SITC 2016

NATIONAL HARBOR, MD
NOVEMBER 9-13, 2016

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Society for Immunotherapy of Cancer

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IL-15 primes an mTOR-regulated gene-expression program to prolong anti-tumor capacity of human natural killer cells

Andreas Lundqvist

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Society for Immunotherapy of Cancer

#SITC2016

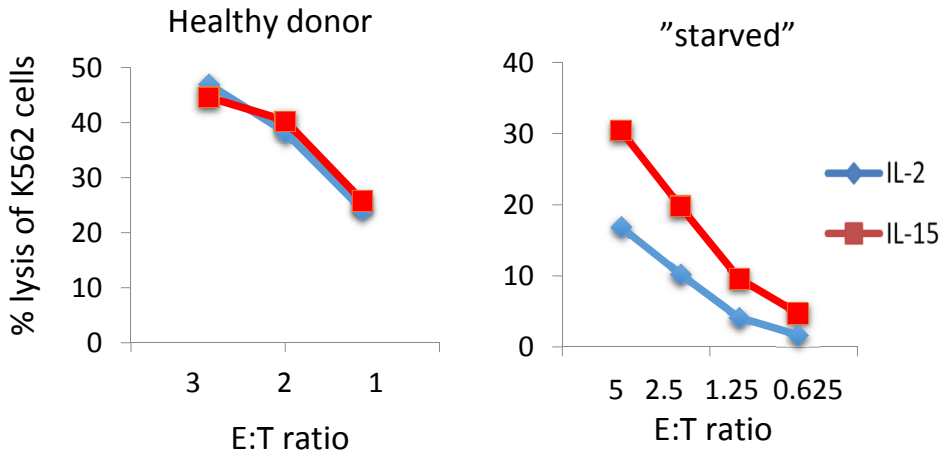
Presenter Disclosure Information

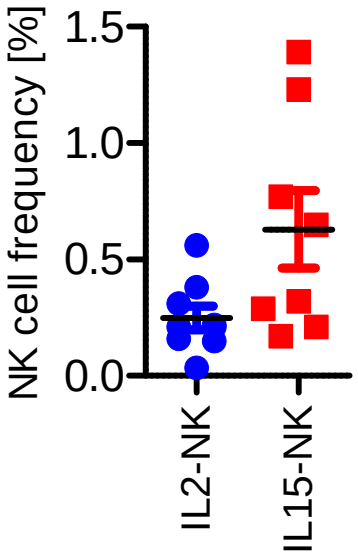
Andreas Lundqvist

The following relationships exist related to this presentation:

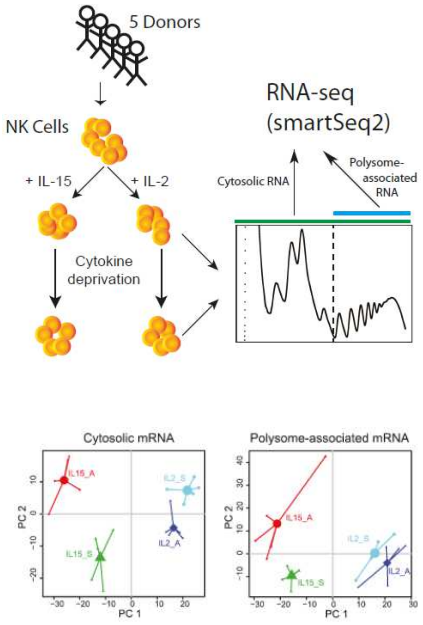
No Relationships to Disclose

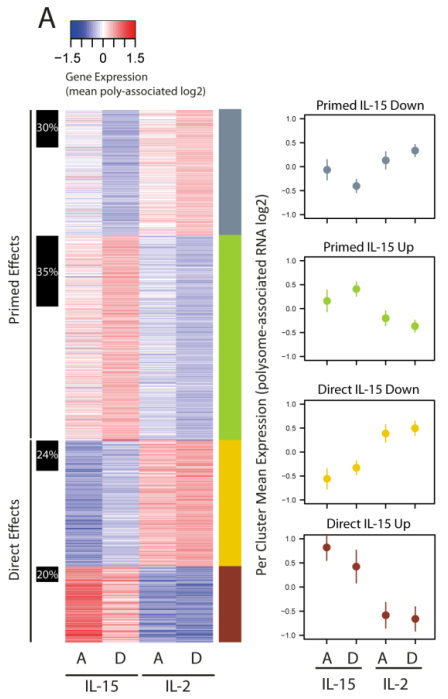
Increased in vivo persistence of IL-15 NK cells compared with IL-2 NK





