ImmunoTools *special* Award 2016

Christian Marx, PhD
Postdoctoral Researcher
Group Prof. Dr. Wang

Leibniz Institute for Age Research–Fritz Lipmann Institute(FLI)
Beutenbergstrasse 11, 07745 Jena, Germany

Metabolism in neurogenesis and degeneration

Since my bachelors thesis I am working with different model systems on mitochondrial metabolism, defects and related diseases. Since July, I have started my ongoing project as a postdoctoral researcher in the laboratory of Prof Dr Wang, at the Fritz Lipmann Institute (FLI) in Jena, Germany, about neurogenesis and neurodegeneration related to metabolic alteration.

Mitochondria are at the center of several cellular pathways and deliver the energy as well as biomolecules for cell growth and maintenance. Their structure and networks within the cell are very important for their proper function and cell vitality. Defective mitochondria produce reactive oxygen species (ROS), which can initiate apoptosis pathways but mitochondria are usually degraded by mitochondrial autophagy, so-called mitophagy. As mitochondria divide or fuse independently of cell divisions, defects would be amplified and given to daughter cells, if mitochondria would not be degraded after they become damaged. Mitochondrial dysfunctions are often also reflected in altered metabolic pathways, for example a shift from respiration to mainly glycolysis and are involved in neurodegenerative diseases like Alzheimer, Cockayne Syndrome (CS), Parkinson and Ataxia telangiectasia (AT).

Neurons and other cells in brain tissue have a primarily glycolytic metabolism. Glucose, lactate and keton bodies can cross the blood brain barrier (BBB) and are the only energy source of these cells. In addition to energy demands, these cells have to generate all of their biomolecules from these short chain carbohydrates. But still, these cells are capable to alter their metabolism to respiration in response to stress, such as starvation. The tricarboxylic acid (TCA) cycle within mitochondria is the hub for nearly all metabolic pathways and mediates metabolic alterations.

Dysfunctional mitochondria cause developmental problems during neurogenesis and cause neuropathologies in human patients and in mouse models. DNA damage response proteins like ataxia telangiectasia mutated (ATM) are involved in neurodegenerative diseases and also metabolic alteration. Recently many

studies show that ATM influences mitochondrial morphology and structure, mitophagy, the activity of electron transfer chain (ETC) complexes and thus, mitochondrial respiration, the pentose phosphate pathway (PPP) and the maintenance of mitochondrial DNA (mtDNA). Hence, there is a clear link between mitochondrial defects, metabolic alterations and neuopathies including neurodegeneration.

In our lab, we use mice, neuronal cell culture and murine fibroblasts as test systems to study inflammatory responses, neurogenesis and neurodegeneration. For my project I would use the reagents from ImmunoTools to investigate Annexin-V positive cells per flow cytometry related to mitochondrial damages and neurodegeneration. The recombinant cytokines would be useful to induce inflammatory responses and to follow up on mitochondrial defects afterwards. With Annexin-V, we would analyze the rate of apoptotic cells under different conditions. The growth factors would be used within our cell culture systems and to induce cell differentiation in cultured neuronal stem cells.

Neurodegeneration and mitochondrial damages can cause immune responses and secretion of inflammatory factors. Inflammation itself induces further processes and metabolic alteration to compete with the changed energy demand. In brain tissue microglial cells mediate immune responses. In collaboration my colleague Dr Nadine Schneble, whose expertise in microglial function, I will investigate the alterations of microglial cells after their stimulation with inflammatory cytokines from ImmunoTools. We would further use your ELISA kits to further investigate TNF-α secretion in neuron and microglial cultures.

ImmunoTools *special* AWARD for **Christian Marx**

includes 25 reagents

FITC - conjugated anti-mouse: isotype control IgG2b, Annexin-V

PE - conjugated anti-mouse: CD11b, isotype control IgG2b, NK-cells, Annexin-V

APC - conjugated anti-mouse: isotype control IgG2b, NK-cells, Annexin-V

mouse ELISA-set for 96 wells: 2x mouse TNF-a, (each 3 reagents)

recombinant mouse cytokines: rm EGF, rm IFNgamma, rm IL-1alpha, rm IL-1beta, rm IL-6, rm IL-10, rm LIF , rm NGF-beta, rm TNFa, rm VEGF-A

DETAILS more AWARDS