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Speaker’s Abstract

Model Systems for Human Health – Opportunities, Limits, Perspectives

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“Translational medicine” aims at developing discoveries of novel disease mechanisms and targets toward new therapies, which can be applied in the clinic. This pathway “from bench to bedside” is a long, often inefficient and costly process. Appropriate animal models that faithfully predict the efficacy and safety of new treatment strategies are critical for the success of translational biomedical research. Although rodent models are widely used, they often do not accurately represent human disease mechanisms and/or phenotypes. Efficient and precise technologies for genetic engineering are now available for tailoring pigs to represent human disease mechanisms on the functional and/or molecular level. These technologies include the use of lentiviral vectors, transposon-based systems, somatic cell clear transfer from genetically modified donor cells, and gen(om)e editing using site-specific nucleases such as CRISPR/Cas. We generated several genetically tailored pig models for diabetes research, including a model with impaired incretin function and a model of permanent neonatal diabetes. These models were used to screen for biomarkers associated with disease progression and for treatment trials with incretin therapies. Furthermore, these pigs may provide new insights into organ crosstalk during the development of secondary complications of diabetes. In addition, we generated tailored pig models for monogenic disease, such as Duchenne muscular dystrophy and cystic fibrosis, which mimic the human disease phenotypes more closely than the corresponding mouse models. Genetically engineered pigs as donors of cells, tissues and organs for xenotransplantation are another topic, which developed rapidly during the past few years and yielded remarkable progress in preclinical islet and heart transplantation programs. Genetically tailored pigs have to potential to bridge the gap between basic research in rodent models and clinical trials with human patients. Future options and perspectives of genetically engineered pig models provided by new research networks such as COST Action BM1308 “Sharing Advances on Large Animal Models – SALAAM” will be discussed.