



4th ESPT summer school: precision medicine and personalised health

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In September 2018, the European Society of Pharmacogenomics and Personalised Therapy (ESPT), with the support of the Swiss Personalized Health Network (SPHN), organized its 4th biennial summer school, entitled 'Precision Medicine and Personalised Health' (Campus Biotech, Geneva, Switzerland; www.esptsummerschool.eu/). The school's comprehensive and innovative educational program aimed to address the fundamentals of pharmacogenomics, the latest knowledge on established and new concepts in the field of precision medicine, as well as its advanced clinical applications in personalized health. The school consisted of 31 lectures, eight interactive workshops, visits to genome center and poster presentations, involving 40 speakers from distinguished international faculties. The meeting was a resounding success by generating informal environments between more than 80 participants from 26 different countries.

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The European Society of Pharmacogenomics and Personalised Therapy (ESPT) was created in 2011 with the aim of extending knowledge and facilitating clinical implementation of pharmacogenomics (PGx) and personalized medicine in Europe. One of the major goals of ESPT is to provide students, clinicians and all health professionals with comprehensive training and updated knowledge in the multidisciplinary field of PGx and personalized therapy. To achieve these educational goals, ESPT has established and organizes every 2 years a comprehensive Summer School in Europe. So far three schools have been successfully organized: in August 2012 in Ljubljana, Slovenia; in June 2014 in Rome, Italy and in August 2016 in Belgrade, Serbia.

The 4th ESPT Summer School took place at Campus Biotech in Geneva, Switzerland, from 24 to 27 September 2018 (www.esptsummerschool.eu/). The event was opened by the chair of the organising committee, Prof Marc Ansari, board member of the ESPT, chairman of the Swiss Group on Pharmacogenomics and Individualised Therapy (SPT) and director of the CANSEARCH Research Laboratory at the Geneva University. He was followed by the president of the ESPT, Prof Ron H van Schaik, and finally by the co-chair of the summer school and the president of the Swiss Personalized Health Network (SPHN), Prof Peter Meier-Abt. The summer school began with two introductory lectures: "Precision medicine and personalised health: concepts, opportunities and challenges" (Urs A Meyer, Switzerland) and "Pharmacogenetics in clinical practice: do you have your DNA passport?" (Ron H van Schaik, The Netherlands). These two lectures aimed to refresh participant's thinking about concepts of precision medicine through examples of successful implementation, recapitulating the basics of personalized health and setting the

overall tone of the summer school by discussing the opportunities and challenges researchers are facing. After these introductory talks, the topics covered by the lecturers of the school were organized into the following ten sessions.

'Omics' overview 1 (Chairs: Marc Ansari, Peter Meier-Abt)

The morning session of the first day included three different lectures: *"Genomics: Medicine & Health"* (Stylianios E Antonarakis, Switzerland), *"Epigenomics: Medicine and Health"* (Ingolf Cascorbi, Germany) and *"Transcriptomics"* (Manolis E Dermitzakis, Switzerland). This session aimed to reinforce basic methodological concepts in these three fields through reviews of methodology development, present their usage for successfully addressing research questions such as cancer drug resistance and discuss future possibilities in light of the accelerated development of technological capabilities and its benefit for drug development.

'Omics' overview 2, the integrome (Chairs: Maurizio Simmaco, Ron H van Schaik)

The first day of the summer school concluded with four afternoon lectures in new and fast developing fields of: *"Proteomics"* (Rudolf Aebersold, Switzerland), *"Metabolomics"* (Maurizio Simmaco, Italy), *"Microbiome"* (Jacques Schrenzel, Switzerland) and *"Nutrigenomics"* (Walter Wahli, Singapore). Like the morning lectures, the aim was to review basic concepts and highlight examples of successful implementation, together with a presentation of the future opportunities offered by these methodologies.

Clinical phenotype (Chairs: Christian Lovis, Antoine Geissbuhler)

The morning session of the second day started with a lecture on *"Clinical Phenotype"* (Christian Lovis, Switzerland) and revolved around questions concerning what a phenotype is, the landscape that it is represented in and the challenges of data representation, interpretation and interoperability. Because the summer school was focused on doctoral and postdoctoral students, a *"Questions and Answers"* (Antoine Geissbuhler, Switzerland) section was dedicated to a free discussion to reinforce and promote the understanding of various concepts. The session concluded with a lecture on the *"Prediction of Metabolic Phenotypes from Genotype"* (Adrian Llerena, Spain) discussing the pitfalls of the current genotyping approach to determining actual enzymatic activities. The whole session was innovative, interactive and truly dynamic.

