Ganglioside-targeted anti-idiotypic vaccination for active cancer immunotherapy

Yoan Javier Machado Hernandez, Centre for Molecular Immunology, Havana, Cuba

yoan.machado@gmail.com

Approaches for cancer immunotherapy based on idiotypic antibodies represents an attractive alternative to classic treatment including chemo-/radiotherapy and use of tumor antigen-specific monoclonal antibodies. Based on Jerne’s concept, the activation of antibody regulatory networks to elicit a specific antibody response to a nominal antigen have been studied extensively.

We have developed a murine anti-idiotype monoclonal antibody (mAb) named 1E10. This mAb (Ab2) is specific to a murine Ab1 mAb, named P3, which selectively binds Neu-glycolyl (NeuGc)-sialic acid on several monosialo- and disialogangliosides, which are antigens expressed in human melanoma, breast, and lung tumors. Vaccination with 1E10 induced anti-anti-idiotype antibodies (Ab3) in cancer patients. These Ab3 generated were characterized by bearing P3 idiotopes (Ab3, Id+). Although a potent anti-tumoral effect in two mouse tumor models was observed, no specific humoral response against NeuGc-containing gangliosides was detected in sera from immunized mice. In contrast, hyperimmune sera from melanoma, breast, and lung cancer patients vaccinated with 1E10 specifically reacted with these gangliosides. Currently, the production process of 1E10 is being transferred from the in vivo (mice ascites fluid) approach to a bioreactor-based method. 1E10 antibodies resulting from both methods have similar but not identical physicochemical properties. However, they show a similar anti-tumoral effect in mice, but 1E10 produced in bioreactor displays lower immunogenicity in preclinical models as compared to ascites fluid-derived 1E10. The impact of structural differences on immunogenicity is presently under investigation.