



# Novel therapy for Parkinson's disease

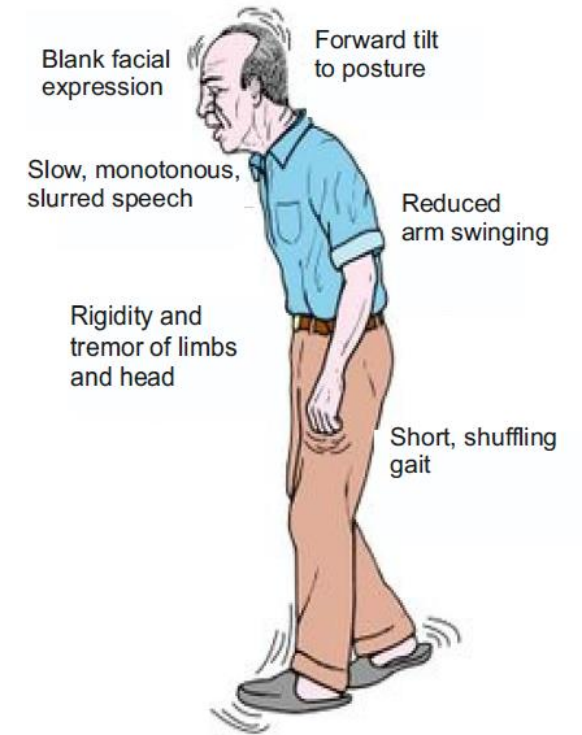
- Neuroprotection and neurorestoration -



BioFit Lille, November 2016

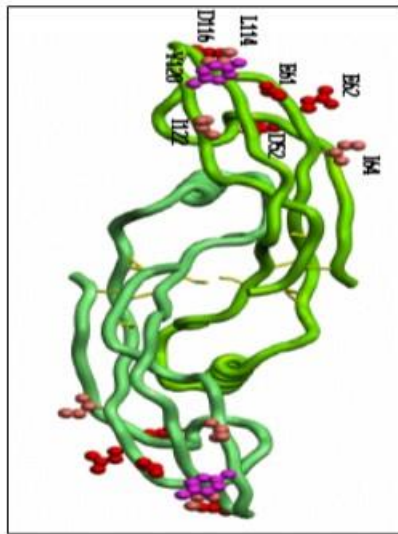
# Parkinson's challenge

- Progressive neurodegeneration of midbrain dopamine neurons
- 0.3% in total population ; 1% in population over 60
- In Europe ~ 1.2 million patients (2015)
- In Europe ~ 13.9B€ for direct and indirect costs
- 6-7 million patients worldwide; may double in 20 years
- Symptomatic relief is on the market but no cure
- Can this neurodegeneration be stopped?

