Abstract: The aim of Personalized Medicine in disease treatment and prevention is to take account of the individual variability in genes, environment and lifestyle for each person. This approach is applied to certain tumours but is still not common for most diseases. On June 18, 2015 the TEDD network (Tissue Engineering for Drug Development and Substance Testing) invited a total of 130 academic and industrial partners to Waedenswil to exchange ideas and discuss promising approaches.

Keywords: Personalized medicine · TEDD

Why don’t we tailor medical therapies to the individual characteristics of each patient and take advantage of our knowledge about a person’s unique molecular and genetic makeup that makes him or her vulnerable to certain diseases? As a result, we could better assess which medical treatments are safe and effective in a particular case of illness. In the scope of the 7th Waedenswil Day of Chemistry, the TEDD network wanted to highlight the potential of Personalized or Precision Medicine.

Joint Effort Crucial to Success

Professor Niko Beerenwinkel, a computational biologist trained at the Max Planck Institute for Informatics, joined the Department of Biosystems Science and Engineering of ETH Zurich in 2007. From his point of view, personalized medicine involves the integration of information about a patient’s genome with clinical and pathobiological characteristics as well as environmental and lifestyle parameters. “Driven by tremendous technological advances in genomics, most notably in DNA sequencing, the goal of personalized medicine is to design individually tailored therapies and preventive measures”, explains the former postdoctoral researcher at UC Berkeley. This new approach is designed to routinely take into account large-scale constitutional genomic information for an individual patient, including somatic genetic alterations and molecular signatures of pathogenic agents, in order to specifically and effectively target a molecularly defined disease while minimizing the chances of adverse events. He is convinced that “the implementation of personalized medicine represents an extraordinary challenge for scientists, engineers, health care providers and the diagnostic and pharmaceutical industry”. “Research in this domain is highly interdisciplinary and includes clinical research, molecular biology and statistical
Diagnostic Tools Reveal Molecular Origin

The medical need for a more patient-tailored approach has resulted in a greater number of targeted therapies focused on better defined patient groups. Within the past few years Roche has embarked on a systematic approach for the development of medicines, interweaving diagnostic and pharmaceutical expertise to pave the way for Personalized Healthcare (PHC). “We have already begun to provide healthcare professionals with more powerful diagnostic tools and targeted treatments that are based upon new insights into how disease arises at the molecular level”, explains Dr. Bruce W. M. Jordan, Business Development Manager at Roche Diagnostics International Ltd. “Up until now, this has happened mostly in the fields of oncology and virology, and new developments will address equally high areas of unmet medical need such as asthma and Alzheimer’s disease.” One focus is on advancing our understanding of the molecular basis of asthma. This may, at least in part, explain the heterogeneity observed in the response to medication. For patients with this disease – in whom exacerbations can still be life-threatening – laboratory testing also has the potential to allow the tailoring of treatment based on individual characteristics, and to improve overall treatment success.

Alzheimer’s disease is a serious burden on patients and society as the overall population ages. The identification of reliable biomarkers of AD has, therefore, become increasingly important, not only for risk prediction and diagnosis in order to provide appropriate care, but also to identify those patients who could be eligible for inclusion in clinical trials of novel therapies being tested at the early stages of the disease when treatments may potentially yield the greatest benefits.

“Is it clear that the growing number of game-changing targeted therapies in development will require ever more innovative diagnostic tools to guide their use”, points out Bruce Jordan. “Their limited number of PHC approaches suggests that there are still many challenges, as well as opportunities in this emerging field of medicine. “

www.roche-diagnostics.ch

Gene Therapy for the Eye: The Target AMD Project

Eye diseases are particularly suitable targets for gene therapy because the eye is easily accessible and treatment effectiveness is readily measurable. Moreover the eye is immune privileged. During the last few years, using virally mediated gene delivery, gene therapy has been successfully applied to the treatment of inherited Retinitis Pigmentosa, for example. One report has also shown that the virally-mediated delivery of the PEDF (pigment-epithelium derived factor) gene intravitreally inhibits choroidal neovascularization (CNV) in neovascular Age-Related Macular Degeneration (AMD) patients. PEDF is a potent inhibitor of VEGF (vascular endothelium growth factor), which is responsible for CNV.

