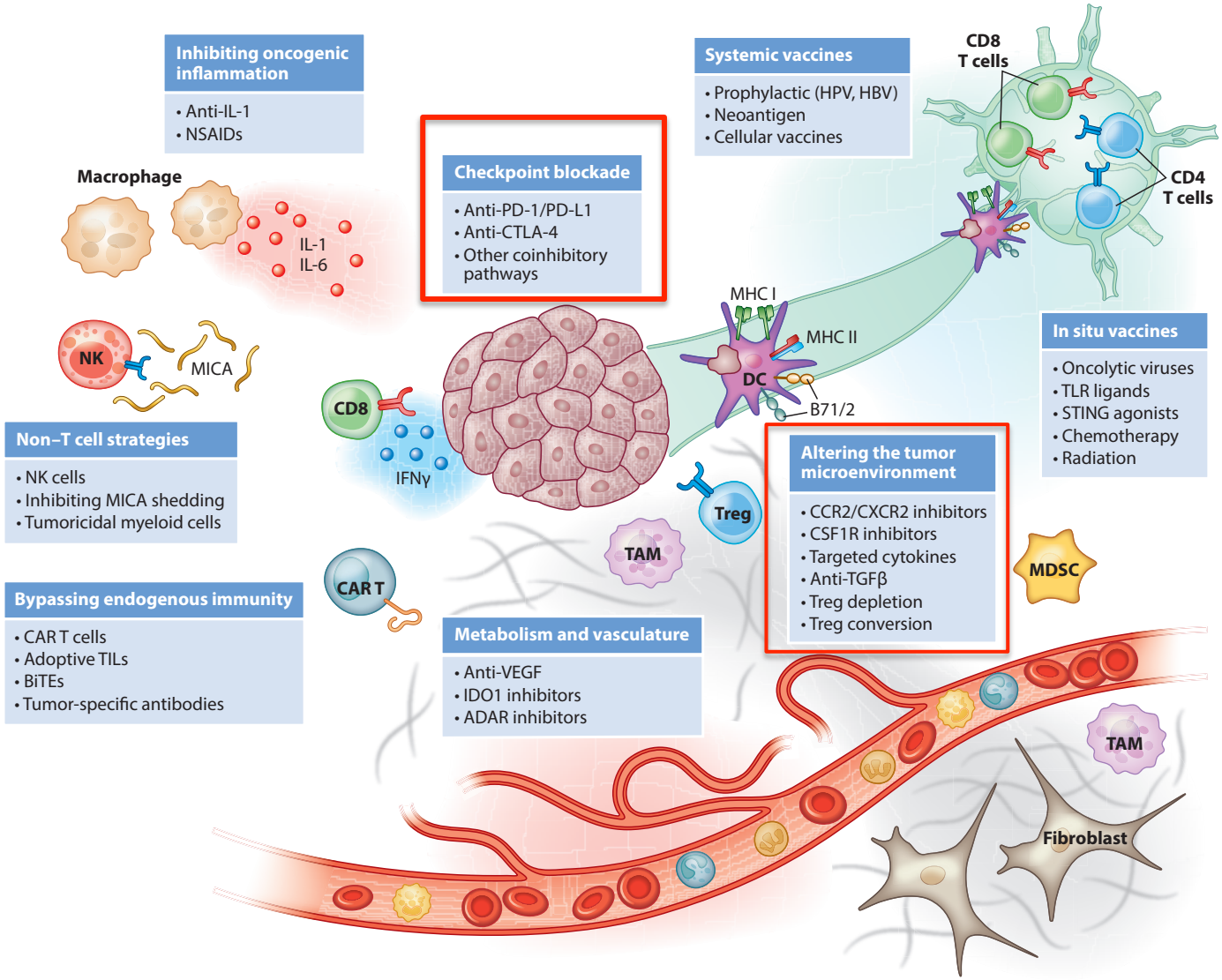
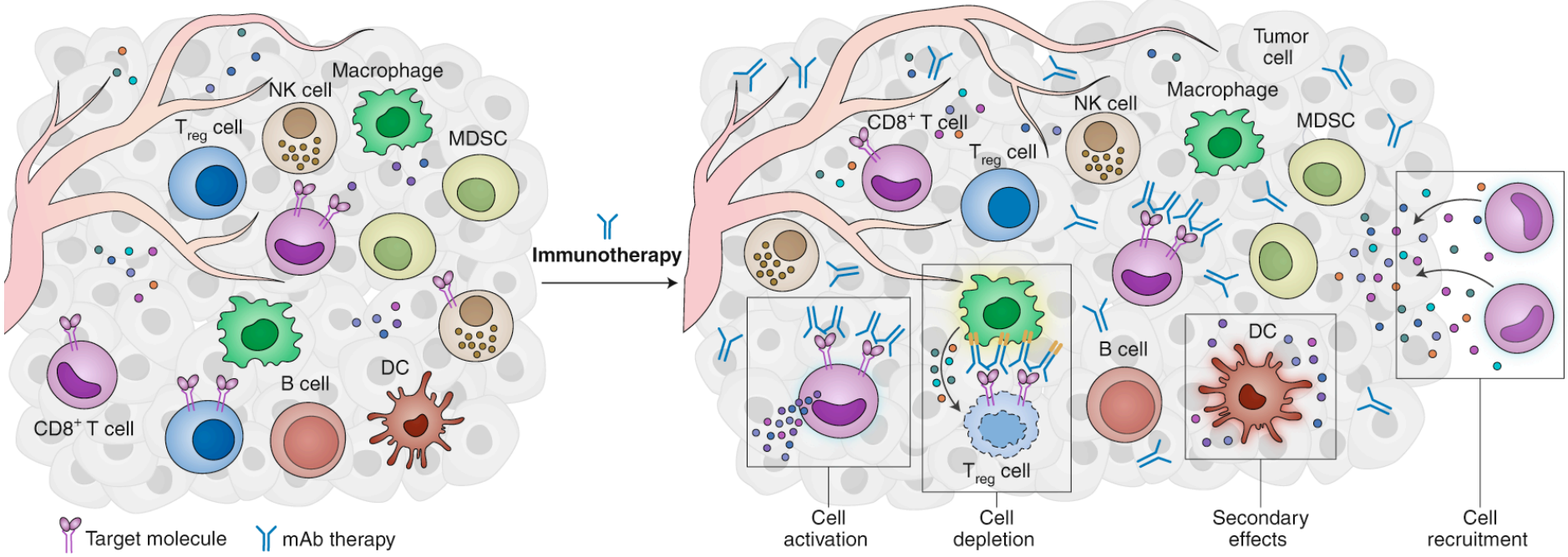
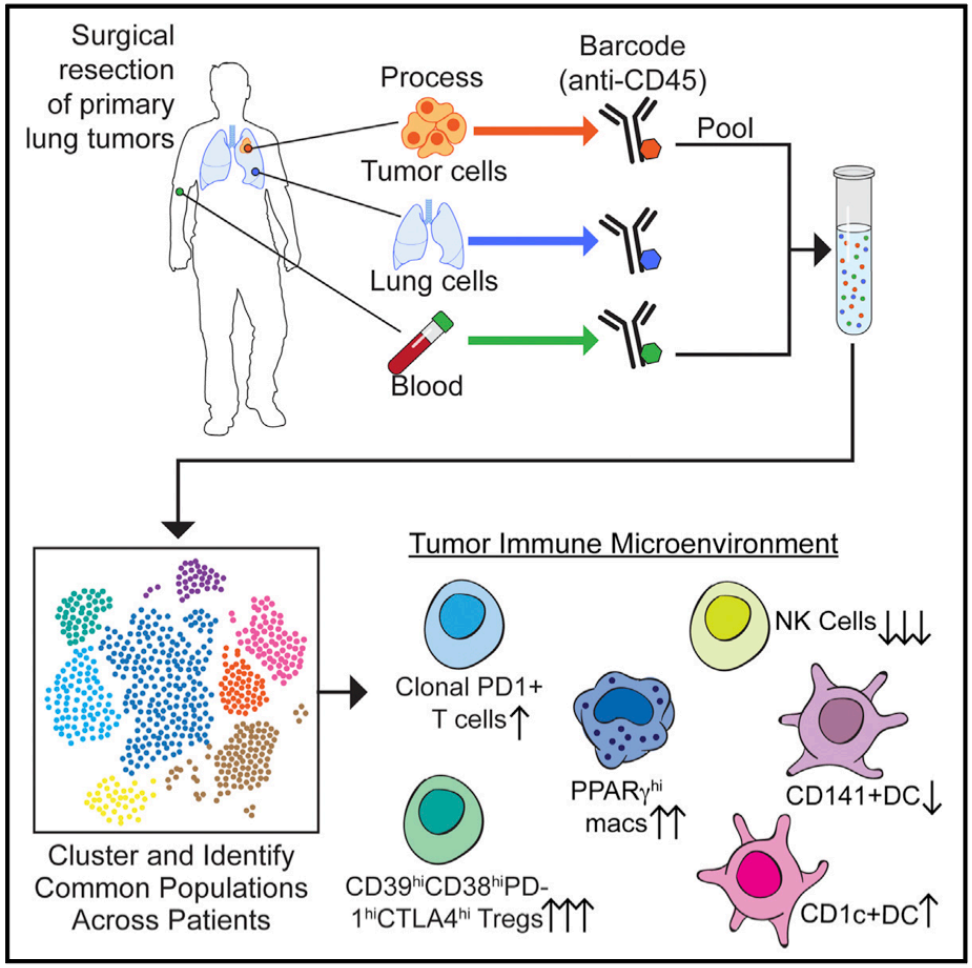
Immunotherapy: beyond checkpoint inhibitors

