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Use of a statistical algorithm to classify influenza infection by lung and plasma cytokine and chemokine production profiles

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Influenza epidemics result in approximately 3 - 5 million cases of severe disease and 250,000 to 500,000 deaths annually. Rapid classification of an influenza infection is of utmost importance in determining the proper treatment regimen. In this study, mice were infected with one of three strains of influenza, 2009 swine-origin influenza A (H1N1) A/California/04/09, seasonal H1N1 A/Texas/36/91, and the highly pathogenic avian (H5N1) A/Vietnam/1203/0 or vehicle control. Levels of thirty seven cytokines and chemokines in lung (6, 12, 24, 72 and 96 hr) and plasma (24 and 96 hr) were measured for 4 days following challenge and analyzed statistically using a support vector machine, a statistical concept using supervised learning methods for classification and regression analysis. Using this method, at a given time point post-challenge, only 2 or 3 cytokines in lung or plasma were needed to predict the influenza type with 100% accuracy at a given time post-infection. Since the exact time of influenza infection is seldom known, the ability of the support vector machine procedure to classify the type of influenza infection independent of the time post-infection was also tested. Combinations of 10 lung or 14 plasma cytokines/chemokines were able to provide a 100% classification accuracy of the influenza type over a 96 hour period post-infection.

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Cell specific gene targeting to the CNS using engineered lentiviruses

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Viral-mediated gene targeting to specific cells and organs is a major challenge for establishment of an efficient gene therapy regimen. In this study we manage to develop a gene delivery platform into cells using lentiviral vectors that are pseudotyped with a sindbis mutated envelope and a single chain variable fragment (scFv). 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 two versions of the receptor-binding domain of the SARS CoV spike glycoprotein were targeted by engineered sindbis pseudotyped lentiviruses that incorporate specific scFvFc attachment moieties. Despite high similarity of the two S1 antigens, gene transfer was obtained with low background of transduction levels, indicating high affinity of the scFvFc to their cognate antigen. Additionally, in vitro targeted gene expression to primary astrocytes was also demonstrated, using engineered lentiviruses that incorporate GLAST IgG. In vivo, lentiviral targeting of astrocytes and oligodentrocyes progenitor cells (OPCs) that express the chondroitin sulfate proteoglycan, NG2 was obtained using viral particles that display an anti-GLAST and anti-NG2 IgG, respectively. Overall, these results demonstrate efficacy of lentiviral vectors as a gene delivery platform. Such a system could potentially be used to mark specific cells populations enabling 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.

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.

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