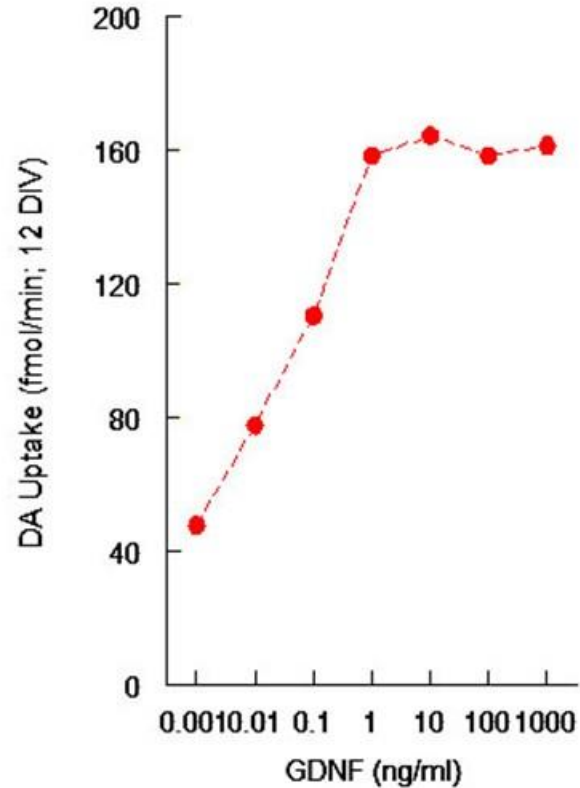


# Trophic support for dopamine in the brain

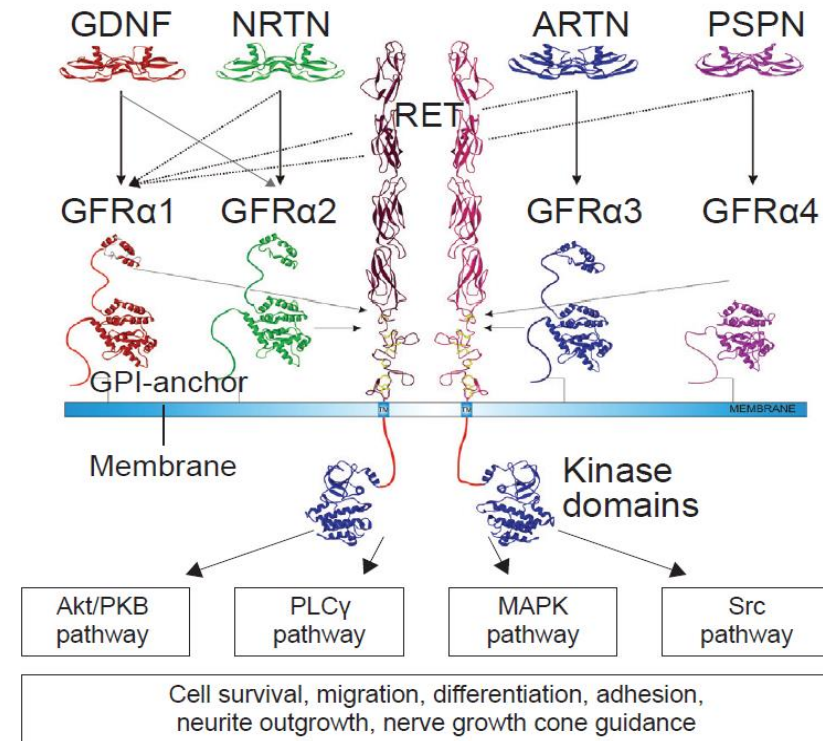
## GDNF Identification



Lin et al., 1994



## Its receptors



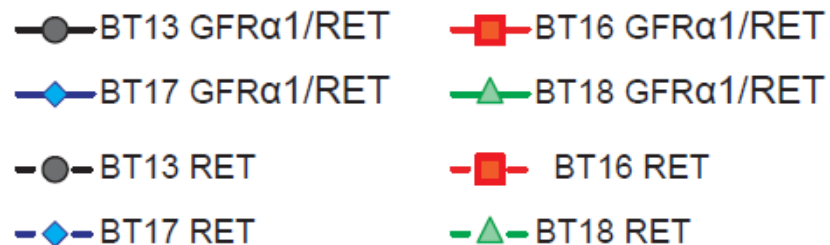
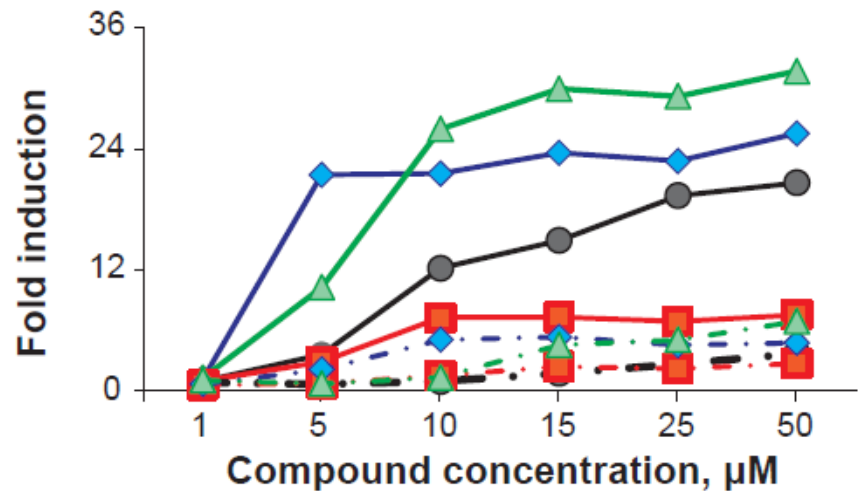
# Finding small molecule GDNF mimics