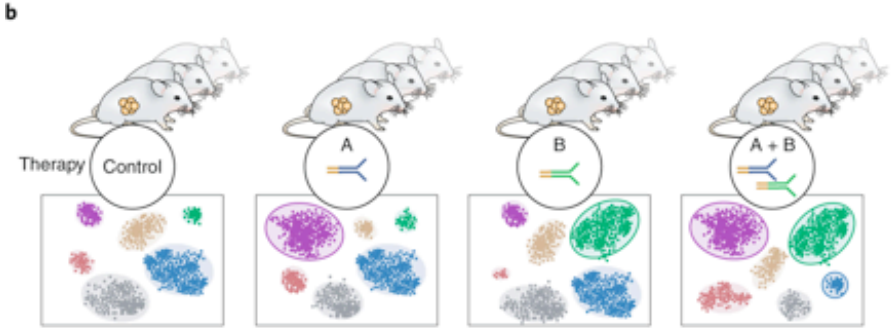


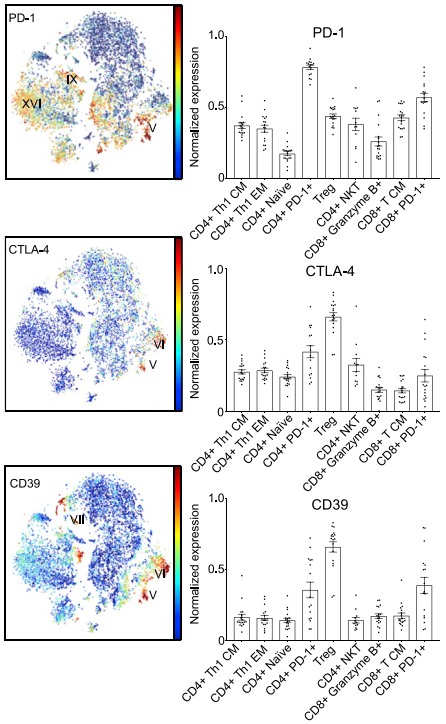
Integration of multiple approaches to understand the effect of immunotherapy combinations on the tumor microenvironment and to predict future targets



