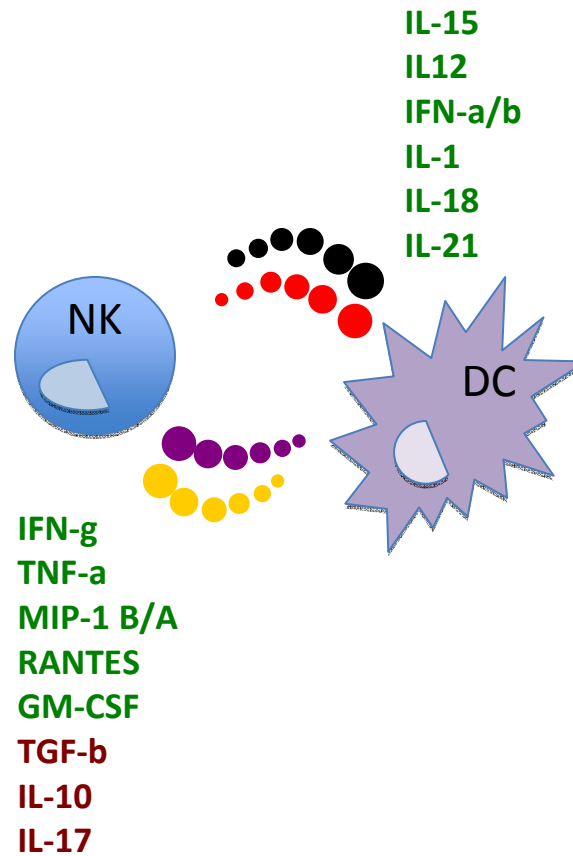


NK cell mediated deletion of Dendritic cell populations

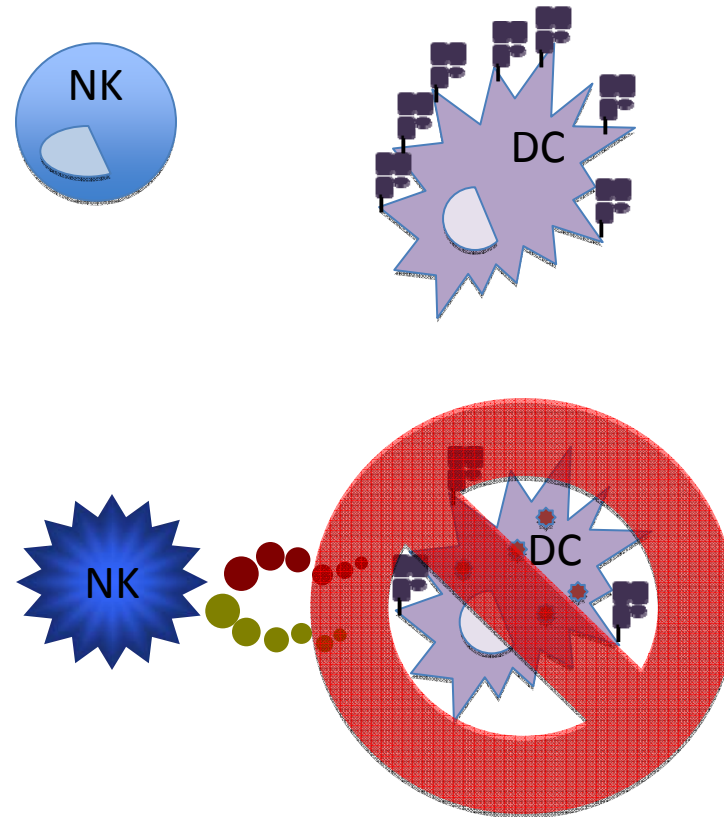
Galit Alter

Partners AIDS Research Center
Massachusetts General Hospital
Harvard Medical School

