CANCER DISCOVERY
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Précis: Single-cell RNA sequencing, immunohistochemistry, and imaging mass cytometry identified immunosuppressive LAG3+ T cells near malignant cells in the MHC class II− classic Hodgkin lymphoma microenvironment.

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Précis: The epigenetic and transcriptional effects of CREBBP hotspot mutations in diffuse large B-cell lymphoma (DLBCL) were reversed by HDAC3 inhibition, which synergized with PD-L1 blockade in a mouse model of DLBCL.

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ON THE COVER Cancer-cell stemness is associated with immunosuppression and poor prognosis in glioblastoma and many other malignancies. Chen and colleagues found that depletion of the circadian-rhythm gene CLOCK in glioma stem cells (GSC) led to reduced self-renewal capabilities and decreased markers of immunosuppressive microglia infiltration. Mechanistically, CLOCK-depleted cells had reduced levels of OLFML3, encoding a secreted protein involved in intercellular interactions. In mouse models, tumors derived from CLOCK-depleted GSCs were less aggressive than those derived from control GSCs, leading to increased survival in mice bearing CLOCK-depleted tumors, and exhibited reduced signs of stemness and microglia infiltration. Bolstering the proposed mechanism, tumors derived from OLFML3-depleted GSCs were also less aggressive than controls. For details, please see the article by Chen and colleagues on page 371.

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