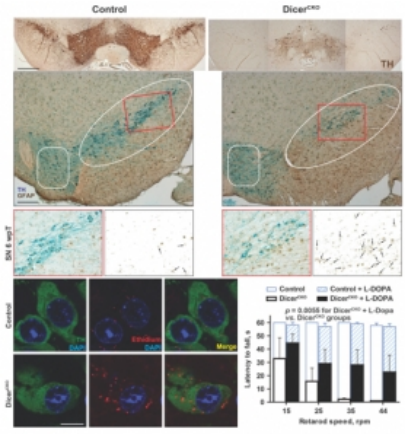
# Shaky matter: How microRNAs can reuvenate our dopamine neurons

P. Chmielarz, J. Konovalova, S. Najam and their colleagues led by Dr. Domanskyi and Dr. Vinnikov just published a paper

**"Dicer and microRNAs protect adult dopamine neurons"**
Chmielarz P., Konovalova J., Najam S.S., Alter H., Piepponen T.P., Erfle H., Sonntag K.C., Schütz G., Vinnikov I.A.*, Domanskyi A.*
SPRINGER NATURE 2017. Cell Death and Disease 8(5): e2813.
*equally contributed corresponding senior authors.
Full text of the publicatior

Download supplementary material

Abstract: MicroRNAs (miRs) are important post-transcriptional regulators of gene expression implicated in neuronal development, differentiation, aging and neurodegenerative diseases, including Parkinson's disease (PD). Several miRs have been linked to PD-associated genes, apoptosis and stress response pathways, suggesting that deregulation of miRs may contribute to the development of the neurodegenerative phenotype. Here, we investigate the cell-autonomous role of miR processing RNAse Dicer in t




he functional maintenance of adult dopamine (DA) neurons. We demonstrate a reduction of Dicer in the ventral midbrain and altered miR expression profiles in laser-microdissected DA neurons of aged mice. Using a mouse line expressing tamoxifen-inducible CreERT2 recombinase under control of the DA transporter promoter, we show that a tissue-specific conditional ablation of Dicer in DA neurons of adult mice led to decreased levels of striatal DA and its metabolites without a reduction in neuronal body numbers in hemizygous mice (DicerHET) and to progressive loss of DA neurons with severe locomotor deficits in nullizygous mice (DicerCKO). Moreover, we show that pharmacological stimulation of miR biosynthesis promoted survival of cultured DA neurons and reduced their vulnerability to thapsigargin-induced endoplasmic reticulum stress. Our data demonstrate that Dicer is crucial for maintenance of adult DA neurons, whereas a stimulation of miR production can promote neuronal survival, which may have direct implications for PD treatment.

Since the discovery of RNA interference, microRNAs are firmly established as crucial factors in development of virtually any kind of tissue in eukaryotes. What about terminally differentiated tissues such as neurons in adult or aged animals?

**The authors show for the first time that microRNA pathway is predominantly depleted in aged dopamine neurons**

**Further, they show that this pathway is essential for maintenance of adult dopamine system**

Even moderate down-regulation of the Dicer1 gene function in these neurons such as during aging or upon homozygous genetic inactivation can result in "pre-symptomatic" neurodegenerative phenotypes

Stay tuned to find out whether it is possible to attenuate these phenotypic changes by restoring relevant microRNAs