DEVELOPMENT OF SIALYL LEWIS^A-BASED ANTI-CANCER IMMUNOTHERAPY

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Sialyl Lewis^a (sLe^a), also known as cancer antigen 19-9 (CA19-9), is a tumor associated carbohydrate antigen. The overexpression of sLe^a on the surface of a variety of cancer cells makes it an attractive target for anti-cancer immunotherapy. However, sLe^a based anti-cancer vaccines and monoclonal antibodies have been under-explored. In this presentation, the development of immunotherapy targeting sLe^a will be discussed.
To develop sLe^a based immunotherapy, sLe^a in a conjugable form is needed. Furthermore, to boost the antibody responses against sLe^a, it needs to be conjugated to an immunogenic carrier. We have developed an efficient stereoselective synthesis of sLe^a with an amine bearing linker by overcoming challenges related to low reactivities of sialic acid donor and stereochemical controls of sialylation. The synthetic sLe^a was conjugated with a powerful carrier bacteriophage Qβ. Mouse immunization with the Qβ-sLe^a conjugate generated strong and long-lasting anti-sLe^a IgG antibody responses, which were superior to those induced by the corresponding conjugate of sLe^a with the benchmark carrier keyhole limpet hemocyanin. Antibodies elicited by Qβ-sLe^a were highly selective toward sLe^a structure, could bind strongly with sLe^a expressing cancer cells and human pancreatic cancer tissues, and kill tumor cells via complement mediated cytotoxicity. Furthermore, vaccination with Qβ-sLe^a or treatment with the anti-sLe^a monoclonal antibodies significantly protected the mice from tumor development in a metastatic cancer model. This is the first time that tumor protection was observed from a sLe^a based vaccine. These results highlight the significant potential of sLe^a as a promising cancer antigen for immunotherapy development.