generation of imaging instruments. With the launch of EAS's Solar Orbiter, this has changed drastically since it allows imaging of the solar corona with a much higher spatial and temporal resolution using its Extreme-Ultraviolet Imager. Already the first data has shown a variety of new and highly active small-scale features such as EUV brightenings. In our current work, we use the most recent data from the Solar Orbiter satellite in combination with data from other satellites to investigate the influence of the smallest know coronal features on the solar wind.

LEGO®-inspired multicomponent 3D-printed bone substitute for personalised facial bone repair

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Introduction: Large bone defects such as trauma, tumour resection, infections or congenital deformities do not have the capacity to heal inherently and therefore cause serious healthcare implications. Reconstruction of large bone defects in the facial area represents a challenging medical condition and requires the implantation of an autologous bone graft. This difficult surgical intervention includes harvesting a piece of bone of the patient's own body to be implemented into the defect site. Autologous bone grafting is the standard of care (SOC) to restore a functional and aesthetic outcome but is unfortunately associated with major drawbacks including limited availability, donor site pain and excessive graft resorption. An alternative SOC is urgently needed to overcome these issues. A tissue engineered approach combines the use of regenerative cells, a supporting scaffold material for mechanical stability and pro-osteogenic factors to create a bone substitute as an alternative. An attractive approach to create personalised scaffolds is the use of 3D printing. The main limitation of 3D-printed bone substitutes is the formation of a necrotic core upon implantation within the body, due to limited diffusion of oxygen and nutrients into the scaffold and poor biological waste removal. Also, delivery of regenerative cells within 3Dprinted bone substitutes remains a challenge, due to the poor cell-adhesion properties of the scaffold. This work aims to create a 3D-printed personalised bone substitute based on a novel combination of materials, to form a scaffold with enhanced mechanical and celladhesion properties and with a configurable layered composition based on the LEGO[®] principle. The layered multicomponent approach allows for improved distribution of cells in the centre of the bone substitute by implementing collagen membranes that not only function as a collection chamber but also promotes cell viability and osteogenic cell response. Collagen is a very important protein for the early regeneration of bone that is produced by the bone cells and is therefore often used for bone tissue engineering.

<u>Methods:</u> The newly developed printable ink is created by mixing a solvent, ethylene carbonate (EC), with poly(lactic-co-glycolic acid) (PLGA, 40% (w/V)), β -tricalcium phosphate (β -TCP, 20% (w/V)), and thermoplastic polyurethane (TPU, 10% (w/V)). EC is a non-toxic solvent that is water soluble which makes it easy to remove after printing. PLGA is a thermoplastic polymer that is biocompatible, bioresorbable and is added to improve printability of the ink and mechanical strength of the 3D-printed scaffold. β -TCP is composed of calcium phosphate, a brittle material with weak mechanical properties, but it provides the necessary osteoconductivity that promotes the formation of bone. TPU is a polymeric elastomer that is biocompatible and improves elastic mechanical properties. The LEGO[®]-like components are virtually designed using a CAD software (Autodesk Fusion 360[®]) and printed into personalised layered scaffolds via solvent-based printing using a RegenHu 3D Discovery[®] Bioprinter. Human bone marrow derived mesenchymal stromal cells (hBM-MSCs, obtained will full ethical approval) can differentiate into different cell types including bone cells and

help with the regeneration of the lost bone tissue. Therefore, they are used in this study to test for the collagen membrane's osteogenic potential by undergoing an osteogenic differentiation experiment for 21 days on two commercially available collagen membranes: 1. Lyostypt (B. Braun) and 2. Collagen Cell Carrier (CCC) (Viscofan Bio Engineering). As last step, the viability of hBM-MSCs on the collagen membranes placed in between 3D-printed scaffold layers is examined after 8 days of cell culture.

<u>Results:</u> Water-mediated solvent removal leads to surface microporosity and roughness, both confirmed by scanning electron microscope, and both favourable properties for improved cell-adhesion and osteogenic cell response. Mechanical compression and drilling tests of the 3D-printed scaffold show improved stiffness and destructibility compared to a commercially available ceramic. Under osteogenic culture conditions, hBM-MSCs placed on collagen membranes show satisfactory osteogenic outcome confirmed by upregulation of important bone markers such as alkaline phosphatase through protein expression and bone sialoprotein through gene expression. Cell viability assays show good hBM-MSCs cell survival on the Lyostypt cultured in between 3D-printed scaffold layers, while a higher number of dead cells were detected on the CCC.