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- **GDNF receptors: a RET kinase moiety and a selectivity –determining part**
- **Agonist screens have been developed to detect GFR/RET receptor agonists**
  
- **18,000 compounds screened; 43 confirmed hits**
- **One series optimized. Best compounds GFLM1 and GFLM2**
- **Compounds are selective (CEREP screens)**
- **Granted patents (US, EU)**

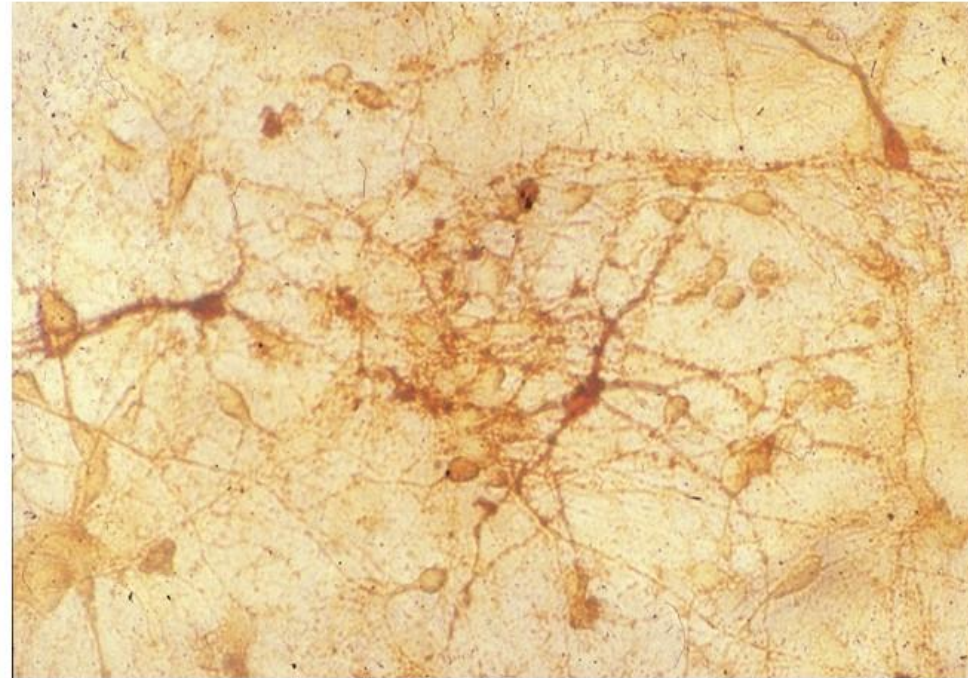
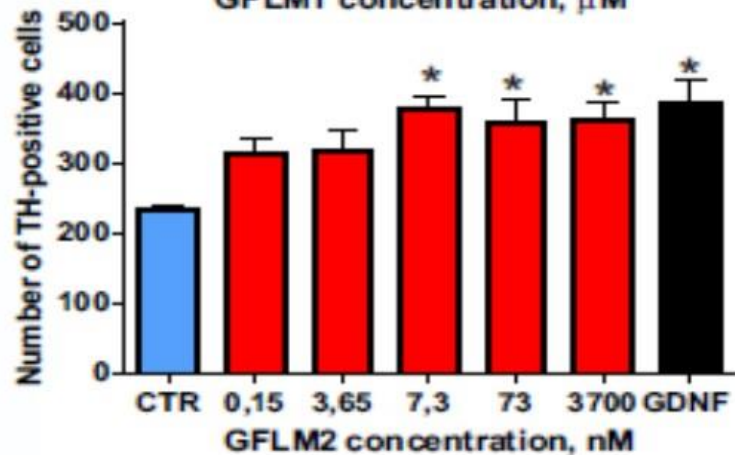
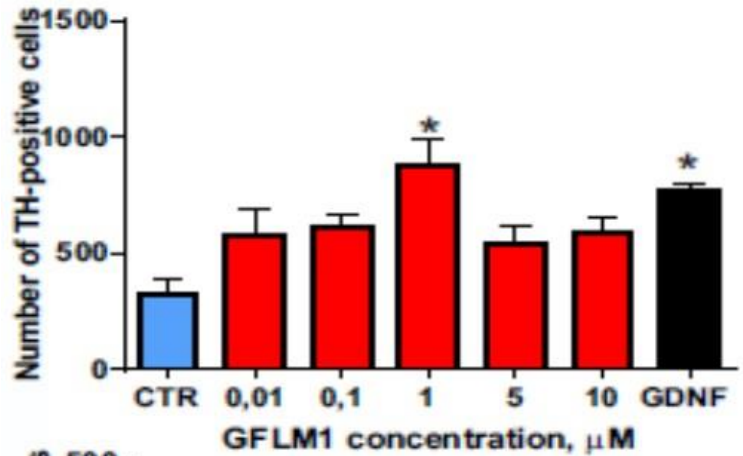
# Lead compound pharmacology