Cytokine-activated NK cells display distinct gene expression programs in response to cytokine withdrawal





n=466 — transcription, cell signaling and developmental processes

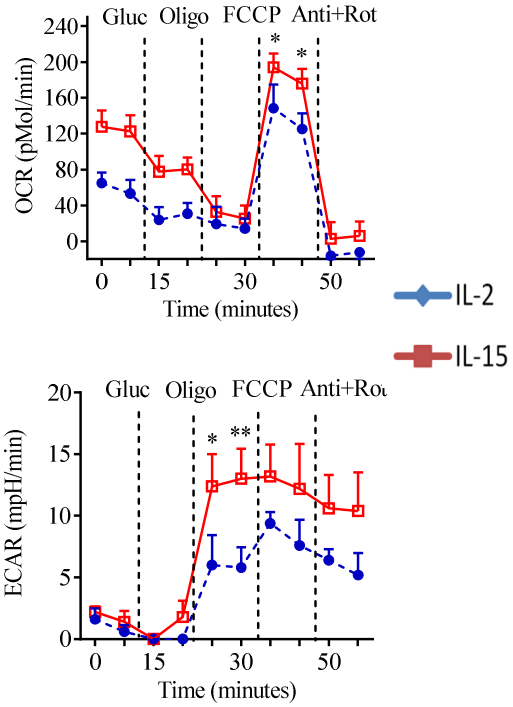
n=286 — respiration, metabolic processes and translation

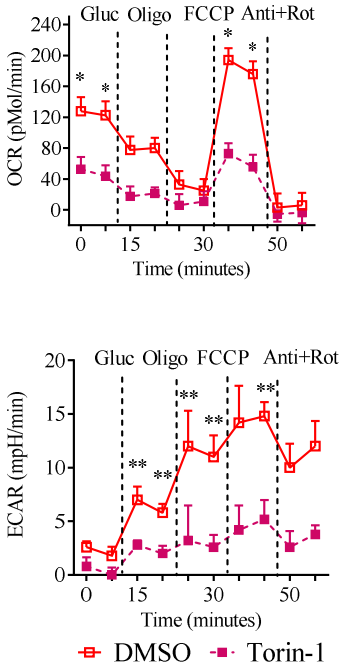
n=173 — cell motility, development and cell signaling

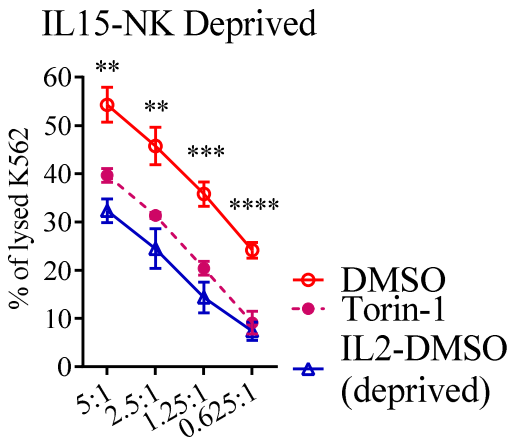
n=287 — cell cycle functions

FDR<0.15 and fold change>1.5

IL-15 sustains anti-tumor functions of NK cells through mTOR-governed metabolic processes.







Mao Y, van Hoef V. Blood. 2016 Sep

NK cell activity is suppressed by prostaglandin E2

Cancer Therapy: Preclinical

Clinical Cancer Research

Human Anaplastic Thyroid Carcinoma Cells Are Sensitive to NK Cell–Mediated Lysis via ULBP2/5/6 and Chemoattract NK Cells

