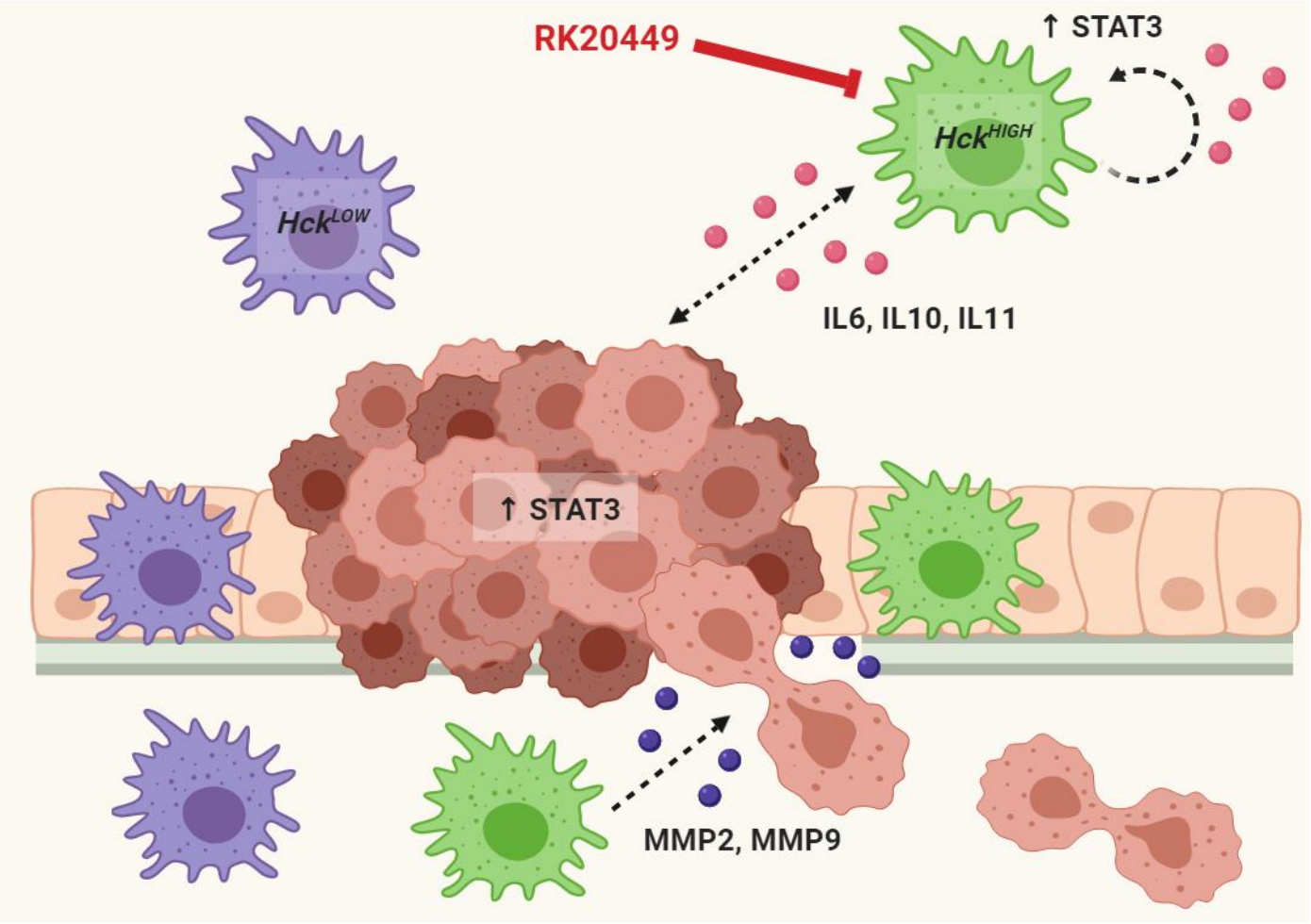
Supplementary Figure 4



Supplementary Figure 4. Excessive HCK activity in bone marrow-derived cells promotes STAT3-dependent gastric tumor development and invasion.

Aberrant HCK activation (*Hck*^{HIGH}) enhances alternative macrophage polarization (AAM, green) and the production of STAT3-stimulatory ligands (including IL6, IL10, IL11), which act on cancer epithelial and immune cells in a reciprocal feed-forward loop to further enhance STAT3 signaling in both cell types. These molecules may also sustain the HCK-STAT3 signaling axis and AAM polarization in a cell autonomous manner. In addition to tumor growth, *Hck*^{HIGH} macrophages show an enhanced ability to support tumor cell invasion through the increased production of matrix-remodelling factors such as MMP2 and MMP9. Accordingly, genetic reduction or pharmacologic inhibition of HCK activity with a small molecule HCK-specific inhibitor RK20449 reduces STAT3-dependent tumor growth. *Figure created in BioRender.*