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Targeting the tumor associated carbohydrate antigens

Somdutta Saha
Duke Human Vaccine Institute, USA

Tumor associated carbohydrate antigens (TACAs) are a class of glycans with important structural and signaling functions playing a major role in cell proliferation, differentiation, and apoptosis relevant to oncology. Tumor cells expressing TACAs influence prognosis and survival of cancer patients. We have used structure-based approaches to study antigen-antibody interactions in the tumor micro-environment and designed a peptidyl ligand that mimics the molecular topology of TACAs even though they are chemically dissimilar but functionally equivalent molecular structures. Our work also suggests that in designing antibodies, careful consideration should be made for somatic mutations that enhance the rigidity of an antibody. Electrostatics play a major role in the recognition of the model antigen examined. Discrimination against wanted targets through repulsive electrostatic interactions might be more fruitful than a strong optimization of target binding whereas increased specificity toward one target leads to decreased affinity toward others. Models for TACA targeting reagents are typified by TACA reactive monoclonal antibodies, lectins, and perhaps oncolytic viruses that target sialylated receptors. Peptides reactive with TACA may, in particular, be interesting carbohydrate binding agents, forming the basis of novel drugs that combine the advantages of antibodies and small molecules. We have developed a peptidyl ligand that binds to the TF or T antigen (Galβ1-3GalNAc). The designed peptidyl ligand was observed functionally to mediate cell signaling of TF expressing cell lines, suggesting that TF antigens might be functionally interesting.

Speaker Biography

Somdutta Saha has completed her PhD degree in Bioinformatics from the University of Arkansas at Little Rock in December 2013. She has investigated the developmental pathway for antibodies reactive to neo-carbohydrate antigens expressed in several metastatic cancers. She is interested in application of Bioinformatic approaches to early stage drug discovery efforts. She was also selected as the first Early Talent Post-doctoral Fellow in GlaxoSmithKline Plc., where she made significant contributions to the understanding of host-microbe interactions via metabolite signaling. Currently, she is a Staff Scientist at Duke Human Vaccines Institute in Durham, North Carolina involved in designing better immunogens for HIV patients.

e: sombioinfo@gmail.com

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