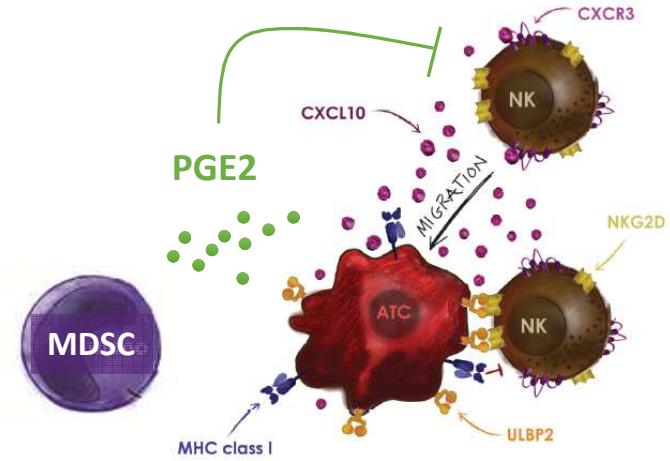
Erik Wennerberg[1], Aline Pfefferle[1], Lars Ekblad[2], Yuya Yoshimoto[1], Veronika Kremer[1], Vitaliy O Kaminskyy[3], C Christofer Juhlin[1], Anders Höög[1], Inger Bodin[1], Vitalijs Svjatoha[1], Catharina Larsson[1], Jan Zedenius[4], Johan Wennerberg[5], and Andreas Lundqvist[1]

Biology of Human Tumors

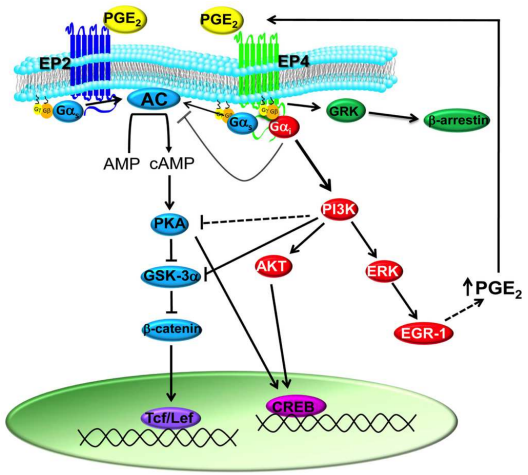
Clinical Cancer Research

Inhibition of Tumor-Derived Prostaglandin-E2 Blocks the Induction of Myeloid-Derived Suppressor Cells and Recovers Natural Killer Cell Activity

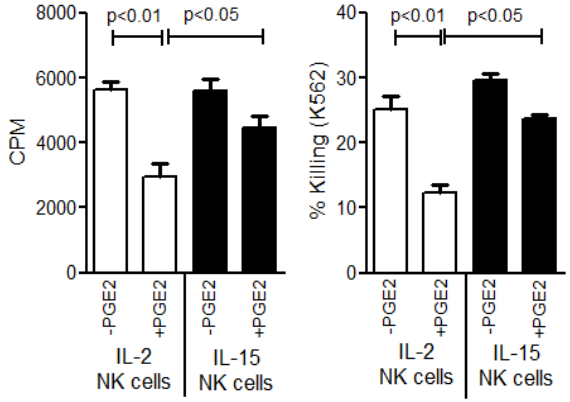
Yumeng Mao[1], Dhifaf Sarhan[1], André Steven[2], Barbara Seliger[2], Rolf Kiessling[1], and Andreas Lundqvist[1]



