Cytokine-induced Hexokinase 3 supports macrophage cell survival

Experimental Hematology/Oncology

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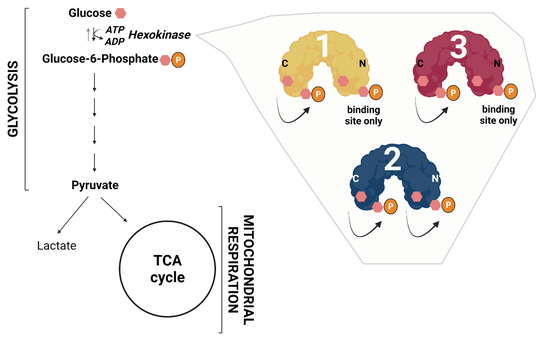
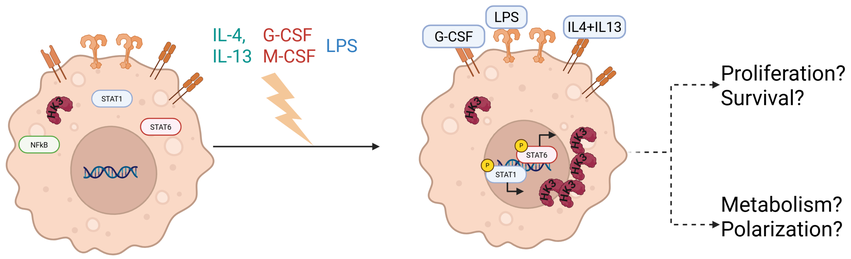
Background

- **Hexokinases (HK) catalyze the first, rate limiting step of glycolysis.**
- **HK3 expression is confined to the myeloid lineage.**
- **The function of HK3 in healthy myeloid cells is largely unknown**

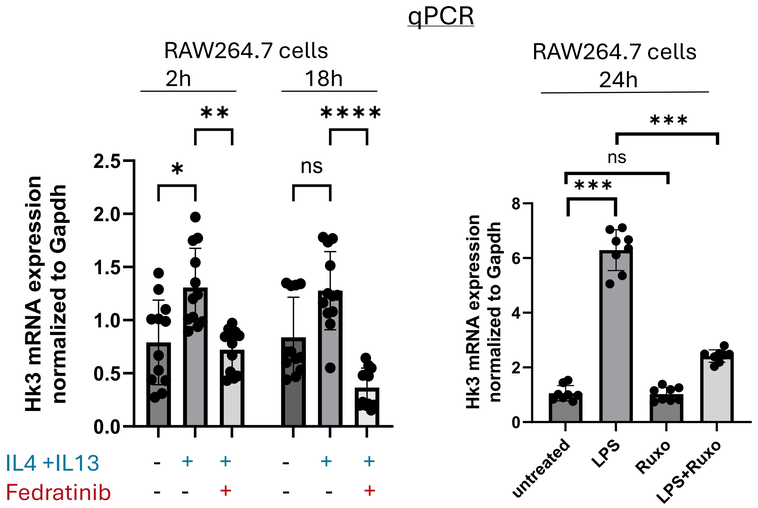


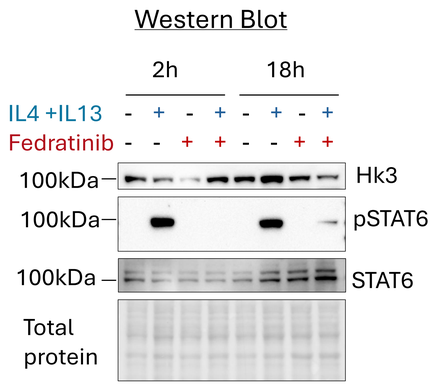
Hypothesis

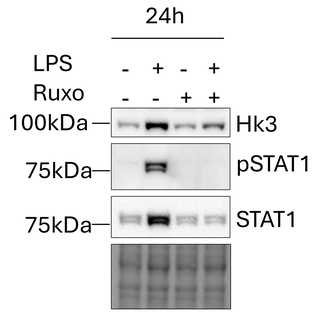


HK3 is upregulated upon cytokine stimulation via the JAK/STAT pathway to promote survival of activated macrophages.