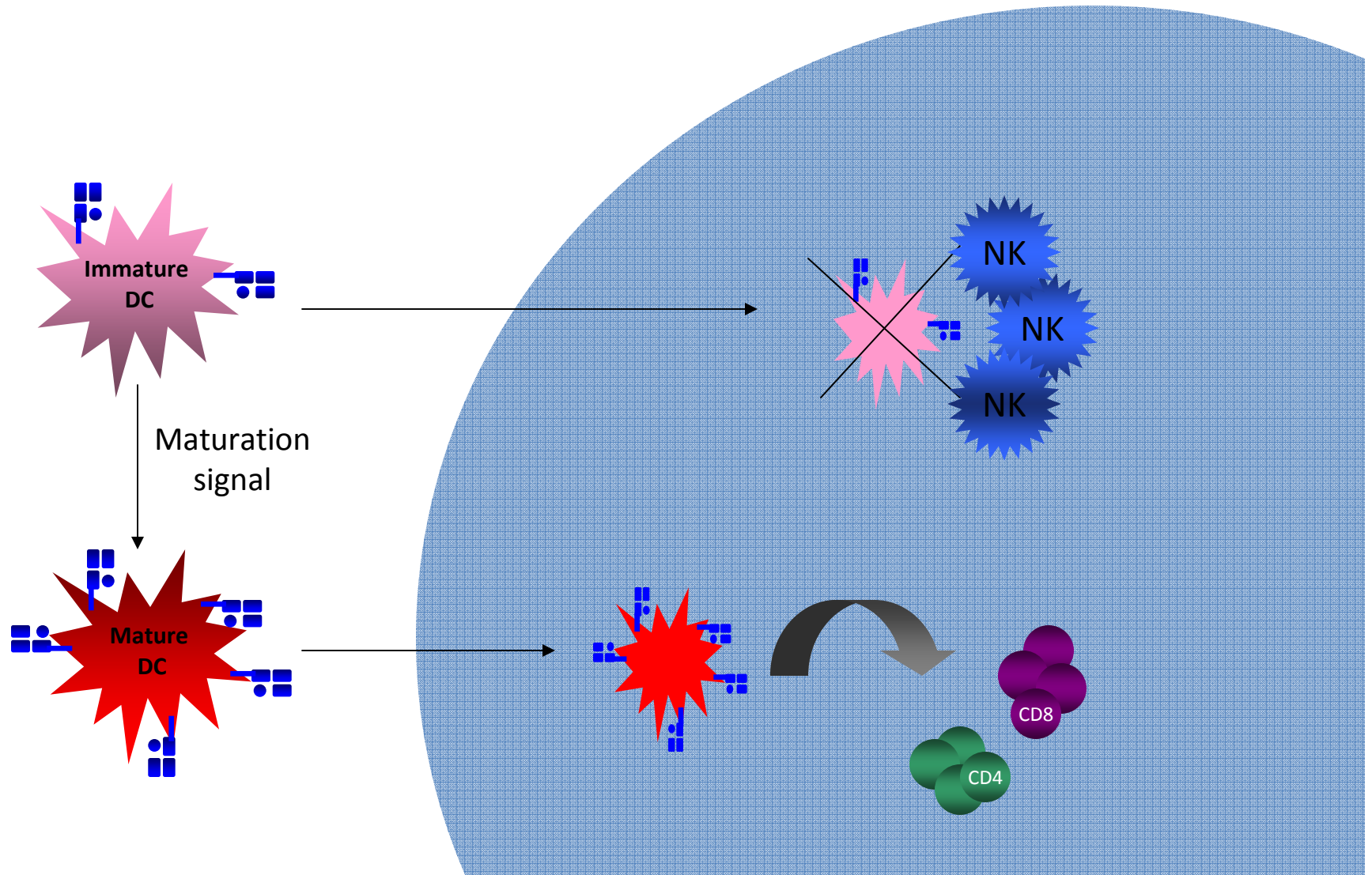
NK cells and DCs potentiate each other during an acute immune response



