

## Retroviral expression of GATA-3 siRNA impairs early T cell development

Hematopoiesis is a complex, highly controlled process, requiring precise regulation of gene transcription at each stage of development. Cells require an evolving pool of transcriptional regulators for progression and survival as they develop.

GATA-3, a Zn finger transcription factor, is expressed throughout the T cell development pathway, and binds to the regulatory regions of multiple T cell specific genes.

To study the role of GATA3 in early T cell development, we are using retrovirally delivered GATA-3 specific siRNA to prevent GATA3 protein synthesis at defined developmental stages. These experiments are done either in the SCID-adh cell line (a DN3-like cell line), or using (day 14) fetal liver derived precursors cultured on OP-9 stromal cell layers.

Cells infected with a GATA3 siRNA producing virus do not survive in numbers comparable to those in control infections, suggesting that GATA3 is critical for survival in these early stage cells. We further detect a block in early T cell development in cells expressing a GATA3 specific siRNA, consistent with an essential role for GATA3 in promoting T cell developmental progression. Our data suggest that GATA3 is critical for early T cells, as its loss affects both viability and progression along the developmental pathway.

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