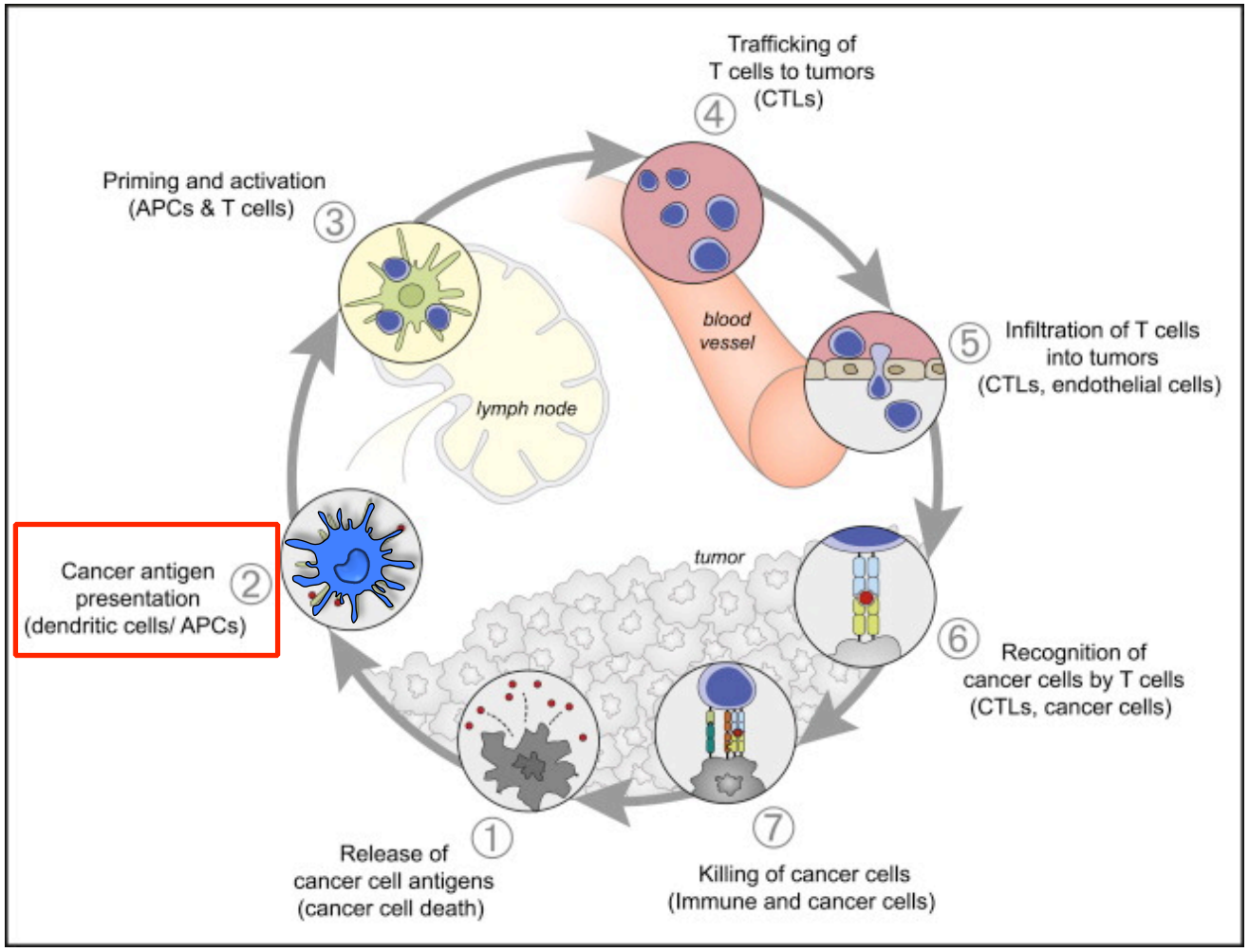
Single-cell approaches are used to understand modifications and to develop new therapies







The cancer immunity cycle



Type 1 dendritic cells (cDC1) and anti cancer responses

Article

Cell

NK Cells Stimulate Recruitment of cDC1 into the Tumor Microenvironment Promoting Cancer Immune Control

Article

Cancer Cell

Tumor-Residing Batf3 Dendritic Cells Are Required for Effector T Cell Trafficking and Adoptive T Cell Therapy

Article

Cell

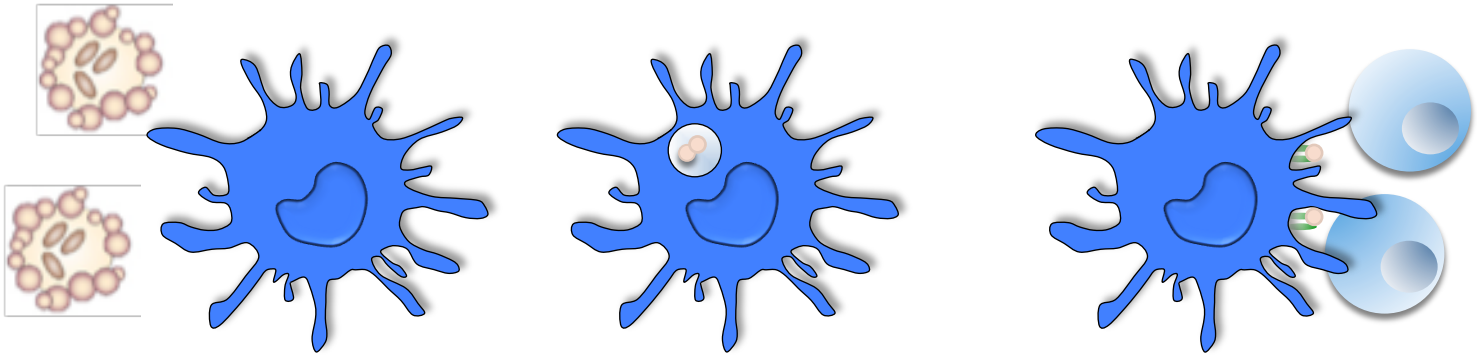
Cyclooxygenase-Dependent Tumor Growth through Evasion of Immunity

