

Principal Investigator: Stephan von Gunten
Grant Title: The sweet touch of tumors: cancer glycosylation effects on NKIS formation

Abstract:

Aberrant glycosylation is a key feature of malignant transformation. We have recently described that sialoglycans expressed on tumor cells are able to dampen anti-tumor immune responses of cytotoxic lymphocytes^{1,2}. This inhibition occurs through the engagement of sialic-acid containing carbohydrates with specific inhibitory receptors named Siglecs. In this work we decided to investigate the molecular events that occur upon interaction between tumor sialoglycans and Siglecs at the contact site between tumor cell and the attacking NK cells. Interactions between NK cells and cancer cells were visualized by confocal microscopy and flow cytometry analysis, and molecular redistribution events at the contact site were analyzed. Our results showed that presence of Siglecs influences the formation and stability of NK-cancer cell conjugates. Accordingly, the functionality of the NK immunological synapse (NKIS) and relevant signal transduction were affected when Siglecs engaged their ligands. Our results highlight the importance of the Siglec-ligand axis in modulating the the NK immunological synapse (NKIS) formation and functionality.



1. Jandus C, Boligan KF, Chijioko O, et al. Interactions between Siglec-7/9 receptors and ligands influence NK cell-dependent tumor immunosurveillance. *J Clin Invest*. 2014;124(4):1810-1820.
2. Haas Q, Boligan KF, Jandus C, et al. Siglec-9 Regulates an Effector Memory CD8(+) T-cell Subset That Congregates in the Melanoma Tumor Microenvironment. *Cancer Immunol Res*. 2019;7(5):707-718.