

The Sartorius Research Xchange Forum 2017:

Trends and Challenges in Oncology

Goettingen, May 2017 – With checkpoint inhibitors, gene therapies and other cancer immunotherapies, the medical field has notched up successes in the recent past that were inconceivable just a few years ago. These advances were made possible only by the close collaboration between academic research at universities and university spinoffs on the one hand and between the pharmaceutical and biotech industry on the other.

The objective of the Research Xchange Forum, a series of conferences hosted by the international pharmaceutical and laboratory equipment supplier Sartorius, is to improve this transfer of knowledge from basic research to applied research and all the way to implementation in industrial manufacture and, ultimately, to translation into marketable products. The theme of the two-day event held at the end of February at Sartorius College of its Group headquarters in Goettingen, Germany, was "Trends and Challenges in Oncology."

At the focus of the Forum were new approaches and options offered by innovative therapy concepts to patients and doctors alike and also to companies in the biotech and pharmaceutical industry. As a consequence, key areas covered by the conference were gene therapies and cancer treatments using monoclonal antibodies, DNA repair mechanisms, innovative approaches for drug delivery and targeted release of active pharmaceutical ingredients, as well as the search for new biomarkers for cancer diagnosis and research on cancer stem cells.

"The discovery and development of new therapeutics is an enduring, complex and laborious procedure. As a biopharma and laboratory supplier, we are well aware of the challenges of translating research findings into clinical practice," stated Karen Storm, Vice President of Marketing in the Lab Products & Services Division at Sartorius. This year's Research Xchange Forum offered attendees from academic research, biotech start-ups and the biopharmaceutical industry a platform to exchange information and new ideas in and around oncology and cancer research. "With new innovative bioanalytical tools and turnkey solutions, our aim is to enable advancements in exactly these fields and help scientists find faster answers to fundamental biological questions", continued Storm.

Twelve internationally recognized scientists engaged in academic research and in industry, provided insights into their lectures and their current studies as well as a comprehensive overview of the progress made in cancer research. Researchers with practical experience in process technology and scientific transfer described strategies on how knowledge and methods developed in the lab can be quickly scaled up from the laboratory level to pilot or commercial scale and how the implementation of new procedures can be successfully translated into marketable therapies and manufacturing processes. During these lectures, it became clear that completely new cancer treatments are likely to be approved and therefore used in clinics.

At the beginning of the conference, Dr. Lothar Germeroth of Juno Therapeutics reported on the advances made using CAR T-cell therapy to combat various types of cancer. He described how such highly individualized gene therapy methods can be implemented in commercial-scale manufacture rapidly, safely and economically. This was also the direction taken by Dr. Henrieta Fraser's lecture, which provided detailed information on the challenges posed by commercial T-cell expansion under GMP conditions. This scientist, who tests and optimizes biotech manufacturing processes at the British company, Catapult, described the advantages and drawbacks of various culture methods.

Dr. Nicola M.G. Smith of the British firm, Immunocore, showed that so-called ImmTACTM molecules could be available in the future as a breakthrough cancer treatment approach. Her company currently uses ImmTACTMs (Immune mobilizing monoclonal TCRs Against Cancer) to develop soluble T-cell receptors, which as cancer therapeutics of the future, are engineered to make completely new target antigens accessible. Dr. Jamel Chargui of Innate Pharma based in Marseille, France, presented on new checkpoint inhibitors that are currently in the clinical testing phase. With lirilumab, monalizumab and other monoclonal antibodies, Innate Pharma has many promising cancer drug candidates in the pipeline for checkpoint inhibition of the immune checkpoint receptors on the surface of natural killer cells. Such candidates as Chargui, impressively demonstrated positive results based on clinical data. These new targets also showed promise of new treatment approaches.

Professor Dr. Maja Köhn revealed the key role that phosphatase PRL-3 plays in the genesis of epithelial tumors. This role makes this enzyme very promising as a target molecule in the treatment of colorectal cancer, for instance. Using data obtained on 3D cell cultures, this research scientist from the University of Freiburg impressively demonstrated the essential role that PRL-3-phosphatase plays in tumorigenesis. In his lecture, Professor Matthias Döbelstein, Dr. rer. med., from the Göttingen Center for Molecular Biosciences (GZMB), shed new light on the tumor suppressor p53, a gene that codes for a protein that regulates the cell cycle. This cancer researcher not only described how the p53 protein as a transcription factor eliminates body cells that have suffered DNA damage, but also showed how the p53 protein together with the Mdm2 protein ensures the integrity of the genetic material DNA and the stability of chromatin.