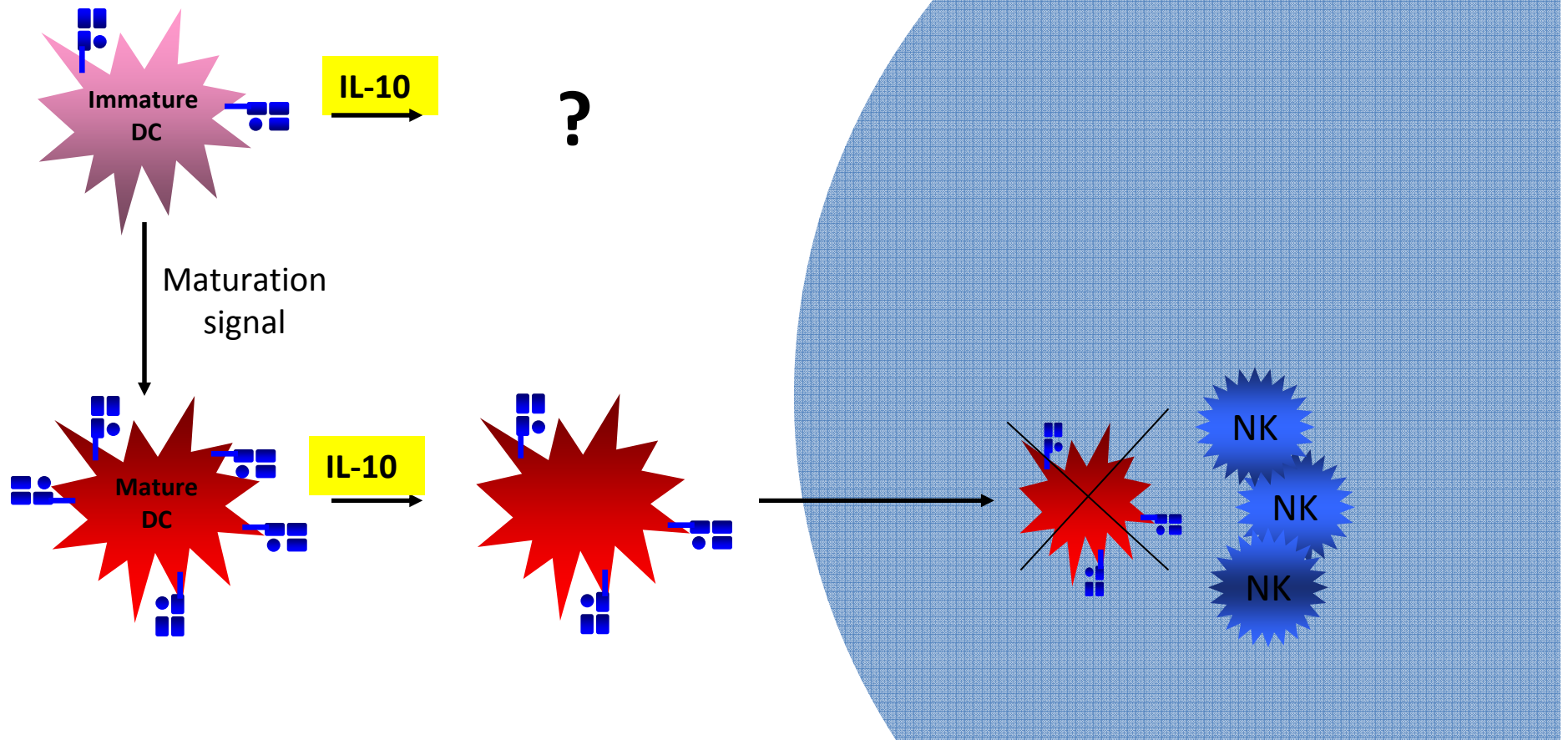
NK cells edit DC populations



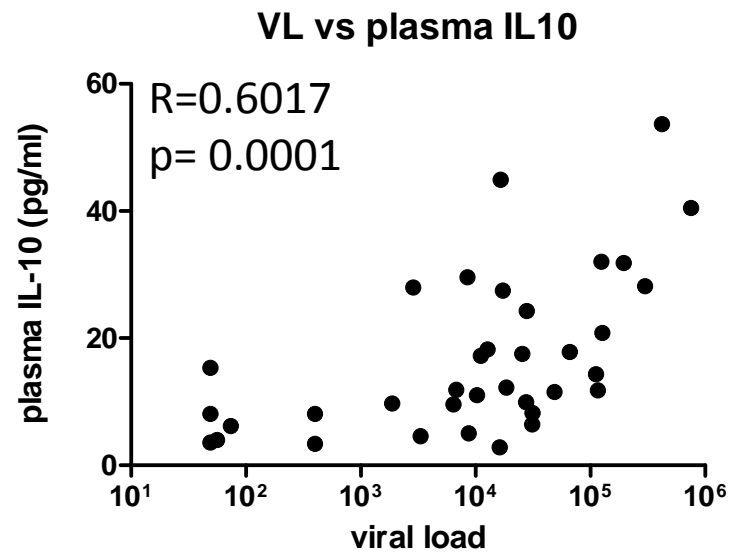
Trincheri Model



What happens in the presence of IL-10?

