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N-glycan cryptic sugar moieties as potential biomarkers of aggressive prostate cancer

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Abstract

Although tumor-associated abnormal glycosylation has been recognized for decades, information regarding host recognition of the evolving tumor glycome remains elusive. We report here a carbohydrate microarray discovery and immunological validation of a number of potential glycan markers of prostate cancer. These carbohydrates are the precursors, cores and internal sequences of *N*-glycans. They are usually masked by other sugar moieties and belong to a class of glyco-antigens that are normally "cryptic". However, viral expression of these carbohydrates may trigger host immune responses. For examples, HIV-1 and SARS-CoV display Man9 clusters and tri- or multi-antennary type II (Galβ1→4GlcNAc) chains (Tri/m-II), respectively; viral neutralizing antibodies often target these sugar moieties. We asked, therefore, whether prostate tumor expression of corresponding carbohydrates triggers antibody responses *in vivo*. Using carbohydrate microarrays, we detected IgG antibodies targeting the Man9- or Tri-/m-II-autoantigens in the sera of men with benign prostatic hyperplasia (BPH), as well as those with cancer. Importantly, these antibody activities were selectively increased in prostate cancer patients. We further verified these observations in a large-cohort of patients, including patients with 100% Gleason grade 3 cancer (N=84), with Gleason grades 4 and/or 5 cancer (N=204), and BPH controls (N=135). Radical prostatectomy Gleason grades and biochemical (PSA) recurrence served as key parameters for serum biomarker evaluation. Progress of this large-scale serological study will be discussed in this presentation.

Biography

Dr. Wang is SRI Distinguished Scientist and Senior Program Director, Tumor Glycomics Laboratory, Center for Cancer research, Biosciences Division. Dr. Wang's long-term research interest is in the carbohydrate moieties that are critical for self/non-self recognition and induction of antibody responses. His team has established multiple platforms of carbohydrate microarrays and introduced these glycomics tools to explore the structural and antigenic diversities of the glycome. The main research focus of his lab is in the immunogenic sugar moieties. In the past few years, his group has contributed to the identification of immunologically potent glycan markers of SARS-CoV, *Bacillus anthracis* exosporium, and a number of human cancers. Dr. Wang received his Ph.D. degree in immunology and glycobiology with the late Professor Elvin A. Kabat at Columbia University (1993). Lately, he entered the developing field of post-genomics research. He served as Head of Functional Genomics Division, Columbia University Genome Center 1998-2003 and Director of the Stanford University Tumor Glycome Laboratory 2007-2010 before joining in SRI International.