Screens with rec. GFR $\alpha$ 1 / RET



- Top selection suitably selective
- Lead compounds readily pass BBB (20%)
- Lead compounds stable in plasma
- Lead compounds are not cytotoxic
- Lead compounds are not very soluble

# Genecode's GDNF mimics exert trophic effects on dopaminergic neurons *in vitro*



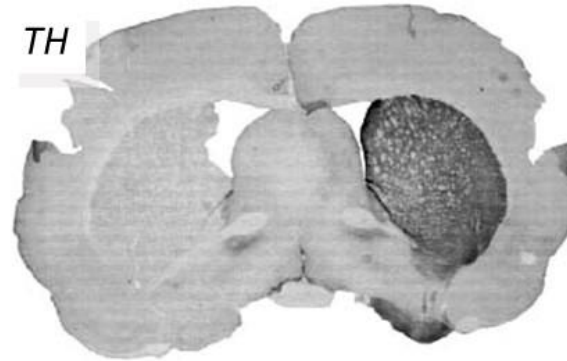
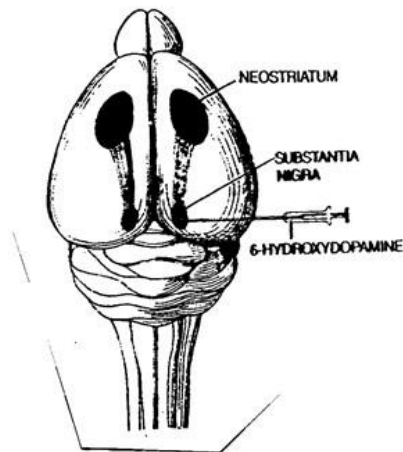
Rat E11 primary dopaminergic neuronal cell cultures stained for TH

# Degenerative animal model for Parkinson

Postsynaptically acting:  
contralateral turning



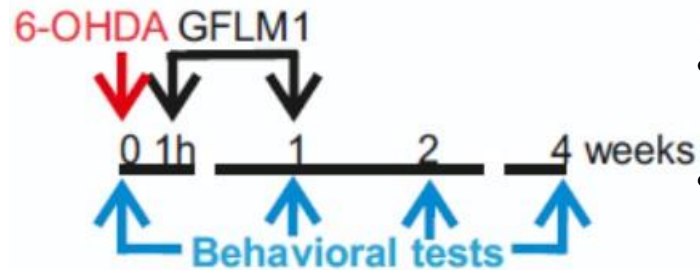
Presynaptically acting:  
ipsilateral turning