Clinical examples (Chairs: Ingolf Cascorbi, Caroline Samer)

The afternoon session on clinical examples included the following lectures: *"Radiology image processing in new precision medicine – new technologies (radio-omics)"* (Xavier Montet, Switzerland) presented examples of how new, advanced technologies are changing the field of medical diagnostics and providing new opportunities for precision medicine. The session continued with a lecture on *"Pathology"* (Thomas McKee, Switzerland) to reinforce the importance of understanding disease etiology and its impact on precision medicine. The presentation of a translational study on *"The Geneva cocktail for cytochrome P450 phenotyping"* (Caroline Samer, Switzerland) continued this session, outlining the development of a highly sensitive clinical test to determine individual cytochrome P450 phenotypes, applying a cocktail of medications in a microdose scale. The session concluded with a lecture entitled *"Biomarkers: discovery & application"* (Denis Hochstrasser, Switzerland), highlighting the importance of biomarkers in medical decision-making and demonstrating the complexity and difficulties associated with such work.

Clinical bioinformatics (Chairs: Manolis E Dermitzakis, Petros Tsantoulis)

With the arrival of new 'omics' approaches, which generate 'big data', this final session of the second day, was devoted to the topic of clinical bioinformatics. Overall, the session aimed to address the *"Clinical perspective of bioinformatics"* (Olivier Delaneau, Switzerland), with the first lecture introducing the basic concepts of bioinformatics through the case study of intra- and inter-chromatin interactions and their effects on gene expression. A second lecture, on *"Clinical Bioinformatics Pipelines"* (Valerie Barbié, Switzerland), gave examples of successful, clinically useful, interoperable tools to support Swiss hospitals in the harmonization, standardization and coordination of their bioinformatics analysis pipelines. These two lectures were followed by a discussion of the *"Clinical perspective"* (Petros Tsantoulis, Switzerland), outlining future implications for clinical practice, and the session concluded with a lecture on *"Artificial intelligence"* (Niko Beerenwinkel, Switzerland). This stressed the importance of methodology, not only in light of the rapid growth in data volumes but also in their complexity, presenting examples of how artificial intelligence can help us understand ever more complex systems. The session concluded with a guided *"Visit of the genome center"* (Manolis E Dermitzakis, Switzerland) at the Health 2030 Geneva Genome Center, which

is the genomic medicine arm of the Health 2030 initiative for Swiss personalized medicine. During the tour, the participants had the opportunity to see the sample processing, equipment and data analysis workflow of a modern genomic facility.

Statistics/experimental design (Chairs: Urs A Meyer, Sanja Stanković)

The morning session of the third day on statistic and experimental design was an extension of the preceding clinical bioinformatics session. The aim of this session was to introduce concepts of *"Digital Epidemiology and Big Data"* (Marcel Salathé, Switzerland), but more importantly, less-discussed machine-learning algorithms were presented, followed by a discussion of how they may impact the field of medicine. Next, the problems surrounding current experimental designs were addressed in detail in three lectures: *"Evidence in personalised medicine: has correlation made experimental design obsolete?"* (Marcel Zwahlen, Switzerland), *"Randomized Real-World Evidence"* (Lars Hemkens, Switzerland) and *"Experimental design for 'omics' studies"* (Ursula Amstutz, Switzerland). In the first lecture, the drawbacks of correlational design were highlighted, using examples of the limitations to current artificial intelligence algorithms for providing causal explanations. The second lecture focused on the big and routinely collected data providing decision-making support for healthcare and health policies. The session concluded with a lecture addressing the issues of good experimental design, particularly those, important for avoiding bias or reducing confounding effects.