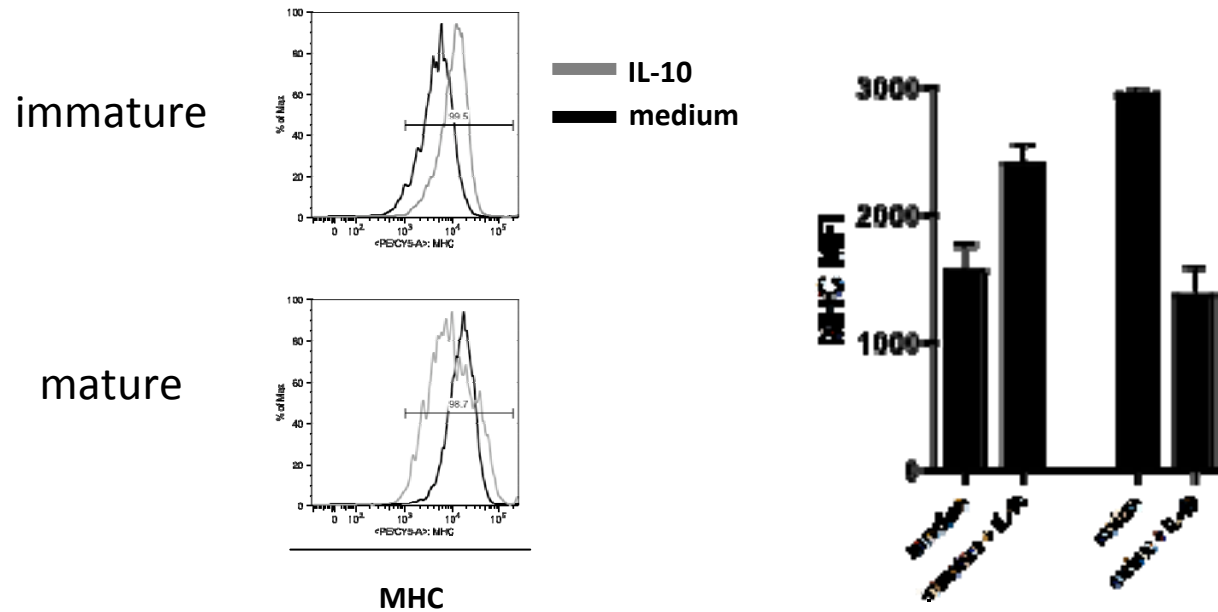


Increased IL-10 secretion with elevated viral loads

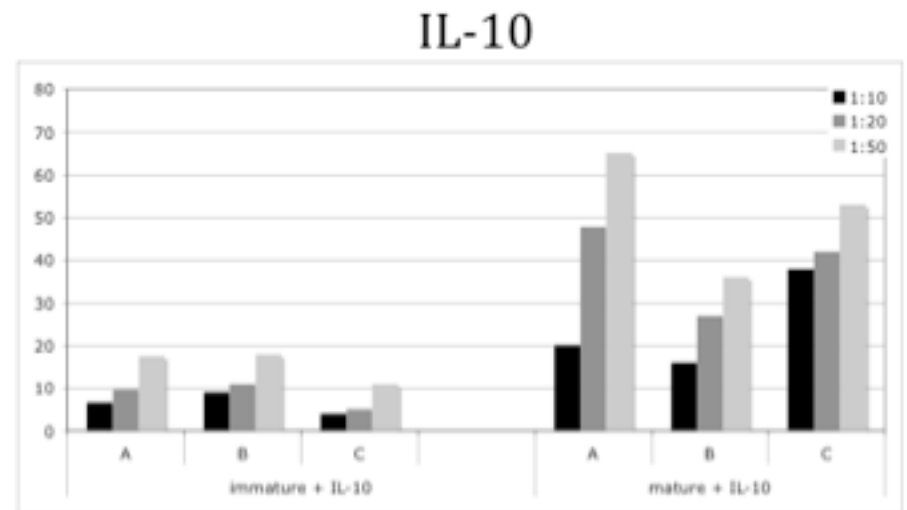
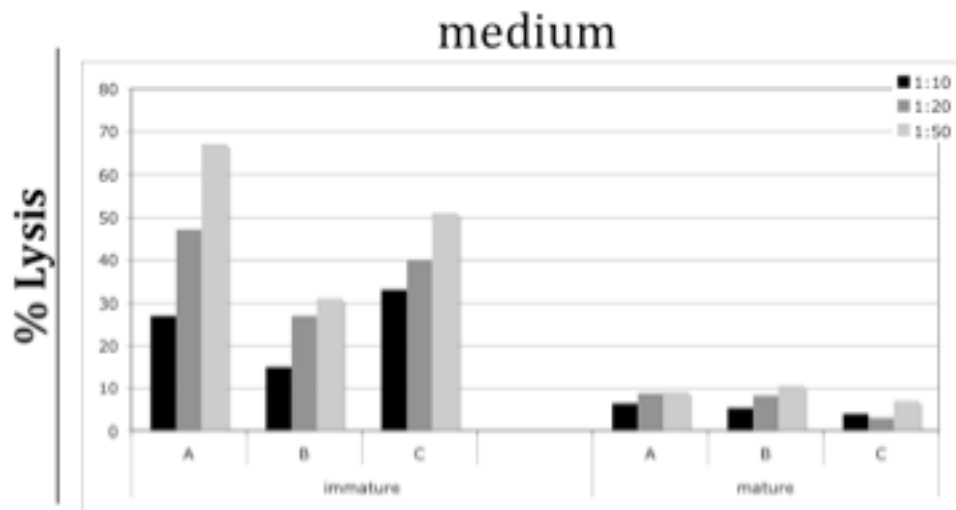


