Does aging compromise our microRNA-mediated protection to kill dopamine neurons?

Dr. Vinnikov and Dr. Domanskyi just published a perspective mini-review paper
"Can we treat neurodegenerative diseases by preventing an age-related decline in microRNA expression?"
Vinnikov I.A.*, Domanskyi A.*
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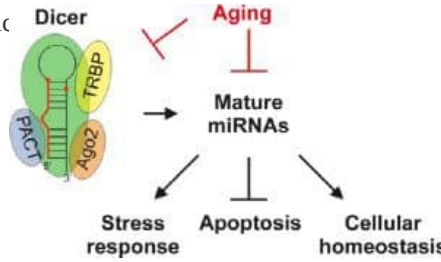
*co-corresponding authors.

Full text of the publicatior

Abstract: MicroRNA pathway is down-regulated in aged dopaminergic neurons: Parkinson's disease (PD) is the most frequent motor neurodegenerative disorder and is morphologically mainly associated with progressive dopaminergic



neuronal loss in the ventral midbrain. The cause of this pathology is unknown, but aging is well established as the strongest risk factor, which by far prevails over gender, environmental and genetic factors. In our recent work (Chmielarz et al., 2017), we have demonstrated that the expression of Dicer, a multidomain ribonuclease III and a key endonuclease in microRNA (miRNA) maturation pathway, is significantly down-regulated in aged mouse midbrain. Further, using a laser-assisted microdissection and quantitative PCR profiling techniques, we analyzed microRNAomes of dopaminergic neurons from the mouse substantia nigra and identified a predominant decrease of miRNA expression in aged dopaminergic neurons. Dicer mRNA levels are also reduced in the ventral midbrain of PD patients (Simunovic et al., 2010). Importantly, several miRNAs have been shown to regulate PD-associated genes, suggesting that age-related deregulation of miRNA signaling may contribute to neurodegeneration (Heman-Ackah et al., 2013).
The two major questions arising from these observations are:

Does the miRNA-mediated regulation provide an essential protection mechanism from neurodegeneration?]

May this protective component be compromised during aging and make the dopamine system more susceptible for other genetic and environmental factors leading to PD?]

In our studies, we attempt to resolve these two challenges. Recently, we have found a way to answer the first of these two major questions: miRNA pathway indeed turned out to be cytoprotective for adult dopaminergic neurons (Chmielarz et al., 2017). An increasing number of published and ongoing studies also start to address the second question, identifying neuronal functions- and survival-regulating genes and pathways targeted by miRNA network in the context of neurodegeneration (Briggs et al., 2015).

May our microRNA-mediated protection be compromised as we age to make dopamine neurons vulnerable against genetic and environmental factors ultimately leading to degeneration and Parkinson's disease?

The question still remains largely unresolved but the authors address several important considerations which might promote further research towards identification of disease-relevant pathological mechanisms and even suggest new ways to halt the disease progression.