<u>Conclusion</u>: Large scale personalised bone substitutes can be successfully printed, assembled, and combined with cell-carrying collagen membranes within the LEGO[®]-inspired interlocking system. We propose a novel tissue engineered approach for large bone reconstruction as an alternative SOC to autologous bone grafting. Ongoing tests aim to demonstrate osteogenic capabilities of the 3D-printed scaffold itself.

How we build scientific theories and the extent to which AI can support us in doing so

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Scientists in all fields are constantly engaged in developing and expanding scientific theories: They recognise relationships, develop new hypotheses, and try to test them. But how exactly do we develop new hypotheses? This is a central question in the philosophy of science and one that I am investigating in my PhD. More specifically, I am investigating abduction. Besides deduction - certain reasoning - and induction - the generalisation of statements abduction is the third, and most powerful, type of reasoning: abduction is the only type of reasoning that allows us to introduce new concepts into a theory. For example, Newton deduced from the fall of an apple that gravity exists, Fleming deduced from spots in a Petri dish that an antibiotic is at work there, and Darwin deduced evolution from the formation of certain characteristics in plants and animals. Abduction thus plays an enormously important role in science, since it is the only way to introduce new theoretical concepts, i.e. to infer from observations to theoretical concepts that describe underlying causes.

Precisely because of its power and complexity, abduction is controversially discussed in the philosophy of science and there are many different manifestations and models, for example a psychologically oriented one by Charles Peirce and an explanation-based one by Peter Lipton. Furthermore, it is controversial whether abduction can be formalised, i.e. whether artificial intelligence can at least theoretically be capable of introducing new concepts in a theory.

In my PhD, I developed a new theory of abduction based on conditionals that builds on existing theories while avoiding their problems such as being able to find only certain concepts or having inherent contradictions. Unlike many other theories, it also allows abductive inference to be formalised. Now that the theory has been developed and successfully published as an article, I would like to prove that it can indeed be formalised and profitably used in science.

To do this, I apply it to a previously unsolved problem in the field of artificial intelligence, the Abstraction and Reasoning Corpus (ARC). The ARC is a kind of intelligence test intended for both human and artificial intelligence approaches. While humans can solve 80% of the tasks on average, the best artificial intelligence approach is around 30%. This is because the intelligence test consists of 1000 individual tasks, all of which are different in nature, and existing artificial intelligence approaches are not able to successfully abstract the solution of one task and transfer it to a new, different task.

Abduction can make a valuable contribution here, as each task involves finding the underlying law that describes the transformation from the problem state to the target state. In other words, an underlying cause must be inferred from observations. The abduction theory developed so far is to be implemented accordingly in the form of a computer programme and applied to the ARC test.

If it is possible to solve the ARC test by means of abduction, it can be shown that the philosophical theory of abduction can be formalised and practically applied, which is an important step in demonstrating its feasibility. Furthermore, the successful implementation would show that the generation of scientific hypotheses can be formalised and that it is in principle possible to use artificial intelligence to develop hypotheses and form new scientific

theories or extend existing theories. This would be a result that has a major impact on all areas of science and should therefore be discussed interdisciplinarily from the outset and developed further in a joint exchange.

The aim of my 10–12-minute presentation would be to introduce the core ideas and present the main results of the research and their implications. The aim is not to discuss individual components of my work in detail, but to show the audience - especially scientists but also the public - how we develop theories further and to what extent artificial intelligence can support us in this.

Thursday, September 22

14:15-15:30

Session 10 Mixed topics ENGLISCH

Chairs: Britta Allgöwer / Academia Raetica, Louise Harra / Physikalisch-Meteorologisches Observatorium Davos / World Radiation Center

Augmented Swiss Heritage

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<u>Augmented Reality:</u> In this project, an AR app for guests and locals of the destination Davos is being created in collaboration with the Kirchner Museum and the Davos Museum of Local History. With the app, the guest experiences Davos' cultural heritage in an immersive and participatory way. In terms of time and content, the app is to be closely linked to the exhibition Europa auf Kur, in which the rise of Davos from a sleepy mountain farming village to a sophisticated spa and tourist resort as well as a meeting point for the European scientific and cultural scene is highlighted. The project pursues to answer three questions:

- 1. Which art historical artifacts, tourist sites and stories are suitable for augmentation (enrichment) on the smartphone?
- 2. Which multimedia forms and formats have to be applied to the virtual content in order to fulfil the quality criteria of composition, immersion and participation?
- 3. Which steps of the production process can be defined and to what extent can the latter be optimised to deliver a high-quality result in a cost-effective and timely manner?