nature COMMUNICATIONS

ARTICLE

DOI: 10.1038/s41467-017-02186-9 OPEN

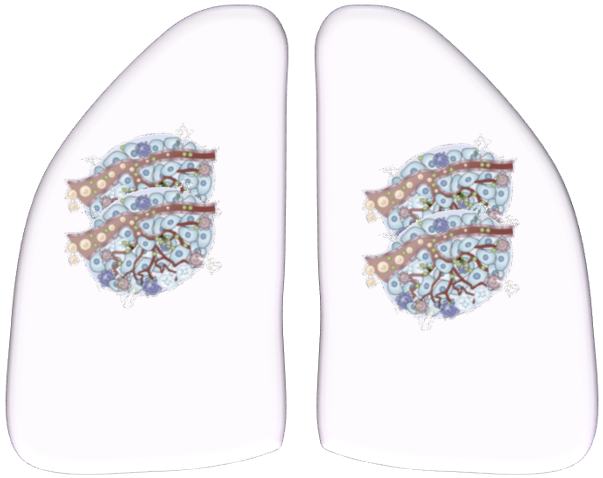
Lipid bodies containing oxidatively truncated lipids block antigen cross-presentation by dendritic cells in cancer

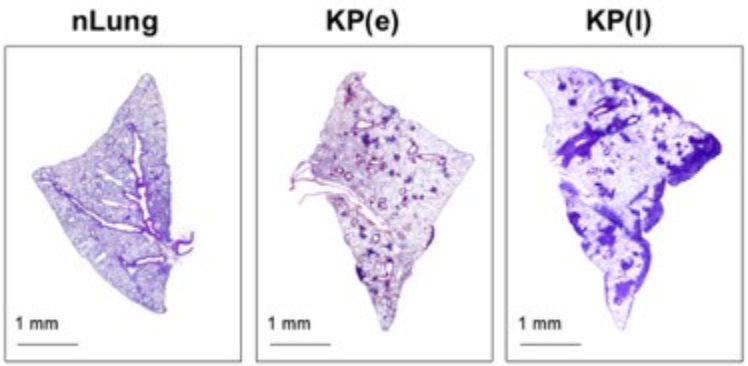


uptake processing presentation

A genetically driven model of lung cancer to study cDC1 function

$Kras^{(12D+)}$ /$p53^{-/-}$ (KP) adenocarcinoma of the lung





Orthotopic implantation

