# HIPPOCAMPAL ASTROCYTES WITH TRIPLE ALZHEIMER'S DISEASE MUTATION HAVE ALTERED MITOCHONDRIAL FUNCTION AND RESPONSE TO POLY (I:C) SIGNAL

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Virus-induced inflammation is known to accelerate progression of the most prevalent neurodegenerative disorder – Alzheimer's disease (AD) [1]. Mitochondria are key players in immuno-metabolic responses and antiviral signaling via mitochondrial antiviral-signaling protein (MAVS) pathway [2]. In AD, neurodegeneration starts from hippocampus, and astrocytes are important mediators of neuronal dysfunction and death [3,4].

In our study, we investigated mitochondrial function and reactive oxygen species (ROS) production in response to virus signal-mimicking polyinosinic:polycytidylic (Poly (I:C) sequence in hippocampal astrocytes containing three AD-related mutations (APPswe/Tau-P301L/PS-1M146V, further referred to as TG). Immortalized hippocampal astrocyte TG and wild type (WT) lines were generated by means of retroviral transfection of SV40 [5], mitochondrial function was assessed by Oroboros oxygraph-2k system, mitochondrial superoxide production was determined by MitoSOX and fluorescence microscope, image processing was performed by ImageJ, and statistical analysis – by SigmaPlot v13 software.

TG astrocytes had suppressed mitochondrial respiration and higher ROS production compared to the WT cells. Moreover, they demonstrated no mitochondrial response to Poly (I:C) treatment, whereas WT cells reacted to the virus primer by decrease in mitochondrial respiration and burst in mitochondrial ROS.

These results suggest that TG astrocytes have mitochondrial dysfunction and therefore respond differently to virus infections comparing to normal astrocytes. Further investigation of the virus-induced mitochondrial changes in hippocampal astrocytes can shed light on the pathogenesis of neurodegeneration.

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