

Research Project

Exploiting the CXCR4-CD44 axis for cancer treatment

Third-party funded project

Project title Exploiting the CXCR4-CD44 axis for cancer treatment

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In the tumor microenvironment (TME), cancerous cells, together with stromal and immune cells are organized within a specific extracellular matrix (ECM) that provides cues orchestrating cell behaviour. Therapies which harness our inherent ability to destroy tumors, such as antibodies that activate cytotoxic lymphocytes (CTL) to re-engage tumor cell killing (immune checkpoint therapy, ICT), are successful in treating some but not all cancer patients. Emerging evidence suggests a key role of the ECM in regulating the crosstalk between cancer and immune cells. Therefore, a more complete understanding of how cells and the ECM in the TME interact will be important to design new and complementary approaches to treat cancer. We propose a signaling axis comprising ECM and CXCR4, involving tenascin-C (TNC), hyaluronan (HA), CXCL12 and CD44, to modulate tumor immunity thereby compromising ICT. We aim at understanding how CXCR4 signaling complexes form and how this impacts CTL behaviour by using proteomics, in vivo targeting and computational modelling. As CXCR4 plays an important role in CTL reactivation, more insight about its regulation in space and time may provide novel information with therapeutic potential for improving ICT.

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