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Carbohydrate based vaccines for the treatment of cancer

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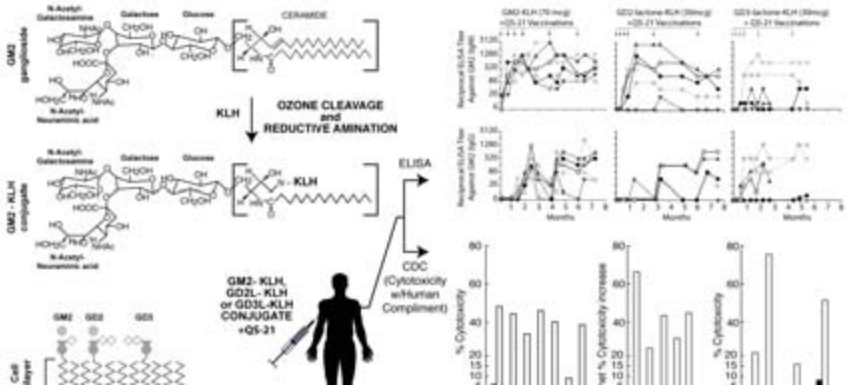
PL and GR are shareholders and paid consultants for MabVax Therapeutics, Inc. who have licensed the KLH-conjugate vaccines from MSKCC, USA

As vaccines against cancers (and infectious diseases) have employed increasingly focused and homogeneous antigens for vaccine construction, the immunogenicity of these antigens has been observed to markedly decrease. This can be offset by conjugating these homogeneous antigens to an immunogenic carrier protein such as keyhole limpet hemocyanin (KLH) or the use of a potent immunological adjuvant such as the saponin QS-21. Especially in the case of vaccines against cancer antigens (generally autoantigens), both carrier protein conjugation and immunological adjuvant have been required. Many of the antigens over-expressed on the cancer cell surface are carbohydrate antigens expressed on cells of particular lineages. These have been surprisingly potent targets for immune recognition and attack by antibodies, both because of their abundance at the cell surface and their unexpected immunogenicity in KLH-conjugate+QS-21 vaccines. Passively administered and vaccine induced antibodies targeting carbohydrate antigens have eliminated circulating tumor cells and systemic micrometastases in a variety of preclinical models. A series of these cancer cell-surface differentiation antigens have now been identified, synthesized, KLH conjugated, and demonstrated to induce antibodies in the majority of vaccinated cancer patients. These include GM2, GD2, GD3, Fucosyl GM1 and sialyl Lewis A (sLea) gangliosides, globo H glycolipid, Tn, sTn and TF blood group related antigens, polysialic acid, and MUC1 peptide. For maximal impact, largely due to tumor cell heterogeneity, polyvalent vaccines will be required. A series of double blind, randomized trials with different polyvalent vaccines designed to test clinical impact against particular cancer types in the adjuvant setting are currently in progress. The trivalent ganglioside vaccine against sarcomas is a good example. It is based on the immunogenicity of each of its 3 conjugates:



Biography

Philip Livingston received his MD degree from and is currently Professor of Medicine in the Joan and Sanford Weill Medical College at Cornell University and Attending Physician and Member in Memorial Sloan-Kettering Cancer Center where he has treated patients and run a research lab for 36 years. His research has focused on: identification of suitable targets for immunotherapy of a variety of cancers, construction of polyvalent conjugate vaccines specifically designed to augment antibody responses against these targets, and identification of optimal immunological adjuvants to further augment the potency of these vaccines. He has over 150 publications and 4 issued and 3 pending patents concerning cancer vaccines. Recently, he helped establish MabVax Therapeutics, Inc., a small biotech company. MabVax supports several randomized Phase II trials with these polyvalent vaccines and establishment of human monoclonal antibodies against cancer antigens from the immunized patients