

# Discovery of a Key Molecule for the Development of Dopaminergic Neurons

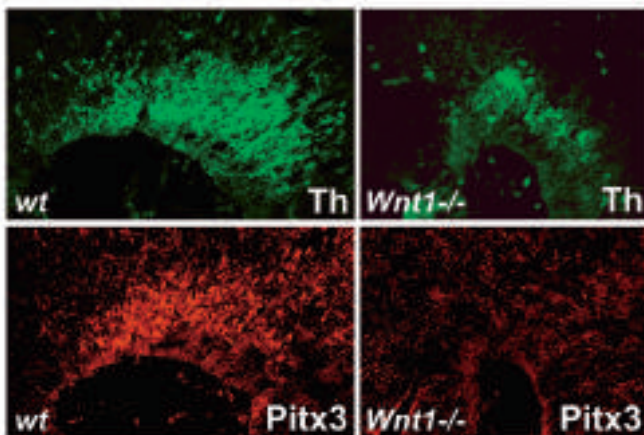
Institute of Developmental Genetics

**P**arkinson's Disease (PD) is the second most common neurodegenerative disease in elderly people. Treatment of PD is difficult and purely symptomatic. In light of the demographic development of our society, finding new and effective therapies for PD has become also of considerable economic relevance. One approach, for example, is the development of cell replacement therapies. To this end, the molecular cues underlying

the development of neuronal populations have to be unravelled. The hallmark of PD is the degeneration of neurons producing dopamine, a key neurotransmitter of the brain. Scientists at the GSF Institute of Developmental Genetics have now shown that the secreted glycoprotein Wnt1 is a key molecule for the development of precisely these neurons in the midbrain.

Wnt1 regulates a genetic network including two transcription

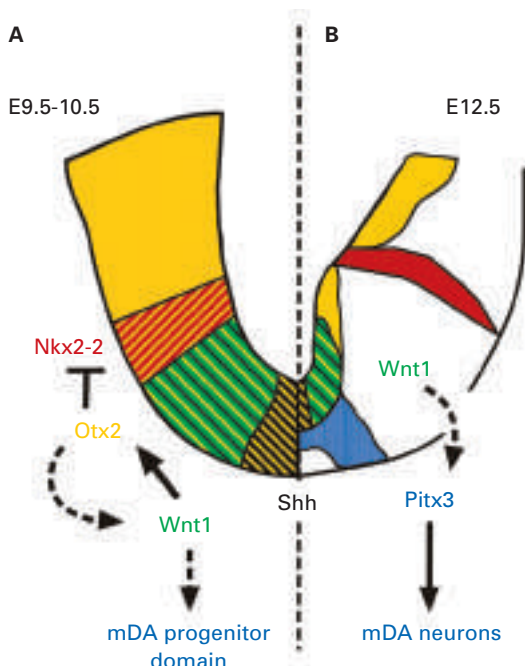
factors, which is essential for the establishment of the corresponding progenitor domain during embryonic development. Furthermore, Wnt1 appears to control the terminal differentiation of dopaminergic neurons in the midbrain at later stages of embryogenesis. These results suggest the signal transduction pathway controlled by Wnt1 to be a very promising target for novel therapeutic approaches in the treatment of PD. One approach would be, for example, the design of therapeutic 'small molecules' that can activate the Wnt1 signal transduction pathway in the adult brain and thereby promote the differentiation of neural stem cells into dopaminergic neurons.



By contrast to wild-type (*wt*) mice, *Wnt1*<sup>-/-</sup> (knock-out) mice lack the gene for *Wnt1*. Hence dopamine-synthesizing cells (green) do not differentiate correctly in these mice, i.e. they do not produce a crucial factor (*Pitx3*, red) required for their survival.

### Literature:

- Prakash, N. et al.: *Development* 133, 1:89-98 (2006)



Wnt1 controls the establishment of the midbrain dopaminergic progenitor domain during early embryonic development (A) and their differentiation into dopaminergic neurons at later stages (B).



Dr. Nilima Prakash

Institute of Developmental Genetics

Telephone +49-89/31 87-22 75  
nilima.prakash@gsf.de