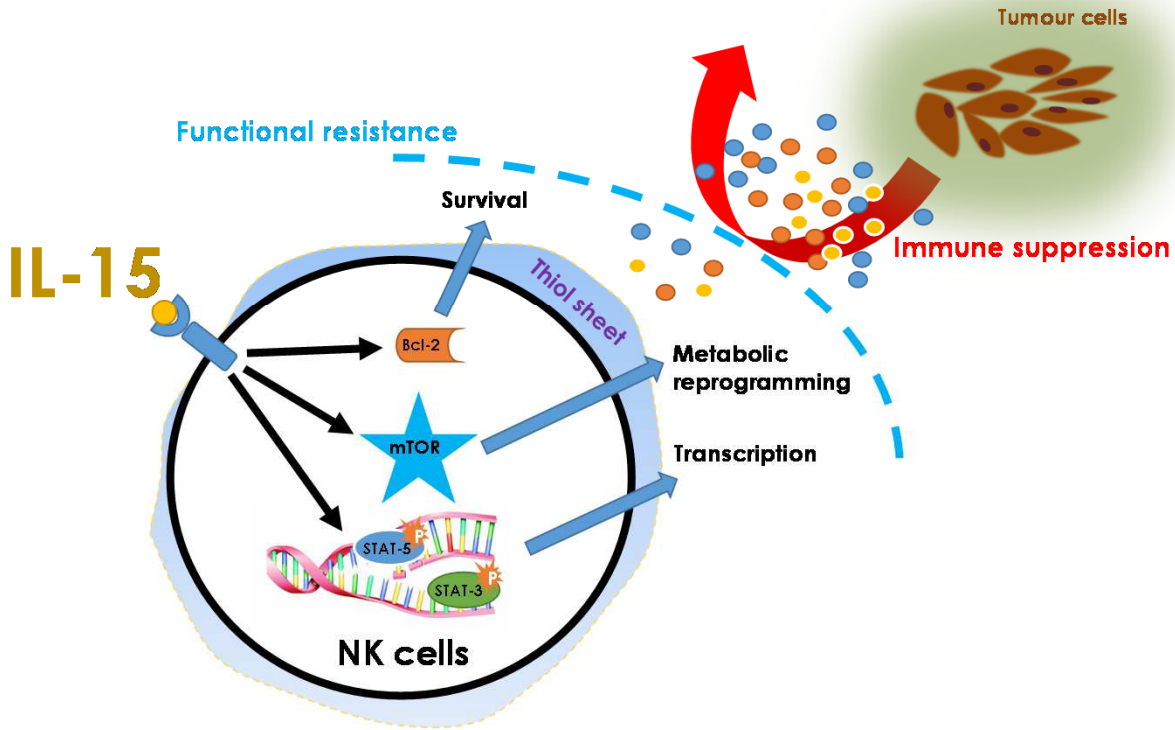
IL-15 NK cells are less susceptible to PGE2-mediated suppression



Changes in gene expression suggesting that IL-15 renders NK cells less susceptible to PGE2-mediated suppression *PKA, CREBBP, CREBRF, CREBZF*



Interleukin-15 potentiates functional persistence of human natural killer cells through mTOR-regulated metabolic control



Lessons and Take Home Messages

- Increased in vivo persistence of IL-15 NK cells compared with IL-2 NK cells
- Cytokine-activated NK cells display distinct gene expression programs in response to cytokine withdrawal
- IL-15 sustains anti-tumor functions of NK cells through mTOR-governed metabolic processes.
- IL-15 NK cells are less susceptible to PGE2-mediated suppression

…

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- Increased in vivo persistence of IL-15 NK cells compared with IL-2 NK
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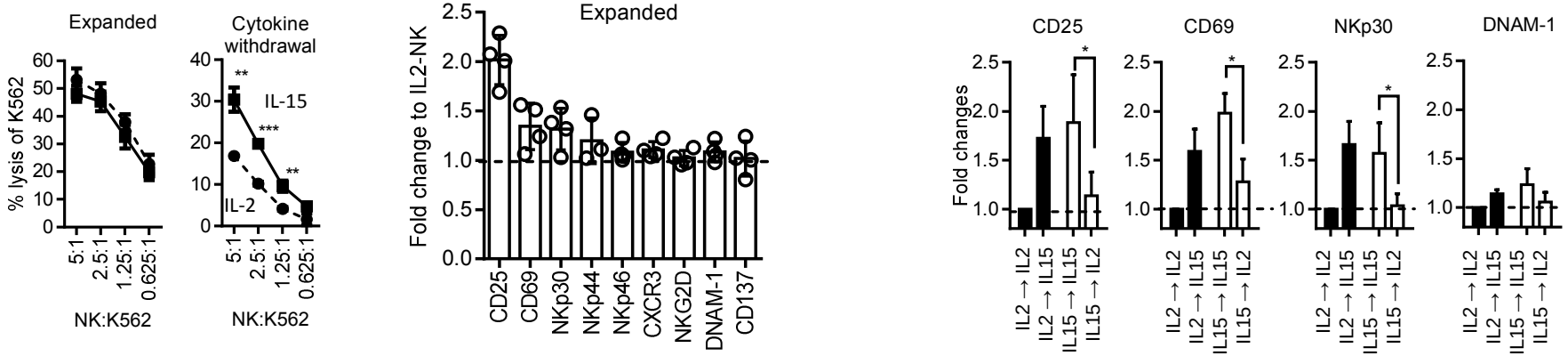
- IL-15 sustains anti-tumor functions of NK cells through mTOR-governed metabolic processes.
- IL-15 NK cells are less susceptible to PGE2-mediated suppression

…Activate/Expand NK cells in IL-15 and not IL-2…

Maintained NK cell phenotype by IL-15



Ackowledgements

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erc
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