Group work (Chairs: Janja Marc, Vangelis G Manolopoulos)

A new concept was introduced to this year's summer school, involving small-group work encouraging students to address their research questions in a more personal, interactive and informal manner. Eight different topics, covering a wide range of subjects, were provided to the participants to work on:

Personalized aging: how to personalize osteoporosis prevention, diagnostics and treatment (Janja Marc, Slovenia);
Precision medicine bioinformatics – connecting diseases, drugs and genes (computer-aided seminar) (Csilla Sipeky, Finland);

How to implement pharmacogenetic testing in clinical practice – the cases of *DPYD* and *UGT1A1* (Mario Pazzagli, Italy);

Pre-emptive pharmacogenomic testing: case study of a workflow from sample to result (Peter Jacobs, The Netherlands);

In silico analyses of DNA–protein, DNA–drug and DNA–DNA interactions – an approach to aid experimental design (Uppugunduri CR Satyanarayana, Switzerland);

Pharmacogenomics–phenotype association: antiplatelet therapy in acute coronary syndrome (Sanja Stanković, Serbia);

Good practices of gene testing in personalized medicine for breast cancer patients (Monica Miozzo, Italy);

Personalized medicine in the diagnostics and monitoring of leukemia (Helena Podgornik, Slovenia).

Group work aimed to address different research problems through the literature searches and the use of computer-aided tools. Each group had 1 day to prepare their topic for presentation at the end of the school. After the presentations, a nominated scientific awards committee presented the travel award, the *"Gérard Siest award"* for the best group-work presentation (group of Uppugunduri CR Satyanarayana, Switzerland), and the best poster award (Fabienne Meier-Abt – *"Transcriptome-Proteome Correlation in Human Hematopoietic Stem and Progenitor Cells"* and Anida Causevic-Ramosevac – *"Association of FTO and GALNT2 Genetic Variants with Type 2 Diabetes-Related Traits in Population from Bosnia and Herzegovina"*).

Biobanking (Chairs: Ursula Amstutz, Ron H van Schaik)

With an ever-increasing array of possibilities with which to analyze biological samples, comes the concurrent need for large number of biological samples and increased quality management. The session on biobanking was designed to give a comprehensive overview of biobanking concepts within the lecture entitled *"Potential and challenges of Biobanks"* (Vincent Mooser, Christine Currat, Switzerland). The session continued with a presentation on the *"Ethical implications related to Biobanking & big data"* (Alessandro Blasimme, Switzerland), with particular weight being put on issues surrounding data sharing, donor's rights to control information about themselves and appropriate forms of governance and oversight for research activities using big data and artificial intelligence. The morning session of the final day concluded with a presentation on the *"Health Economics of Personalised Health"* (Thomas Szucs, Switzerland). Participants were introduced to the basic concepts of health economics and efforts

to position the role of personalized medicine at its core. Subsequently, several case studies involving personalized medicine were examined, concluding the lecture by demonstrating how the concept of personalized medicine and PGx can help to control the increasing costs of healthcare.

Pharmacogenomics (Chairs: Janja Marc, Vangelis G Manolopoulos)

The lecture on "*Cardiovascular Pharmacogenomics*" (Vangelis G Manolopoulos, Greece) was used to discuss the main general concepts of PGx through well-studied examples of the drugs used to treat cardiovascular conditions. In addition, some examples of study designs and useful approaches to address the hereditary components of drug metabolism were presented. The lecture concluded with a discussion of how to overcome obstacles to the implementation of current PGx knowledge in clinical protocols.

Closing unifying lecture (Marc A Rubin)

The summer school was concluded by the closing keynote lecture "*Precision Health Care: Connecting the patient to a global genomic community*" (Marc A Rubin, Switzerland) summarizing major messages for participants. Within the lecture, Prof Marc A Rubin reiterated the main concept and stressed major conclusions of the summer school, the need for further development of precision medicine. The lecture focused on other successfully delivered messages during the summer school: the challenges associated with the development of new methods in precision medicine and the new methodologies with which to overcome some of them. The summer school ended by general agreement regarding the need for collaboration and data sharing, by presenting many examples of joint, nationwide projects in Switzerland in order to demonstrate how collaboration facilitates solutions and new findings for precision medicine.

The ESPT summer school was followed by the joint Federation of European Academies of Medicine (FEAM) and Swiss Academy of Medical Sciences (SAMS) conference, to which all the ESPT summer school participants were invited.

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