



Marie Curie Host Fellowships for Early Stage Research Training:

Interdisciplinary, international PhD-program of the
Center for Systems Neuroscience Hannover
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Project No 6:

Genetically modified dopaminergic progenitor cells – morphometrical and functional evaluation after intrastriatal transplantation in the rat model of Parkinson´s disease

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Goal of this project is the growth factor-mediated increase of the survival of dopaminergic neurons after transplantation and functional integration into the host striatum in the rat model of Parkinson´s disease.

Dopaminergic neurons are important regulators of motor control, behaviour, motivation, emotion, and cognition. In Parkinson´s disease (PD) progressive cell loss of these neurons in the substantia nigra leads to severe motor dysfunction. Exogenous cell replacement represents a possible new clinical therapy for late stages of PD. Stem cells are a promising cell source for grafting. Neuronal progenitor cells display not the disadvantages of embryonic cells like chromosomal aberrations, tumor formations, immunological problems, and ethically controversial discussions.

In our group, we establish the use neuronal progenitor cells as a standardized cell source in combination with neurotrophic factors which promote dopaminergic differentiation and stimulate survival of grafted cells. Work in the project includes cell culture, molecular biology, in vivo experiments in a rat model of PD, morphological and behavioural studies.

Grothe,C., Schulze,A., Semkova,I., Müller-Ostermeyer,F, Rege,A., Wewetzer,K.: The high molecular weight FGF-2 isoforms (21,000 mol.wt and 23,000 mol.wt) mediate neurotrophic activity on rat embryonic mesencephalic dopaminergic neurons in vitro. *Neuroscience* 100, 73-86, 2000.

Timmer,M., Kloth,V., Scholz,T., Winkler,C., **Grothe,C.CA***, Nikkhah,G.*: Enhanced functional recovery and reinnervation of intrastriatal dopamine-grafts co-transplanted with physiological Schwann cells over-expressing high molecular weight FGF-2 isoforms. *Exp. Neurol.* 187(1):118-36, 2004. CA Corresponding Author; * contributed equally.

Grothe,C., Timmer,M., Scholz,T., Winkler,C., Nikkhah,G., Claus,P., Itoh,N., Arenas,E.: Fibroblast growth factor-20 promotes the dopaminergic differentiation of Nurr1-overexpressing neural stem cells. *Neurobiol. Dis.* 17, 163-170, 2004.

Timmer,M., Großkreutz,J., Wesemann,M., Just,L., Cesnulevicius,K., Bufler,J., **Grothe,C.**: Dopaminergic properties and function after grafting of attached neural precursor cultures. Neurobiol. Dis., 2005 Oct 24; [Epub ahead of print].

K. Cesnulevicius*, M. Timmer, M. Wesemann and **C. Grothe**: Transfection of primary mesencephalic progenitors: efficient non-viral gene delivery in vitro. Submission in January.

The PhD-project will be embedded in the area of research 3 of the ZSN, restoration of neuronal functions in movement disorders.