M. Brockman & D. Kwon et al. unpublished

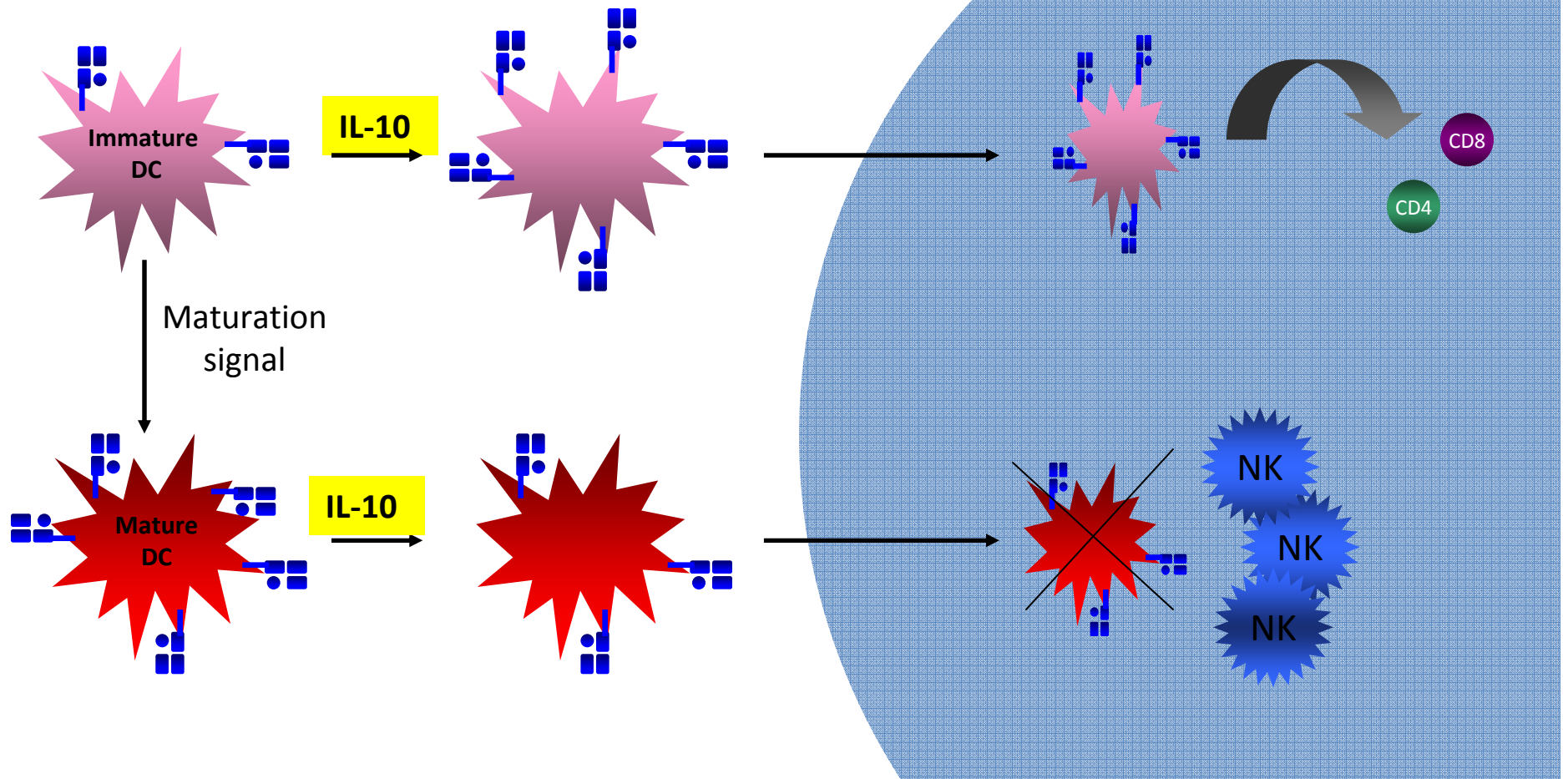
Inverse effects of IL-10 on mature and immature mDCs