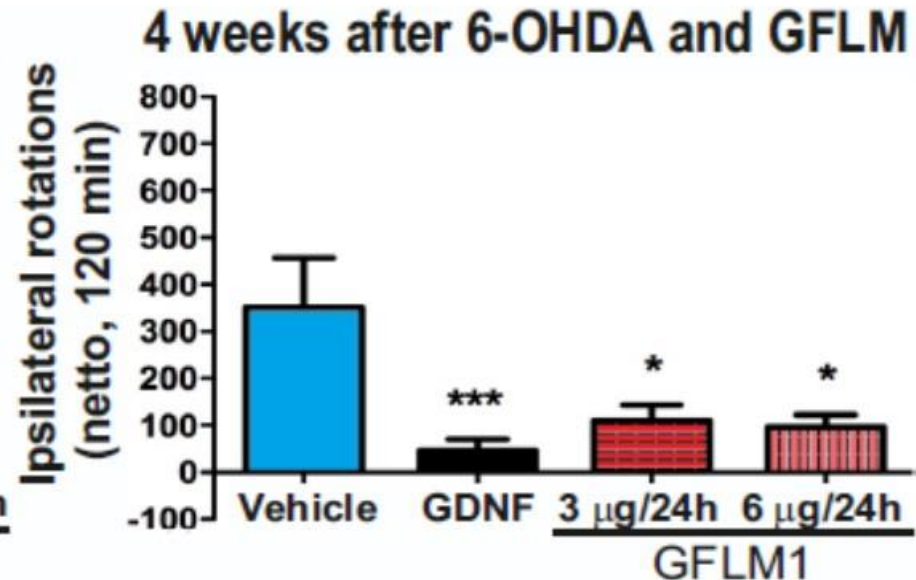
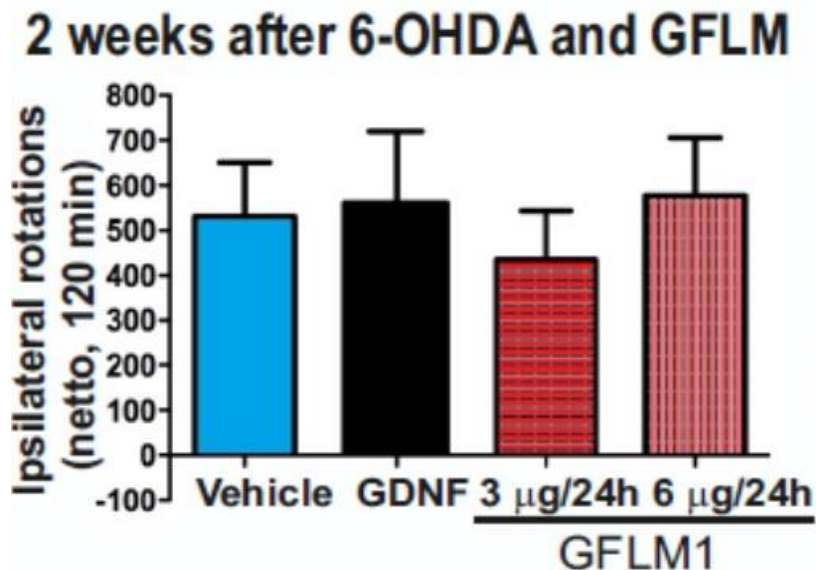
Selective unilateral loss  
of dopaminergic inner-vation of  
the striatum as revealed by  
immuno-cytochemistry.



