A sugar-enzyme link to tumour growth suppression

A chain of sugar molecules attached to proteins may hold the key to fighting cancer. These sugar-protein chains, regulated by an enzyme called beta1,4-galactosyltransferase-3 (B4GALT3), have surfaced as crucial players in various cancers, particularly impacting survival rates in immunotherapy-sensitive cancers like neuroblastoma, cervical, and bladder cancer. Yet, the specific role of B4GALT3 within the tumour immune microenvironment (TIME) remained enigmatic.

In a recent study, researchers have unravelled the mystery behind B4GALT3's role within the TIME. They discovered that a deficiency of B4GALT3 in mice's TIME leads to the inhibition of tumour growth. This study underscores the significance of glycosylation, a form of protein modification, on the surfaces of T cells. It has revealed that when glycosylation is significantly reduced, it paves the way for increased infiltration of CD8+ immune cells into tumours. In the case of B4GALT3 knockout (KO) mice, these findings offer a new avenue for manipulating T cell surface glycosylation, presenting a promising approach to cancer immunotherapy.

To understand the sugar-protein connection, the research team used a method involving the purification of membrane proteins and enzymatic cleavage to enrich glycopeptides. This allowed them to identify the sites and structures of glycans – complex, highly branched sugar chains – and quantify glycoproteins.

The study's experimental approach involved the subcutaneous transplantation of tumour cells, both weakly and strongly immunogenic, into B4GALT3 knockout and wild-type mice to investigate tumour growth. Only the knockout mice exhibited suppressed growth of highly immunogenic tumour cells. Furthermore, the knockout mice showed elevated levels of CD8+ T cells, which secreted potent anti-cancer compounds, including Interferon-γ and Granzyme B.

These remarkable findings open new possibilities for cancer immunotherapy, emphasizing the pivotal role of B4GALT3 in the battle against cancer. It suggests that manipulating glycosylation of T cell surfaces could be the key to enhancing the immune response against tumors and holds promise for the future of cancer treatment.

Journal article: Wei, H., et al., 2023. Beta-1,4-galactosyltransferase-3 deficiency suppresses the growth of immunogenic tumors in mice. *Frontiers in Immunology*.

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