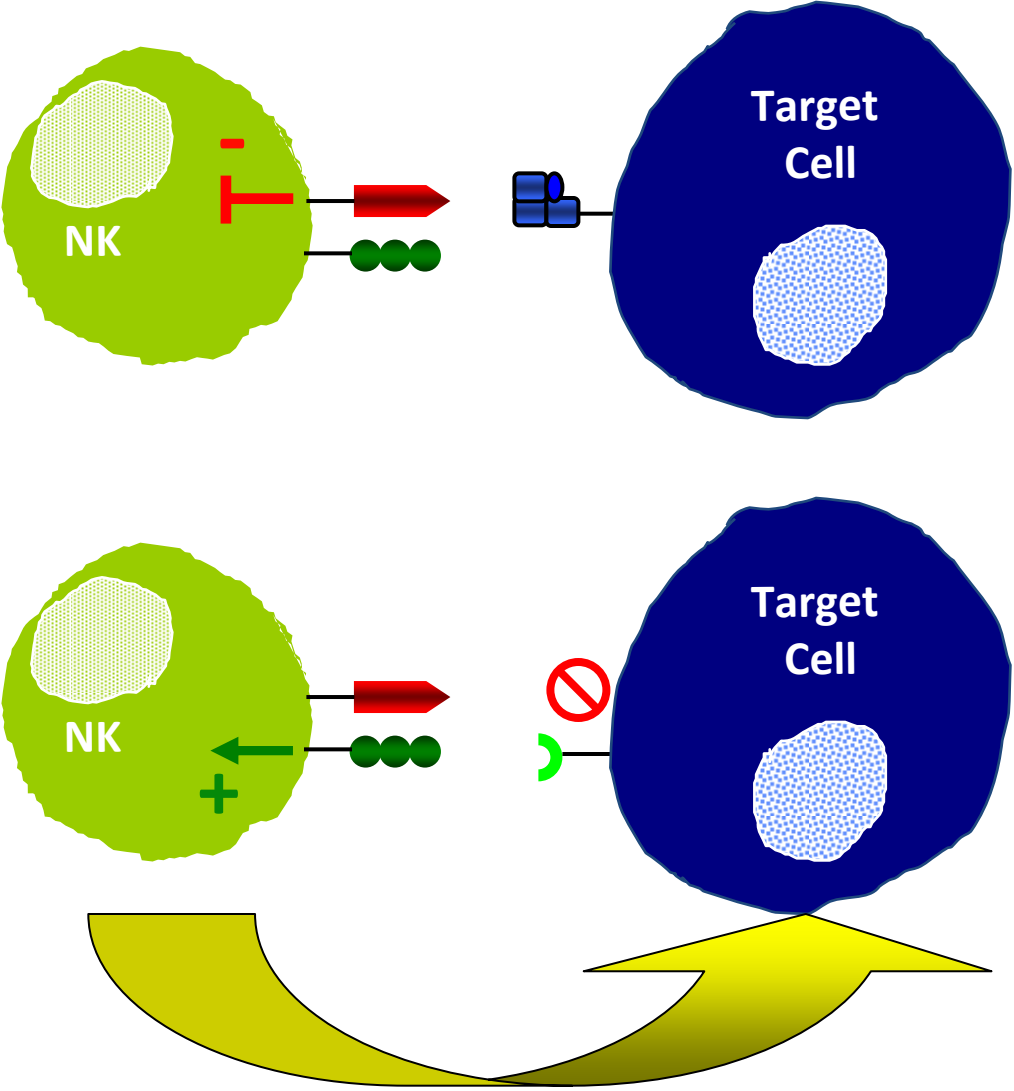
IL-10 protects immature mDCs but renders mature mDCs susceptible to NK cell lysis



IL-10 may skew the repertoire of DCs that reach the lymphnode to induce adaptive immune responses