↓

Tissue dissociation

↓

Identification of bone fide cDC1

↓

Cell sorting

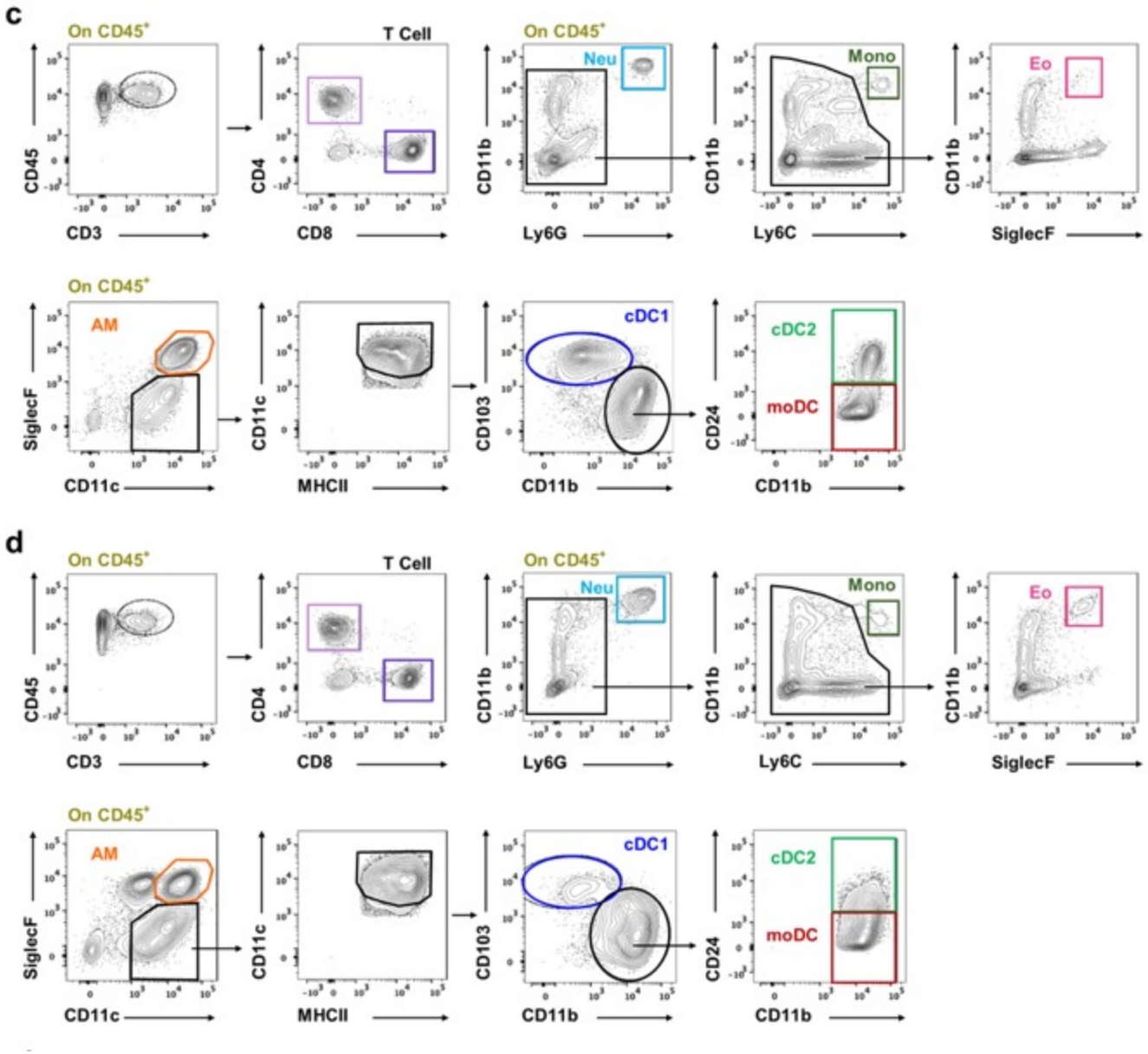
↓

Gene expression analysis

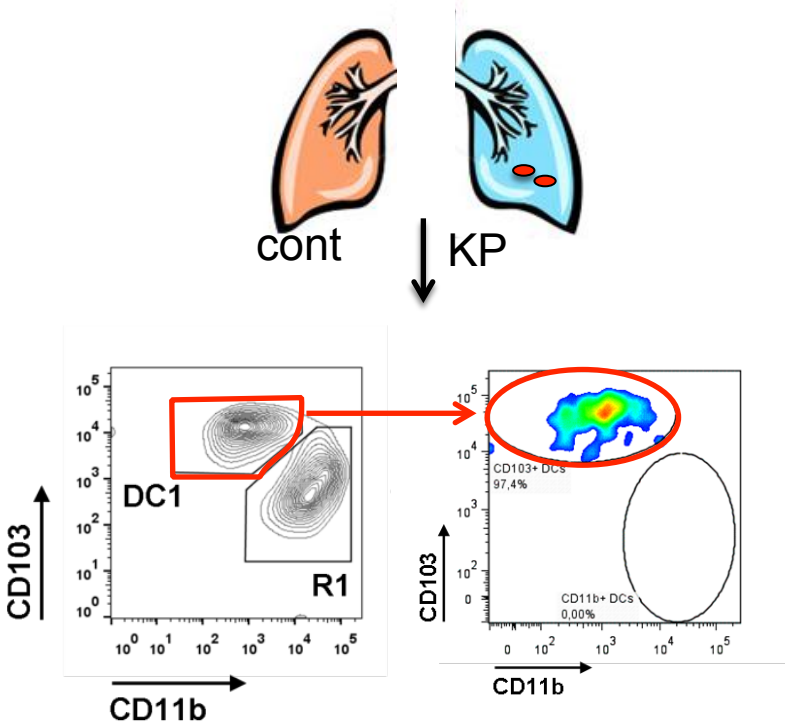
↙ ↓ ↘

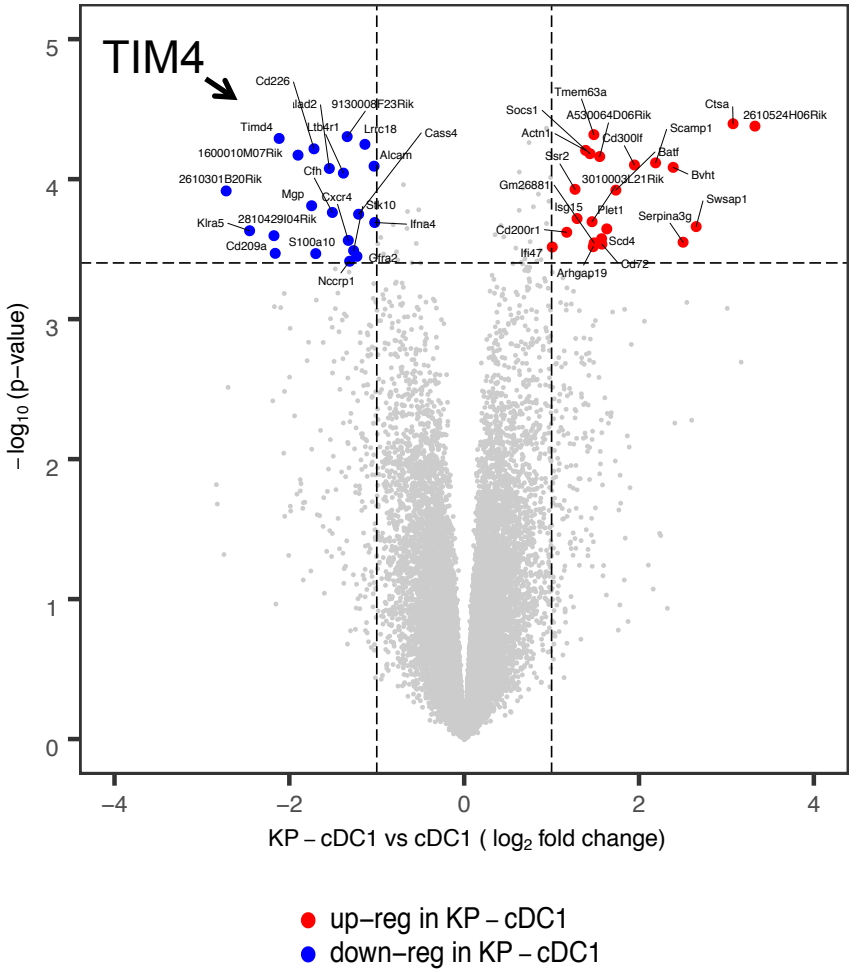
Functional validation

Multiparametric flow cytometry

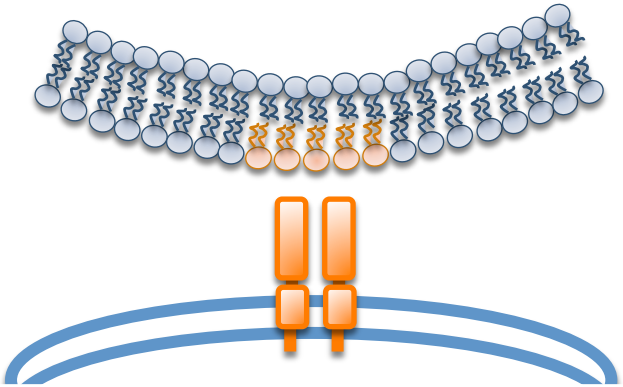


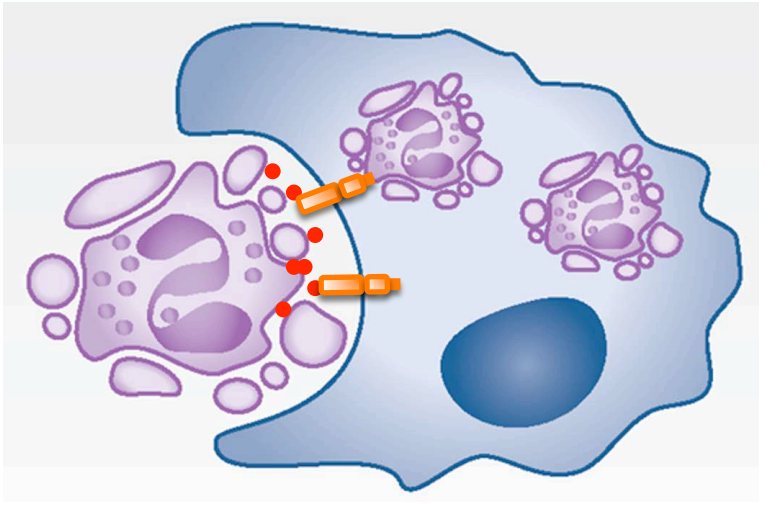
Differential gene expression in cDC1 from tumor free and tumor bearing lungs