With the EU-funded Target AMD project (AMD = age related macular degeneration), involving 13 partners and seven countries, the consortium plans to transplant PEDF-transfected cells to the subretinal space of neovascular AMD patients. To safely transflect pigment epithelial cells, Target AMD will use transposon-mediated gene delivery using pFAR4 plasmids. “Specifically, retinal and iris pigment epithelial cells will be transfected with the PEDF gene using the enhanced Sleeping-Beauty (SB100X) transposon system”, explains biologist Dr. Martina Kropp of the Department of Ophthalmology of the University Hospitals of Geneva, and a participant in this EU project. “The latter integrates the gene into the host cell’s genome and provides a safe and efficient alternative to viral systems.” The use of pFAR4 miniplasmids will further increase the safety and quality of gene integration. With the proposed Phase Ib/Ila clinical trials in Target AMD with the harvesting, transfection and transplantation of autologous cells during a single surgical session, the consortium would implement the first European clinical trials using the SB100X transposon system in humans. “In vitro studies in our laboratories have demonstrated long-term PEDF gene expression and protein secretion by SB100X-mediated transfection and, during in vivo studies with animal models of neovascularization, the transplantation of PEDF-transfected cells reduced neovascularization significantly”, concludes Martina Kropp.

http://www.hug-ge.ch/ophtalmologie
www.targetamd.eu
How to Model Cancer Progression

Professor Gerald Schwank of the Institute for Molecular Health Sciences of the ETH Zurich, ranks as a pioneer in stem cell research and was the first person to repair a genetic defect present in the lung disease cystic fibrosis. He focuses on diseases where regulatory mechanisms are disturbed. In a research study with the University of Cambridge and the University Medical Center Utrecht he is developing a method to expand human intestinal stem cells in culture over long periods as genetically and phenotypically stable three-dimensional epithelial organoids. These so-called ‘miniguts’ comprise nearly intact physiology and consist of all major intestinal cell types, including Lgr5 positive stem cells. “We used the CRISPR/Cas9 system for genome editing in organoids”, he explains. “The system allowed us to introduce tumour driver mutations into organoids to model cancer progression and to functionally repair disease-causing alleles such as CFTR mutations in organoids derived from disease modelling and gene therapy by CRISPR/Cas9 genome-editing in stem cell organoids.” This research work contributes to the advancement of regenerative and personalized medicine and its use in the three-dimensional reconstruction of cellular structures, especially in the field of embryonic and tumour stem cell research.

http://www.mhs.biol.ethz.ch/research/schwank.html

The Swiss Platform for Personalized Medicine

“Tonight, I’m launching a new Precision Medicine Initiative to bring us closer to curing diseases like cancer and diabetes – and to give all of us access to the personalized information we need to keep ourselves and our families healthier.” This was the statement issued by President Barack Obama in his State of the Union Address on January 20, 2015. The project is backed up with passion by Francis S. Collins, Director of the National Institutes of Health (NIH). It is currently funded to the tune of US$ 215 million. Europe is also preparing for the future with Horizon 2020, the biggest EU Research and Innovation programme ever, with nearly EUR 80 billion of funding available from 2014 to 2020 – in addition to the private investment that this money will attract. From introducing safe and effective innovative treatments in multidisciplinary standard care, we expect more breakthroughs, discoveries and world-firsts by taking great ideas from the lab to the market.

In Switzerland, the international Competence Centre TEDD – Tissue Engineering for Drug Development and Substance Testing – provides the ideal platform where innovative technologies for personalized medicine can be developed and translated into pioneering technology leaps on the international markets. As an example, close cooperation exists between the applied and pre-clinical research of Professor Dr. Ursula Graf-Hausner, Head of the TEDD network at the Zurich University of Applied Sciences (ZHAW), and Professor Dr. Bruno Fuchs, Head of Tumor Surgery and Research at the University Hospital Balgrist and Head of the Sarcoma Center Zurich (www.sarkomzentrum.ch). The common objective is to develop reliable and robust in vitro 3D micro-tissue models to improve the current standard treatment of osteosarcoma patients, based on the drug sensitivity of patient-derived material obtained at initial diagnostic biopsy. Osteosarcoma is a severe, but rare, bone cancer that is still associated with poor outcome in the event of metastasis formation. The search for new drugs that efficiently disrupt metastasis is therefore essential. Both research institutions evaluate scaffold-free 3D cell culture platforms to produce reliable and reproducible micro-tissues from osteosarcoma cell lines for drug assessment. Potential in vitro evaluated drugs will be tested in orthotopic osteosarcoma mouse models to assess their in vivo efficacy. The use of primary patient-derived material for micro-tissue production will further foster personalized medicine.

www.icbc.zhaw.ch/tedd

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