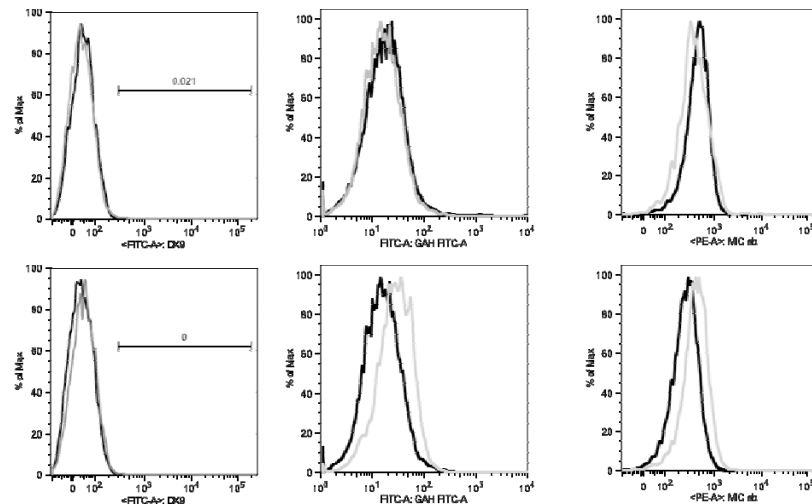


Natural Killer Cell Recognition of Target Cells



What are the NK cells recognizing on the DCs?