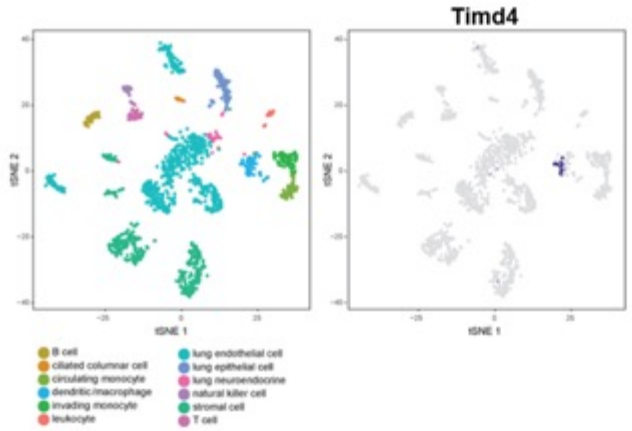
TIM4 is a receptor for phosphatidylserine implicated in the uptake of dying cells (efferocytosis) by macrophages

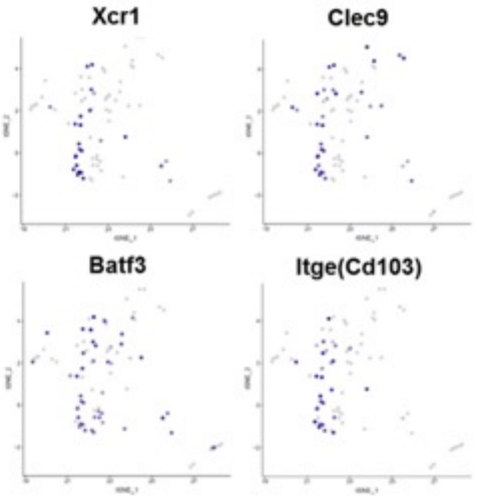


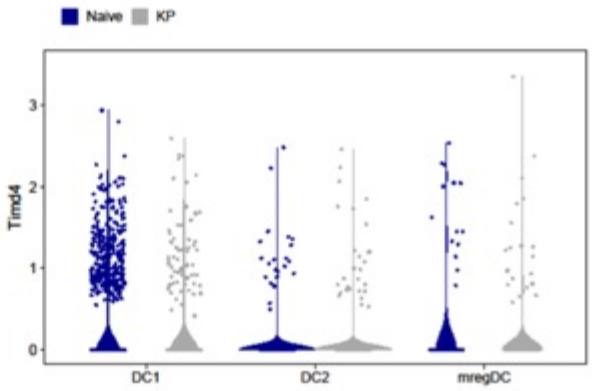


T-cell immunoglobulin
and mucin domain containing
molecule

TIM4 is exclusively expressed by lung cDC1







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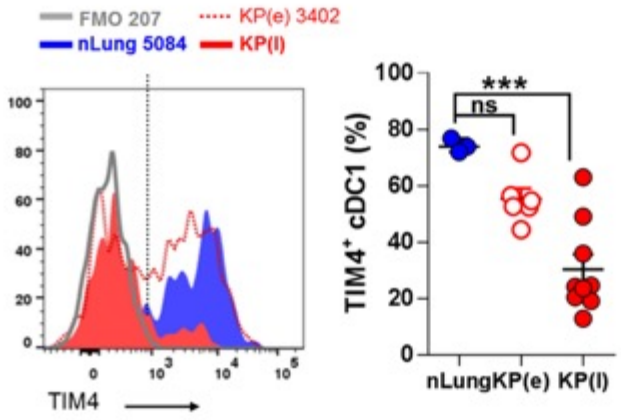

