GLIA 67:E125–E766 (2019)

GLIA

Poster Presentations

Poster topic 01 | Cell migration

T01-001A

Redox regulated migration of glia cells

C. Wilms[1], K. Lepka[1], L. Pudelko[2], L. Bräutigam[2], F. Häberlein[3], B. Odermatt[3], O. Aktas[1], C. Berndt[1]

[1]*Department of Neurology, Heinrich-Heine University, Düsseldorf, DE*
[2]*Medical Biochemistry and Biophysics, Karolinska Institutet, Stockholm, SE*
[3]*Institute of Anatomy, Rheinische Friedrich-Wilhelms-University, Bonn, DE*

Reversible oxidative modifications regulate protein activity. Oxidoreductases such as Glutaredoxin 2 control the thiol redox state of proteins. Here, we demonstrate that Glutaredoxin 2 modifies the cytoskeleton and thereby migration capacity of glia cells. The lack of Glutaredoxin 2 decreases transmigration of mouse primary oligodendrocyte progenitor cells, whereas enhanced levels of Glutaredoxin 2 increase migration. In both, transmigration and scratch closure Glutaredoxin 2 is able to overcome the inhibitory effect of Semaphorin 3A. We found that Glutaredoxin 2 levels control expression of NG2. Therefore, enhanced levels of Glutaredoxin 2 not only affect migration, but also block differentiation of oligodendrocytes in the NG2-glia state. The importance of Glutaredoxin 2 during migration and differentiation of progenitor cells was confirmed in zebrafish with manipulated Glutaredoxin 2 translation. Since NG2/CSPG4 is associated with metastasis/invasion of cancer cells, we investigated the impact of Glutaredoxin 2 on migration and invasion of glioblastoma cells. Injection of patient derived glioblastoma cells with or without manipulated expression of Glutaredoxin 2 into developing zebrafish embryos revealed that Glutaredoxin 2 is essential for metastasis/invasion of glioblastoma cells. Via the migration of glia cells, our data connect specific redox regulation with physiological and pathological processes during development of the myelin sheeth, tissue regeneration, and glioblastoma invasion.

Acknowledgement

For financial support we thank the German Research Foundation (SPP 1710) and iBrain (Heinrich-Heine University).

DOI 10.1002/glia.23675

overexpression causes structural and functional abnormalities in myelination. To develop a therapeutic strategy for CMT1A, we evaluated potency of miRNA in regulation of PMP22 expression. We isolated several miRNAs such as miR-381 that were down-regulated in a CMT1A mouse model. Overexpression of miRNAs in Schwann cell reduced PMP22 expression. In vivo efficacy of miRNAs was assessed by administration of miRNAs expressing lentiviral vectors (LV-miRNAs) into the sciatic nerve of CMT1A mouse model. Administration of LV-miRNAs reduced expression level of PMP22 along with elevated level of miRNAs in the sciatic nerve. Rotarod performance analysis revealed that locomotor coordination of LV-miRNAs administered C22 mice was significantly enhanced from 8 weeks post administration. In addition, improvement of myelination was observed by electrophysiological and histologic findings. Thus miRNA-mediated regulation of PMP22 expression could reduce the expression level of PMP22, thereby alleviating the demyelinating neuropathic phenotype of CMT1A. These data suggest that miRNA can be used as a potent therapeutic strategy to control the disease phenotype of CMT1A.

Acknowledgement

This study was supported by grants (HI14C3484 and HI16C0426) of the Korean Health Technology R&D Project funded by the Ministry of Health & Welfare. It was also supported by grants (NRF-2016R1A5A2007009, NRF-2017R1A2B2004699, and NRF-2018R1A4A1024506) of the National Research Foundation of Korea (NRF) funded by the Ministry of Science and ICT (MSIT).

T08-020A

The human Schwann cell transcriptome: species-specificity, long-term stability and changes with differentiation

P.V. Monje[1,2], D. Sant[2], N.D. Andersen[3], V. Camarena[2], G. Wang[2]

[1]Department of Neurological Surgery / Stark Neurosciences Research Institute, Indiana University, Indianapolis, US
[2]University of Miami, Miami, US
[3]Universidad Nacional del Sur, Bahia Blanca, AR

Cultured Schwann cells of human origin differ from those isolated from experimental animals in both phenotype and function. However, the basis for this divergence and its significance to potential clinical applications of the primary cells are not fully understood. In this study, we used RNA-seq to comprehensively analyze the human Schwann cell transcriptome and compare it to that of rat cells. We also studied the transcriptomics profiles of human Schwann cells subjected to: (1) the pro-mitogenic effect of growth factors in cells undergoing serial passaging in vitro, and (2) the pro-differentiating action of cAMP, a signal known to promote myelin gene expression in rodent cells. Despite the human Schwann cell transcriptome differed as much as 44% from that of rat Schwann cells established under identical conditions, the human cells maintained their expected Schwann cell identity regardless of sub-culture and the continued influence of mitogenic factors. Strikingly, the transcriptomes of low passage (proliferative) and late passage (senescent) human Schwann cells were essentially undistinguishable with the exception of roughly 100 differentially expressed genes in the senescent populations. On the contrary, the human Schwann cell transcriptome was readily and persistently shifted in response to a single treatment with cAMP analogs as highlighted by the >1,300 genes that were upregulated and the >1,700 genes that were downregulated within 1-day post-stimulation. In sum, these results confirmed that human Schwann cells maintain their typical gene expression profiles in culture unless challenged with a strong pro-differentiating stimulus. The observed stability of the human Schwann cell transcriptome in the face of expansion and mitogenic stimulation adds a level of safety for the use of these glial cells in clinical transplantation.