Targeting a lynchpin to treat cancer and autoimmunity

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Abstract

Cancer and autoimmune disease are two sides of the same coin. Autoimmune diseases, such as diabetes, arthritis, and inflammatory bowel disease, are caused by overactivation of the immune response while cancer cells downregulate the immune response in order to promote their own growth. One attractive therapeutic target, lymphotoxin β receptor (LT β R) on the cell surface, is central to both processes but its detailed signaling mechanisms have remained unclear, making it difficult to target the pathway. Now, researchers have identified a way to alter the strength of LT β R-mediated signaling. Using drugs to lower the cholesterol levels in the plasma membrane they showed that the lipid content of the cell membrane affects LT β R-dependent signaling and LT β R internalization. Depleting membrane cholesterol caused increased LT β R signaling through the well-known canonical NF- κ B signaling pathway suggesting that cholesterol depletion could be used to augment LT β R-based therapies for cancer and cholesterol levels may also affect the outcome of treatment for autoimmune disease. Although further mechanistic details remain to be uncovered this discovery could help improve immune-targeting therapies, improving the chances of success in cases where traditional treatment has failed. Banach-Orlowska, et al. "Cholesterol restricts lymphotoxin β receptor-triggered NF- κ B signaling." *Cell Communication and Signaling* (2019).