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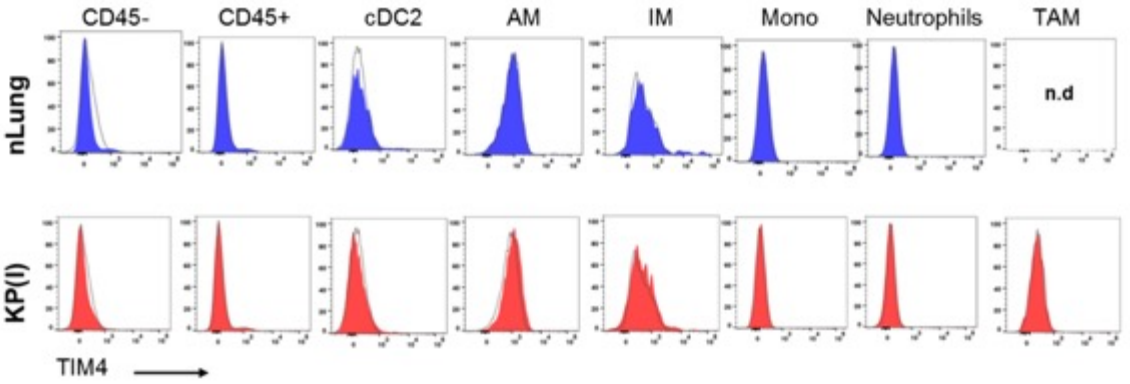
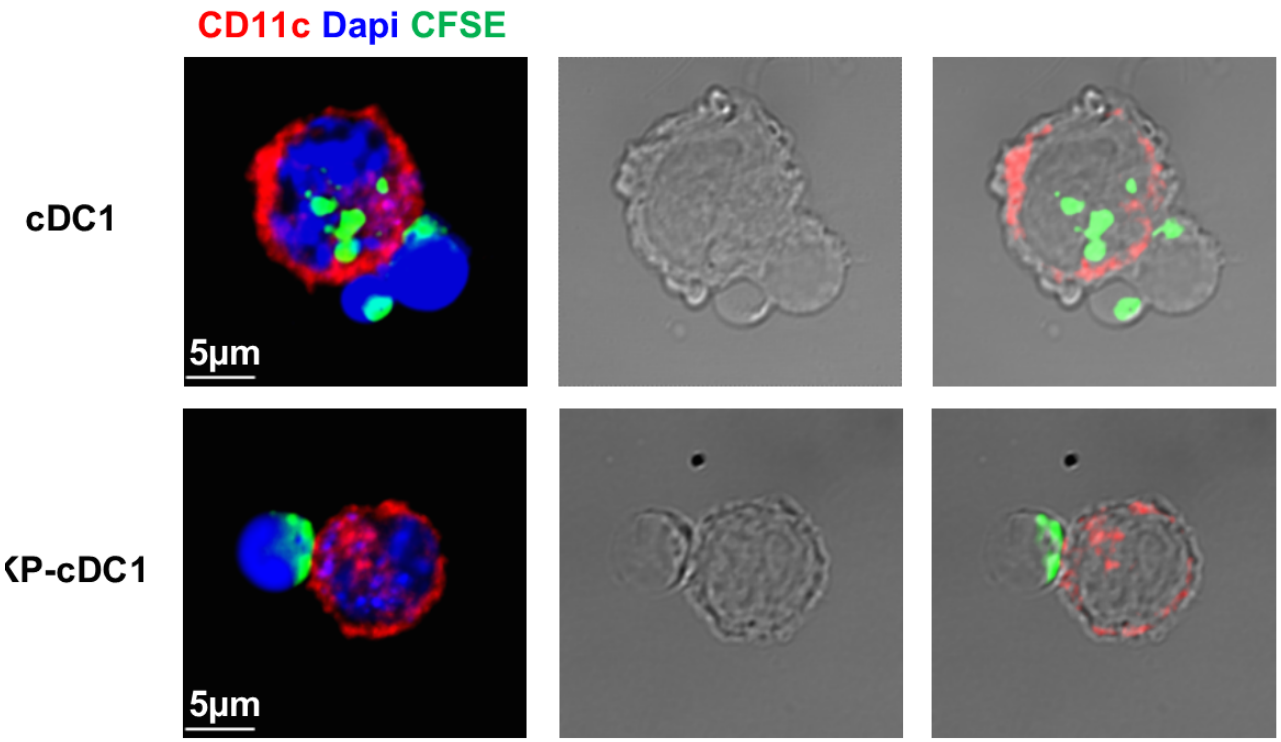
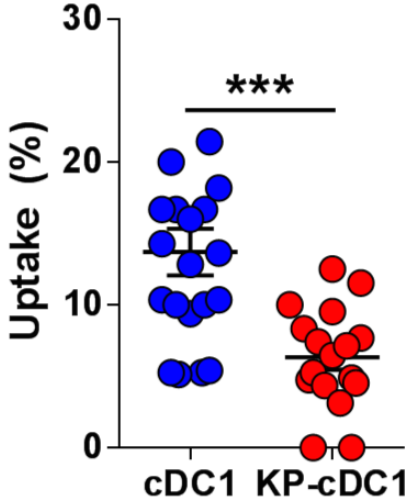
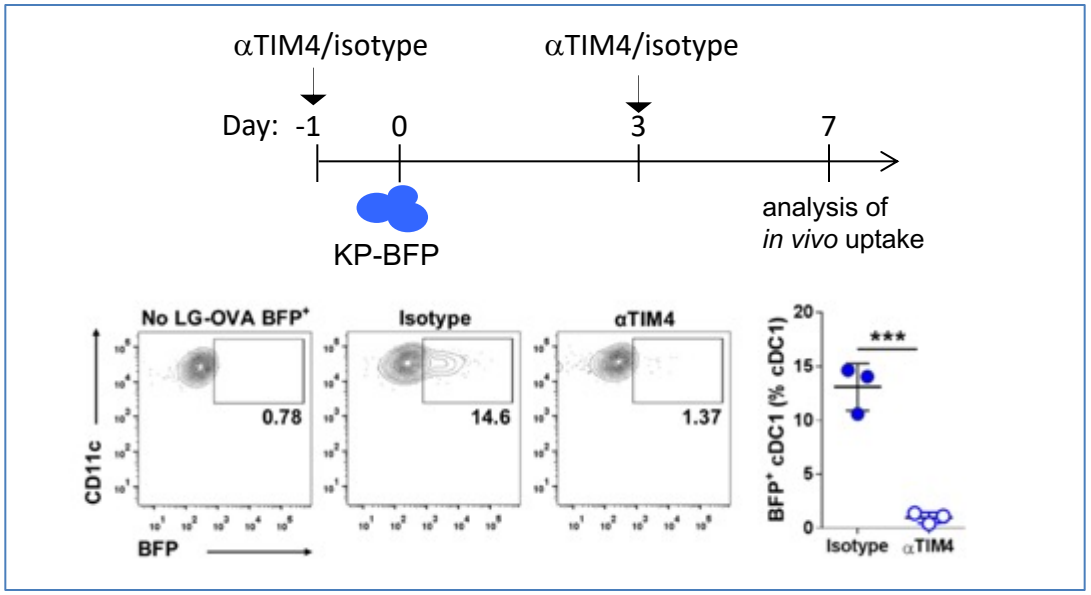