The project investigates how sights, art, history as well as tangible and intangible socialcultural knowledge about Switzerland can be made accessible through AR in the form of new user experiences for a tech-savvy target group. It explores and elaborates the production process from curating the content to digital augmentation and delivery to the smartphone app and ultimately its distribution through the platform discover.swiss, providing a template for replicability by other destinations.

<u>Methodology</u>: The innovation consists of making content that is hardly known or accessible to humans, avail- able to them and of presenting this virtual content audio-visually in a composition with reality. Young people in particular dislike reading long texts and prefer visual presentations. Consequently, the aspect of scene composition is very important. Ronald Azuma (1997) succinctly defines it as follows:

«AR allows the user to see the real world, with virtual objects superimposed upon or composited with the real world. Therefore, AR supplements reality, rather than completely replacing it. Ideally, it would appear to the user that the virtual and real objects coexisted in the same space».

Immersion is equally important in AR than in VR. Two factors must be ensured: The «illusion of place» and the «illusion of plausibility» (Slater 2009). «Illusion of place» requires that the user really has the feeling of being in the virtual place. The «illusion of plausibility» is given when the users get the feeling that the events around them are true.

The current state of research regarding especially intangible cultural heritage suggests that, at a deeper level, commodification of heritage can be interpreted as marking needs for identity, and the finding of the true self through the appropriation of pastness (McIntosh and Prentice 1999, 590). In general, there has thus far been little emphasis on the consumers' perspective or, indeed, that consumers have different perspectives, expectations, and needs (de Faucon-berg, Berthon and Berthon 2017, 6). Heritage sites are

often built on the memories and remains of previous societies and production processes but are given new meanings in contemporary contexts (Heldt Cassel and Pashkevich 2014, 1625). Consequently, the presented research project closes a gap in research regarding its methodological approach; researchers from UAS of the Grisons form a so-called «community of practice» with well-informed stakeholders (mainly locals), which allows the fostering of associations and ultimately, the generation of new and highly transdisciplinary data (Gautier et al. 2021).

<u>Technology (Gain of knowledge)</u>: In the pilot phase, a smartphone app (Android, iOS) is used, but the goal is a progressive web app (PWA). The app enables users to view 2D/3D animated and/or interactive digital models, (persistent content). All users can view the same model in the same place (shared content, allowing to design experiences for families and groups). The content is located on discover.swiss, an open back-end service platform based on Microsoft Azure Spatial Anchors for locating the models and AR Cloud for retrieving the models.

<u>Social Relevance</u>: The project brings Switzerland's cultural and historical heritage, both tangible and intangible, to the public in an educational and entertaining way and raises awareness among the Swiss population for novel technologies. With the app and the various augmented Swiss Heritage experiences, artwork, buildings, and various other artefacts that have disappeared or have been damaged are made visible and tangible in their full glory. Events come to life; guests can even be taken on a journey through time. It is precisely the quality feature of participation that promotes the social and societal sustainability outlined here, as active participation and engagement with content from history, politics, natural and cultural history, or art are specifically supported. In addition, an innovative contribution is made to the preservation of the material and immaterial heritage of Switzerland.

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Influence of snow cover duration on the abundance and distribution of alpine marmots

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The harsh environmental conditions found in mountain ecosystems present special challenges to species living in such environments. Temperatures are low, solar radiation is high, winters are long, and summers are short. Animals living in the mountains have evolved strategies to deal with such unfavourable conditions. Climate change is expected to change these conditions substantially. Some mountain-adapted species will profit from the new circumstances, while the vast majority will experience negative consequences.

In this study we investigated how environmental and climatic factors affect the distribution and abundance of alpine marmots. One particular focus of our study was the influence of snow cover duration. If the snowpack melts too late in spring, vegetation is delayed, and marmots are not able to store enough fat reserves for the following winter. However, adequate snow cover is required during winter to insulate the burrow. Earlier snowpack cover therefore leads to higher winter survival.

In summer 2021 we surveyed marmots in the region of the Swiss National Park. We modelled the distribution and abundance of marmots as functions of environmental and climatic conditions. Besides snow cover we also analysed the influence of land cover, summer temperature, vegetation phenology and topography. We used existing environmental data alongside variables derived from Sentinel-2 satellite images.

The number of counted marmots is not only influenced by how suitable the habitat is, but also by how likely we were to detect a marmot during the survey. To correct for this observation bias, we used an approach called distance sampling, which explicitly models how the detection probability of a marmot decreases with distance from the observer. Correcting the number of counted marmots by the proportion that was missed produces accurate abundance estimates.