immature



IL-10
medium

mature

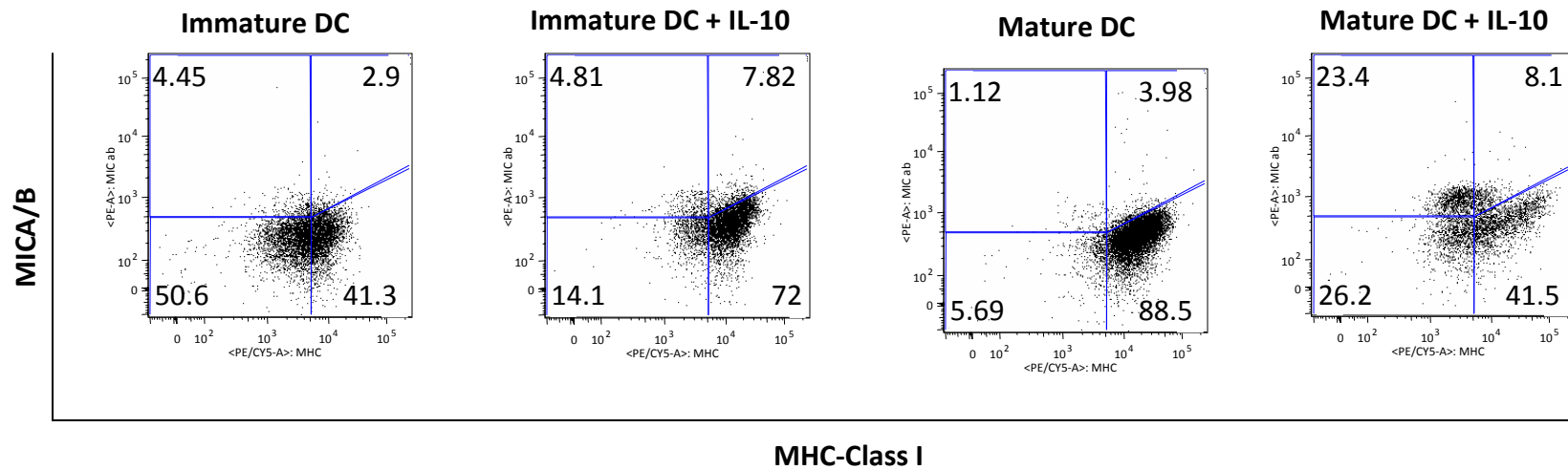


NKp30-FUSION
CONSTRUCT

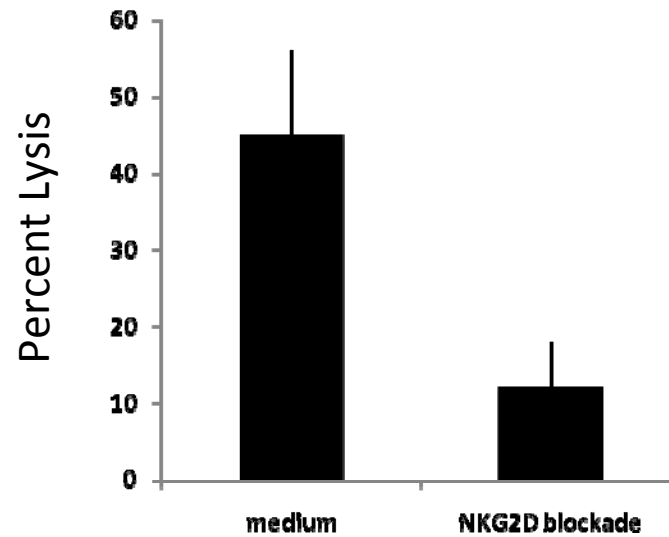
NKG2D-FUSION
CONSTRUCT

MIC A/B

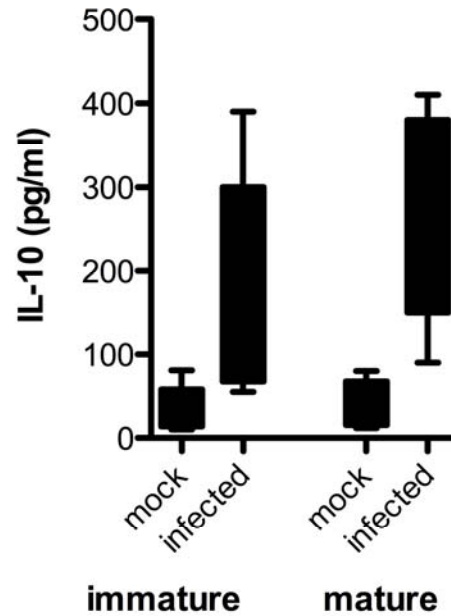
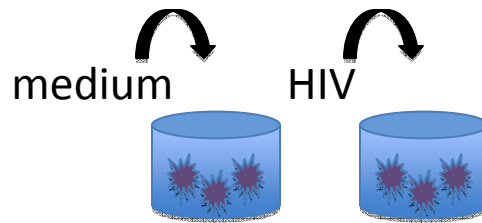
Increased expression of MICA/B on MHC-low mature DCs



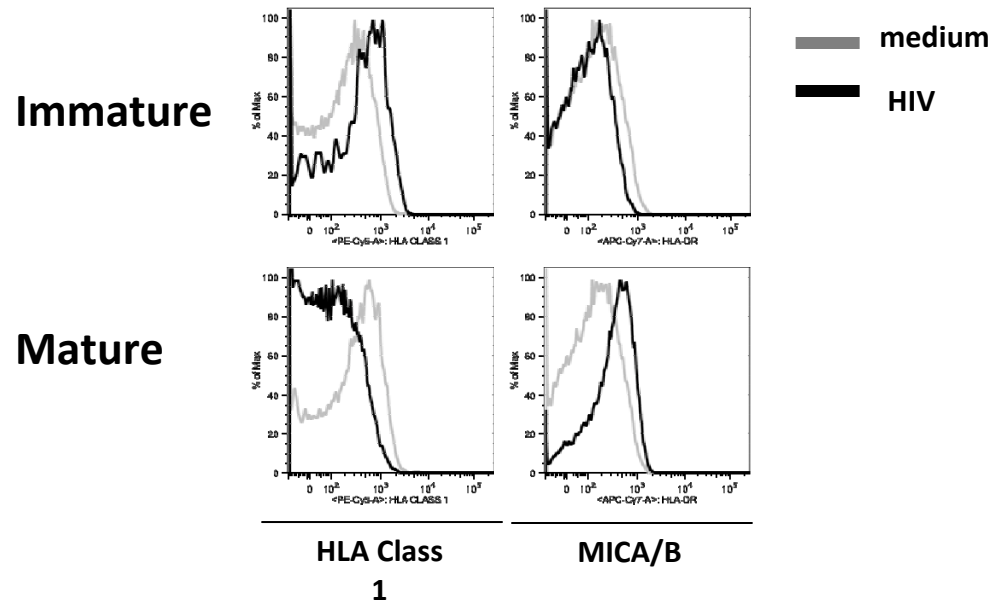
NK cells lyse IL-10 treated mature DCs in an NKG2D-dependent manner



HIV infection results in robust IL-10 production by DCs



HIV infection results downregulation of MHC and upregulation of MIC-A



Summary

- IL-10 skews DC populations, rendering mature DCs vulnerable to NKG2D-dependent NK cell mediated lysis, and protects immature DCs
- Exposure of DCs to HIV results to significant release of IL-10- responsible for aberrant NK cell editing
- Aberrant deletion of mature DCs by NK cells during HIV-1 infection may result in a deficit of highly immunogenic DCs required for the effective generation of adaptive immune responses
- Skewed accumulation of immature DCs may induce toleragenic signals that induce dysfunctional adaptive immune responses

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