How can active molecules of a cancer drug delivery system be transported to and directly released at the site of or within tumorous tissue cells to ensure the bioactive efficacy of such molecules? This was the question that Dr. Laurent Sagalowicz and Zaki Sellam explored in their lectures. Laurent Sagalowicz described the potential of so-called "cubosomes" for delivery and targeted release of active molecules of cancer drugs directly at the site of or inside a tumor. The delivery system expert at the Swiss Nestlé Group, Sagalowicz explained how the stability of "cubosomes", which are self-assembled structures stabilized by ligands, can be influenced so that cancer drugs can be delivered and released depending on the environmental conditions.

Zaki Sellam, also from Switzerland, presented the concept of Antibody Drug Conjugates, ADCs, for cancer treatment. ADCs can be used to deliver and release a chemotherapeutic directly at the site of or inside tumor tissue, which is bound to tremendously improve the side effect profile of cytotoxic drugs, according to the founder and CEO of Avicenna Oncology. More than 70 of such ADCs are already undergoing clinical trials, and numerous other combinations of antibodies, active molecules and linkers are conceivable.

The "umbrella" diagnosis of intrahepatic cholangiocarcinoma currently leaves much to be desired, as Dr. Jesper B. Andersen distinctly stated. An associate professor of the University of Copenhagen, Andersen clearly advocated differential diagnosis of cholangiocarcinoma to be able to offer patients more precision-based therapies. The mutation-dependent markers required for such treatment options are available, as Jesper B. Andersen pointed out. Dr. Ondrej Slaby addressed the significance of non-coding RNAs, called ncRNAs, for regulation of cell metabolism. Together with his research group at the Czech Central European Institute of Technology (CEITEC), Associate Professor Dr. Slaby is also working on methods that enable ncRNAs to be used as biomarkers for cancer diagnosis and as target molecules for future cancer treatment approaches.

Dr. Thordur Oskarsson of the German Cancer Research Center (DKFZ) in Heidelberg, Germany, very impressively described how breast cancer tumors are able to metastasize. According to Dr. Oskarsson, disseminated cancer stem cells use a special extracellular matrix to create their own microenvironment which promotes metastatic colonization. It is important to consider such findings to effectively prevent breast cancer progression and metastatic relapse.

Towards the end of the Research Xchange Forum, the presentations moved from theory to tangible and practical processes when Dr. Alex Chatel introduced the ultra scale-down approach to process design. This method permits industrial-scale simulation of biologics, for instance, in the production of monoclonal antibodies according to Dr. Chatel, a translational research manager from the University College London (UCL). Based on data obtained from ultra scale-down studies, the bioprocessing technology required for production, concentration and purification of new therapeutic candidates can be predicted early; selected and optimized.

The participants of the forum repeatedly discussed the key question of how transfer of knowledge from basic research to commercial-scale production can be improved and thus applied to clinical use and to therapy of patients. Professor Dr. Kilian Bizer of the Innovation Campus of Lower Saxony (SNIC), Dr. Lothar Germeroth and Associate Professor Dr. Jesper B. Andersen, among others, were available at the podium discussion to deliver answers and explanations. During this discussion moderated by Dr. Reinhard Baumfalk, Vice President of R&D Instrumentation & Control at Sartorius, it became clear in the controversial approaches taken that transfer of knowledge and technology is not only a technical, legal or economical issue. Rather, translating research findings into clinical trials and commercial-scale manufacture is also a challenge facing society. According to the podium group, the public needs to be intensively educated to gain their acceptance of innovative procedures and complicated, expensive research. After all, basic research serving as the bedrock for new

cancer treatments is primarily financed by taxes. In the end, all agreed on one point: more intensive communication and a regular exchange of information constitute the basis for the success of such endeavors.

For details on the content discussed and lectures held, click on:

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