While the strongest explanation for marmot distribution was vegetation; areas with earlier snow melt were also inhabited by more marmots. However, the number of marmots was only weakly associated with the date of snow onset. Furthermore, Temperature and weather conditions during the survey affected the distance at which marmots could still be detected.

Climate change is changing the temperature and snow regime in the mountains. I will discuss the implications of our results in relation to climate projections over coming decades and if marmots may cope with future climatic conditions.

A German vocabulary intervention in heterogeneous Romansh primary school classes

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The canton of Grisons in Switzerland promotes Romansh-German bilingualism with unique school models in traditional Romansh-speaking areas (cf. Furer, 2005, p. 9). In those areas, the minority language Romansh is the school language in primary schools. At secondary school levels, however, school language is switched to the majority language German (cf. Cathomas, 2005, p. 160ss.). Differences in contact with German outside of school settings (and therefore differences in German knowledge) lead to heterogeneous class constellations during German lessons from the third grade on. Although children with another first language (L1) than Romansh or German (often Portuguese) show similar qualifications in Romansh compared to classmates with Romansh or German as L1, they perform on average significantly worse in German reading and writings tests (cf. Peyer et al., 2014, p. 41). This may indicate a significant need for support in German for children with another L1 than Romansh or German.

The aim of my doctoral project is to examine the role of the school language regarding learning of vocabulary in another language. Studies have shown glossing (i.e. word explanations at the margin of a text; cf. Choi, 2016; Laufer & Shmueli, 1997; Samian et al., 2016; Zhang & Ma, 2021) and the use of the L1 (cf. Lee & Macaro, 2013; Schmitt, 2008, p. 337s.) to be efficient for vocabulary acquisition in the second language (L2). I investigate whether this is also the case for the school language Romansh (L1 or L2). For this purpose, I developed teaching materials with German texts and exercises for expanding German vocabulary based on scientific recommendations (cf. Elleman et al., 2019) and feedback from teachers from the context. In order to compare the effect of glossing and word explanations in the target language German with the school language Romansh, half of the teaching materials have Romansh and German word explanations, respectively. During spring semester 2022, 5th and 6th class teachers from six Romansh schools used my materials during 18 German lessons. By means of a within-subject-design (cf. Vanhove, 2020, p. 67ss.), each class and therefore each student goes through both conditions (bilingual vs. monolingual) and the effects of conditions will be shown with pre-, post- and follow-up-vocabulary tests. Questionnaires, teacher interviews, some films during instruction and group interviews give a qualitative insight into the intervention.

Here I present the context, theory, research questions, methods and first results of the investigation.

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A pilot study on the (physiological and psychological) effects of therapeutic body wraps ("kalter Ganzkörperwickel") in psychiatric inpatients

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<u>Background:</u> Some traditional therapeutic applications from the era before psychopharmacology are still being used in psychiatric hospitals. One such treatment is called "therapeutic body wrap" ("kalter Ganzkörperwickel"), TBW. While its long-standing use appears to support its therapeutic usefulness, little is known about its actual effects on body and mind, and no study was ever carried out to formally prove its efficacy. The Psychiatric Services of Grison (PDGR) currently run a pilot study to better understand the effect of this treatment in psychiatric inpatients.

<u>Method</u>: In pilot study, the physiological and psychological effects of TBW were first studied in psychiatric inpatients. The early piloting phase (Feb-May 2022) was used to critically reflect on the feasibility of the design and to refine research hypotheses for future studies.

In this sub-study, the first case with a completed treatment series (five TBW applications) is presented.

Physiological effects were studied by continuous recordings of heart rate, respiratory rate and skin temperature before, during and after each TBW treatment using the Equivital system with the software LabChart software for analyses of heart rate variability (HRV). In addition, physiological stress parameters (alpha amylase, cortisol) were measured.

A range of psychological measures were assessed in parallel with the physiological markers. These included: perceived stress, state anxiety, somatic perception, and quality of life. Special focus in this sub-study was given to the reactivity of HRV in response to the treatment with TBW.

<u>Results:</u> The critical analysis of the early pilot phase demonstrated the feasibility of the study design and resulted in suggestions for optimising the study protocol, including refined research hypotheses.

In a 32-year-old male inpatient with severe depression, HRV parameters changed in response to the treatment. For most parameters, a typical response pattern evolved only over time, typically during the 3rd TBW, and in parallel with the patients' subjective ratings of "feeling relaxed".