# Neuroprotection and neurorestoration - I

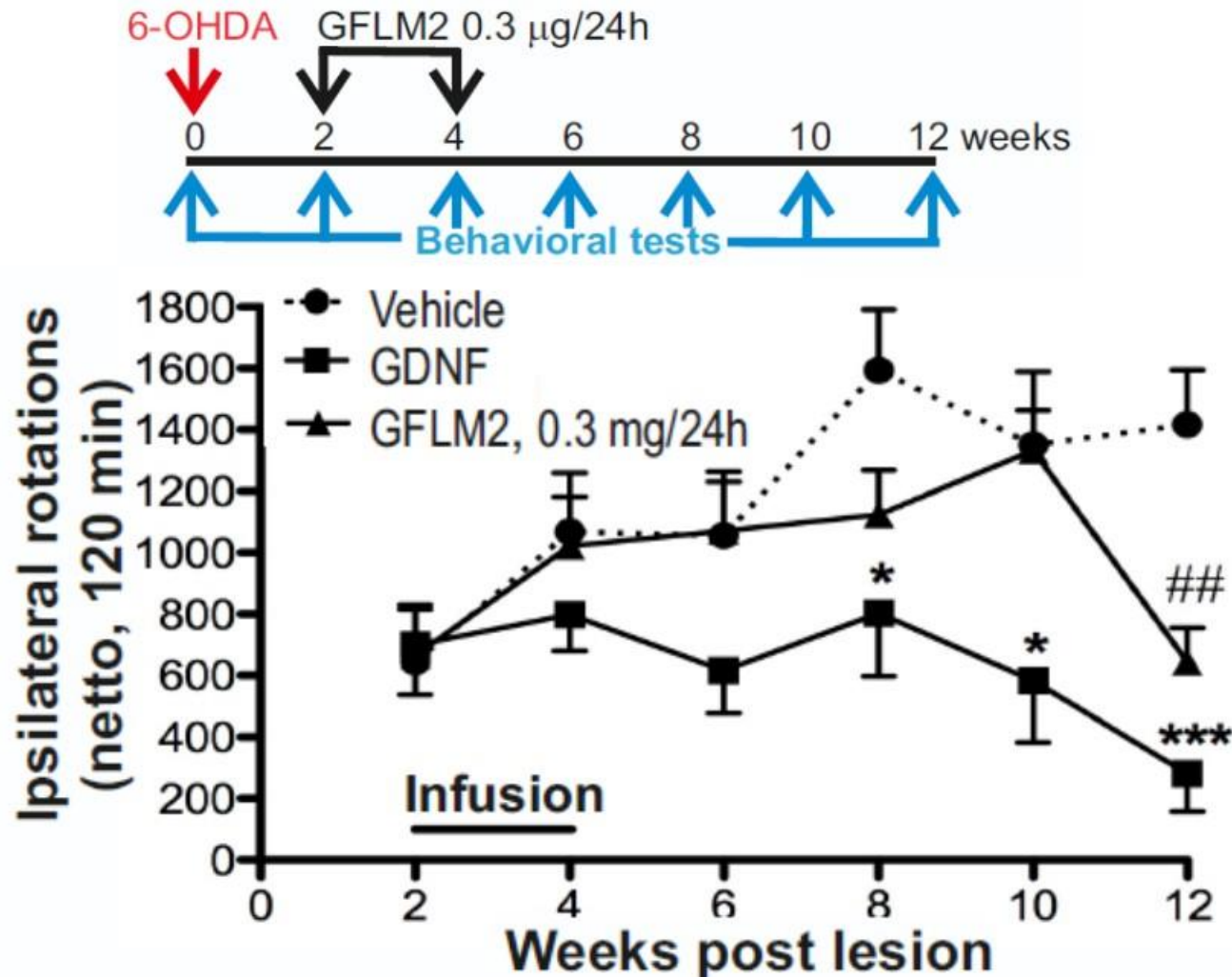


- Rotation behavior develops in unilateral 6-OHDA lesioned rats
- Small molecule GDNF mimics restore aberrant behavior to normal in 4 weeks time, similar to striatal GDNF injections





# Neuroprotection and neurorestoration - II



- Lead compound is active two weeks after lesioning
  - curbs asymmetry development
  - Normalizes rotation behavior
- Lead compound compares well with GDNF

# Genecode team

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## **Genecode management**

**Mehis Pilv, CEO**

**Piia Pilv, Chairman of the board**

**Eric Ronken, operations**

**Janika Leoste, communications**

## **Scientific board**

**Prof. Dr. Mati Karelson, Tartu university, Estonia**

**Prof. Dr. Mart Saarma, University of Helsinki, Finland**

**Dr. Yulia Sidorova, University of Helsinki, Finland**

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# Thank you

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