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Selective lentiviral mediated targeting of glia cells in the central nervous system

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In a complex tissue of the central nervous system (CNS), cell cross-talk is essential to preserve normal functions. Current tools for dissecting the molecular mechanisms that mediate cell-cell interactions within the brain include molecular genetics, imaging and use of transgenic animals. However, these are technically challenging, time consuming and difficult to control. In this study we report the establishment and validation of a lentiviral-mediated gene-targeting platform to specific cells in the CNS. It combines unique features of self-inactivated lentiviruses that promote stable gene delivery into non-dividing cells and efficient display of single-chain variable region human fragments (scFv) or soluble IgG on the surface of viral particles. In vitro, cells that express the receptor-binding domain of the SARS CoV spike glycoprotein were targeted by engineered sindbis pseudotyped lentiviruses that incorporate specific scFvFc attachment moieties. Additionally, in vitro targeted gene expression to primary astrocytes was also demonstrated, using engineered lentiviruses that incorporate Aquaporin 4 IgG. In vivo, lentiviral targeting of oligodentrocyes progenitor cells (OPCs) that express the chondroitin sulfate proteoglycan, NG2 was obtained using viral particles that display an anti NG2 IgG. We conclude that this genetic delivery tool can be used for specific targeting of several genes into different cell populations. Moreover, it will enable efficient fating and imaging studies during CNS development, as well as enhance the understanding of the molecular mechanisms that mediate cell communication in healthy and diseased brain. Importantly, it can open a window for the development of novel strategies for treating CNS pathologies.

Biography

Michael Fassler received his M.Sc degree in 2010 from the Department of Virology, Faculty of Health Science, Ben-Gurion University of the Negev, Beer-Sheva, Israel. He is currently completing his Ph.D. degree in the Department of Virology, Faculty of Health Science, and in the Department of Physiology and Neurobilogy, Ben-Gurion University of the Negev. His research work involves developing a gene-targeting platform using lentiviruses that can mediate specific gene delivery into cells of the CNS.