<u>Conclusion</u>: Studying traditional treatments in Psychiatry, such as TBW, with modern research methods is feasible and promising. Such studies may help to improve the application of traditional treatments and increase their efficacy in psychiatric patients. HRV parameters could be useful markers of treatment response.

Regulation of ACE2 mRNA and protein isoforms in viral and allergic inflammation

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infects airway epithelial cells via the main receptor Angiotensin-converting enzyme 2 (ACE2). ACE2 can be expressed in various isoforms (protein variants), which were found to be differentially regulated. One thereof called short ACE2 was found to be interferon regulated and does not possess the full N-terminal part, harboring the peptidase domain. Short ACE2 is not able to serve as a SARS-CoV-2 receptor, but was speculated to possess antiviral functions due to its interferon regulation. Expression of ACE2 mRNA by classical PCR and RNA-sequencing methods during the pandemics did not distinguish between different ACE2 isoforms on the mRNA level, leading to the contradictory results and especially concerns in interferon clinical trials in COVID-19 patients. The interaction between asthma, it's viral or allergen-induced exacerbations and COVID-19 are still unclear. IL-13, the major type 2 asthma cytokine, was shown in mechanistic studies to inhibit SARS-CoV-2 infection in airway epithelium. Contrastingly, IL-13 has also been shown to be a major driver of COVID-19 severity and anti-IL4/13 treatment to have positive effects in COVID-19 clinical trials. Moreover, infection with rhinovirus was shown to inhibit SARS-CoV-2 infection by inducing interferons which act antiviral. On the other hand, we recently reported that co-infection of rhinovirus and SARS-CoV-2 leads to greater RIG-I inflammasome dependend damage in the airway epithelium in patients with asthma.

Therefore, since regulation of ACE2 isoforms in asthma has not been extensively studied, we investigated the impact of the major type 2 asthma cytokine (IL-13), house dust mite extract (HDM) exposure and viral infection by rhinovirus (RV-A16) on ACE2 in gene and protein expression. We used primary human bronchial epithelial cells from control and patients with asthma, grown and differentiated in air-liquid interface (ALI). These cells differentiate into basal (stem-cells), mucus-producing goblet- and ciliated cells and resemble the human bronchial epithelium as one of the most physiologically relevant model available to date.

By reverse transcription PCR (RT-PCR) we distinguished between long *ACE2* and truncated (short) *ACE2* mRNA transcripts and found that long ACE2 was downregulated by IL-13 treatment, whereas short ACE2 was upregulated by rhinovirus infection. ACE2 protein isoforms and posttranslational modifications (N-linked Glycosylation) were examined by western blotting, where we found IL-13 to reduce the amount of long glycosylated ACE2. Interestingly, we did not observe a significant change on short ACE2 protein level upon rhinovirus infection, as it was anticipated by observation on the RNA level. This suggests a high protein turnover with low protein stability, translation repression or mRNA degradation of this truncated isoform.

In view that IL-13 led to the decreased amount of long glycosylated ACE2, we continued to explore mechanisms which let to such alteration. By means of confocal microscopy on transversal cryosections of ALI cultures, we observed ACE2 to localize predominantly, but

not restricted to the apical site of ciliated cells. IL-13 induced substantial morphological changes in the bronchial epithelium, which led to a redistribution of ACE2 signal. Apical ACE2 intensity, measured on top-view acquisition of ALI cultures, significantly dropped, which hints for less surface available ACE2. Additionally, we found IL-13 to induce changes in genes involved in ion- and transmembrane transport, lipid metabolic processes and protein glycosylation by using our bulk-RNA sequencing data of primary bronchial epithelial cells stimulated with IL-13.

We then screened for effects of IL-13 on other SARS-CoV-2 related host molecules in our bulk-RNA sequencing dataset and found besides others, TMPRSS2 and NRP1 to be differentially regulated. TMPRSS2 is a host protease which facilitates fusion of SARS-CoV-2 with the cellular membrane and NRP1 was shown to serve as an additional SARS-CoV-2 receptor. In a previously published dataset of bronchial epithelial cells infected with rhinovirus, we also found these two molecules to be differentially regulated. Therefore we also investigated the protein of TMPRSS2 and NRP1 by confocal microscopy and western blotting. We found TMPRSS2 and NRP1 both to be localizing apically on ciliated cells and nuclei, and remarkably strong signal of NRP1 in ciliae, making ciliated cells most susceptible for SARS-CoV-2 infection. By quantitative western blotting, we found alterations in their protein level to be negligible in any experimental condition. Overall, the regulation of ACE2 and other host factors was comparable in bronchial epithelial cells from control individual and patients with asthma.