JAK/STAT activation induces Hk3 expression



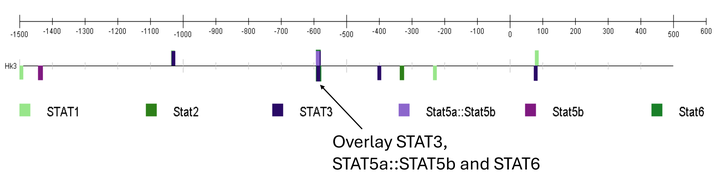


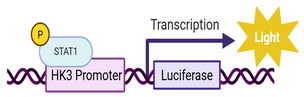


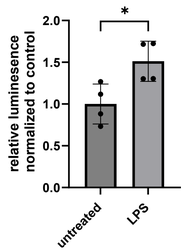
- **Increased Hk3 mRNA and protein levels in RAW264.7 cells upon cytokine stimulation.**
- **Hk3 upregulation is inhibited by JAK inhibitors.**

HK3 promoter is activated by STATs

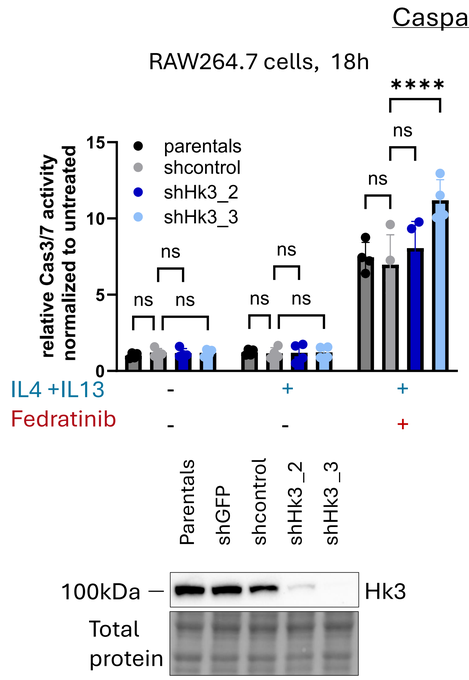
Luciferase promoter assay showing activation of Hk3 promoter upon 24h LPS stimulation

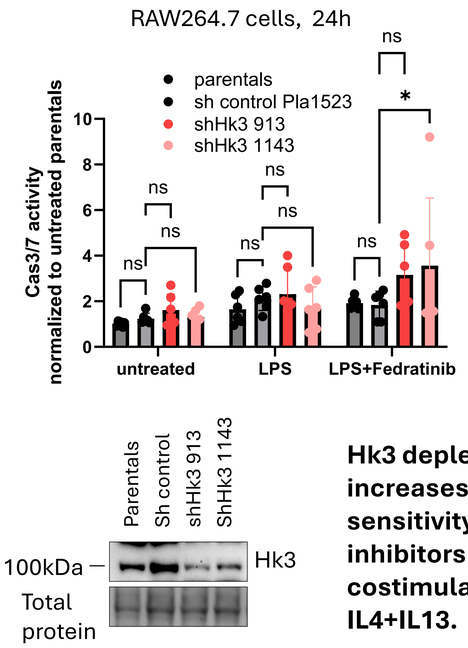






Prosurvival role of Hk3 upon Cytokines





Hk3 depletion increases sensitivity to JAK inhibitors upon costimulation with IL4+IL13.

Conclusion

Transcriptional regulation of Hk3

- Hk3 is upregulated upon cytokine stimulation.
- The data suggests Hk3 upregulation via JAK/ STAT signaling.

Prosurvival function of Hk3

- Hk3 KD decreases cell survival upon fedratinib in combination with IL4+IL13 treatment.

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Reliable hexokinase 3 protein detection in human cell lines and primary tissue European Journal of Histochemistry March 2025