Bavarian Research Network: Induced Pluripotent Stem Cells (ForIPS)

Speaker
Prof. Dr. med. Jürgen Winkler

Address
Division of Molecular Neurology
Schwabachanlage 6
91054 Erlangen
Phone: +49 9131 8539324
Fax: +49 9131 8534672
juergen.winkler@uk-erlangen.de
www.forips.med.fau.de/?lang=en

Aims and structure

The Bavarian Research Network ForIPS was funded by the Bavarian State Ministry of Education, Science, and the Arts from 2013 – 2017 with almost four million euros and had the major and long-term goal to establish human cellular disease models and novel intervention strategies for sporadic and chronic disorders of the brain with its current focus on sporadic Parkinson's disease (PD). The first task of the ForIPS consortium was to establish a biobank for human induced pluripotent stem cells (IPSC) of PD patients and healthy controls at UK Erlangen including the implementation of important quality controls in terms of genomic and transcriptional stability as well as the development of non-integrating reprogramming strategies. Reprogramming of mature cells of the body into so called IPSC represents one of the most innovative biomedical developments in recent years (Nobel Prize in Medicine, 2012). Using this technology, connective tissue cells of patients were obtained and reprogrammed to the stage of pluripotency. As a result, patient specific stem cells were generated and in the framework of ForIPS further differentiated to neurons. Using this technology, ForIPS was able to generate IPS-derived neurons from affected patients. These cells may serve as an ideal cellular model for the analysis of individual disease mechanisms, in particular with regard to the individually underlying pathogenesis of the patient, thus enabling the development of novel treatment strategies.

Research

ForIPS focused on the most prevalent neurodegenerative movement disorders of Western industrial countries, the sporadic PD, first described by James Parkinson in 1817. This disorder is characterized by specific motor deficits, such as bradykinesia, rigidity, and resting tremor. Throughout the disease course, in particular, however, in the premotor stage, nonmotor symptoms such as hyposmia, autonomic dysfunction, disturbed gut mobility, and cognitive deficits are observed. The goal of the ForIPS network was, based on PD-derived cells, to characterize the molecular and cellular mechanisms, which are crucial for the etiology of the disease. To this aim, ForIPS provided the individual projects with primary skin fibroblasts or with IPSC. The projects headed by Prof. Dr. A. Reis (Institute of Human Genetics) and Prof. Dr. M. J. Riemenschneider (UK Regensburg) were analyzing the genetic and epigenetic stability and alteration of IPSC and its cellular derivatives. The scientific questions of other projects were covering in particular functional studies on neural cells and focusing on neuronal compartments such as neurites and synapses Prof. Dr. J.H. Brandstätter (Chair of Animal Physiology, Faculty of Sciences), Prof. Dr. J. Winkler (Division of Molecular Neurology), on intracellular organelles such as mitochondria Dr. D. Vogt-Weisenhorn, Prof. Dr. W. Wurst (TU Munich), on intraneuronal mechanisms such as autophagy Prof. Dr. J. Klucken (Division of Molecular Neurology), Prof. Dr. D.C. Lie (Professorship of Molecular Medicine with focus on Molecular Imaging) as well as on proteins such as TAU Dr. S. Schwarz, Prof. Dr. G.U. Höglinger (TU Munich). In addition, the project of Prof. Dr. M. Wegner (Chair of Biochemistry and Pathobiochemistry) was focusing on the generation of enteric nervous tissue, in particular in the light that the gut may be one of the first sites for the onset of PD. The functional assessment of astrocytes, underlying specific Parkinson-associated neurodegenerative processes, was examined by Prof. Dr. M. Götz (LMU Munich). The inflammatory interplay between neuronal and glial cells was the major task the ForIPS project of Dr. I Prots and Prof. Dr. B. Winner (Division of Stem Cell Biology), whereas Prof. Dr. F. Edenhofer (JMU Würzburg) aimed at developing transgene-free reprogramming strategies and at studying age-dependent processes in cell culture models of PD. Furthermore, in situ reprogramming strategies of pericytes and the differentiation of IPS to specific striatal interneurons were developed in the project of Dr. M. Karow (LMU Munich) and Prof. Dr. B. Berninger (JGU Mainz). Based on the common source of patient-derived cells, there was a high interaction within the research network; furthermore a long-lasting biobank of IPS with its cellular derivatives was established at UK Erlangen. Novel technologies in life sciences, such as the IPSC-technology, are positioned in our society and raise important ethical questions, which were covered by two projects in particular focusing on the internal and public discussion as well as on aspects of biopatenting and commercialization (PD Dr. A. Manzeschke, TTN Munich, Prof. Dr. P. Dabrock, Faculty of Humanities, Social Sciences, and Theology).

Teaching

The research network ForIPS, coordinated by Dr. R. Lederer together with the administrative assistance of J. Burczyk-Schuster (Division of Molecular Neurology), was undergoing large efforts in activities for the education and training of young undergraduates, graduate students, as well as postdoctoral fellows. By offering seminars at UK Erlangen, the participating scientists were enabled to learn the technology of human IPSC, thus standardizing the cell culture models and transferring this technology to all other Bavarian sites. In addition, two PhD seminars with different topics in stem cell biology and neurodegeneration took place as well as an international symposium and a public hearing with the topic "Human biobanking for stem cell research".