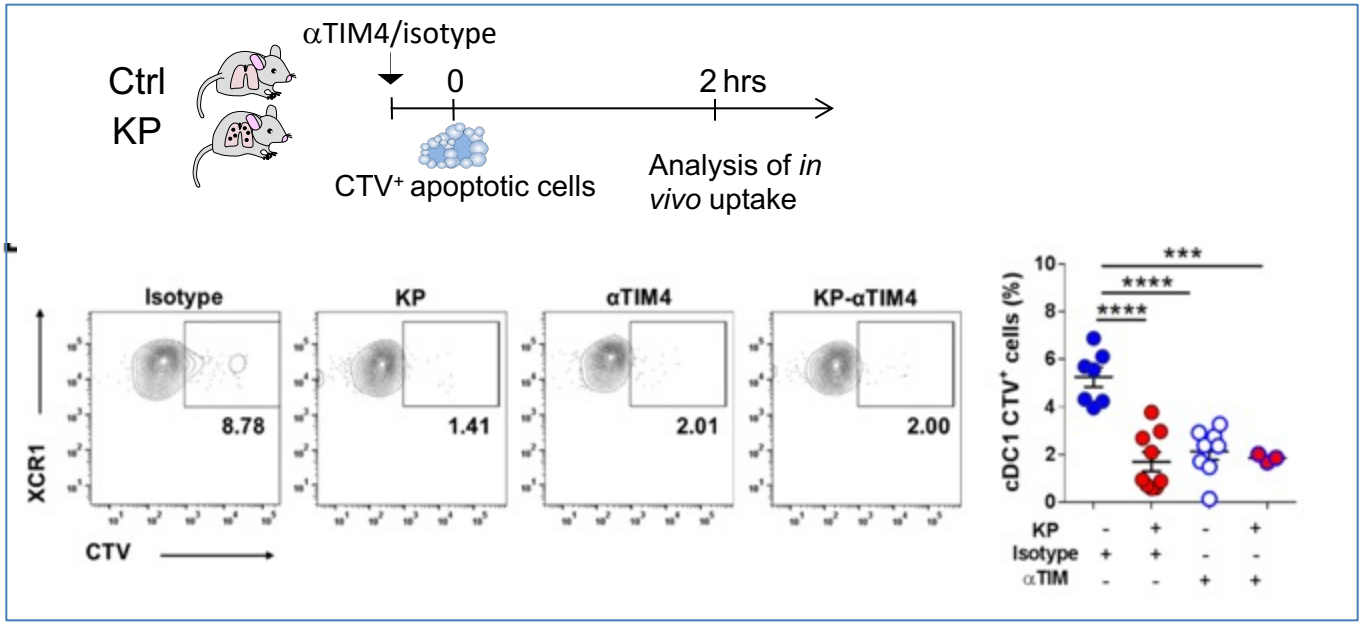
TIM4 controls efferocytosis by lung cDC1



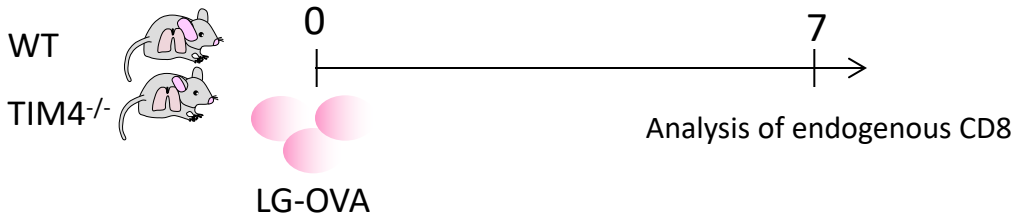


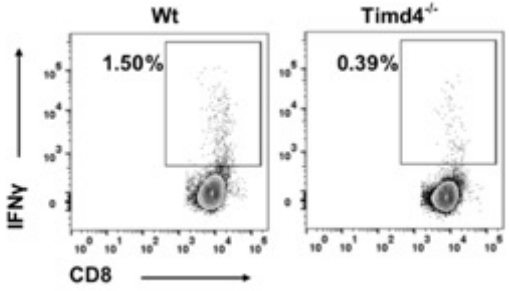
TIM4 controls uptake of tumor cells and apoptotic cells

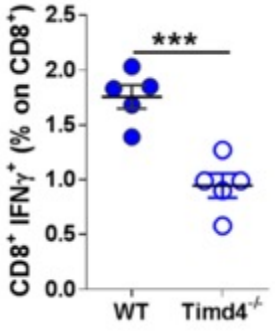


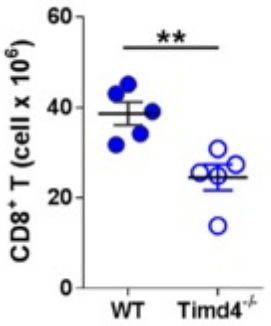


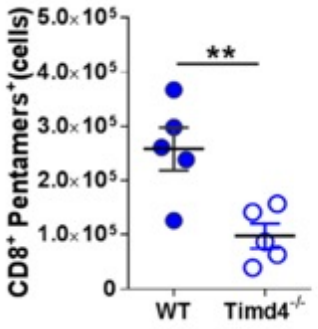
TIM4 controls activation and expansion of tumor specific CD8



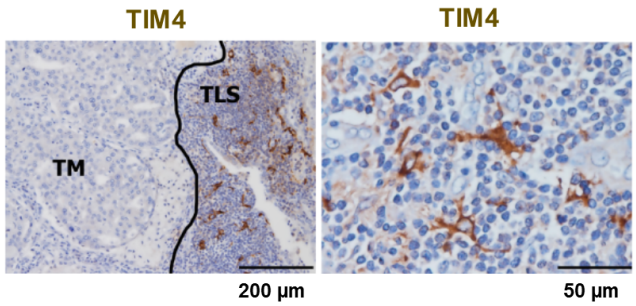


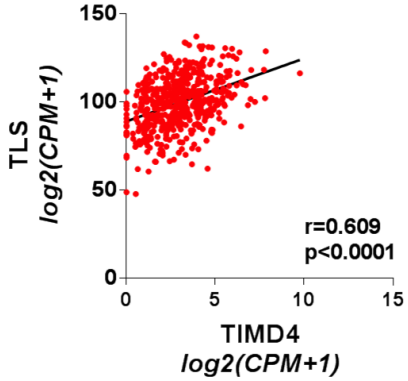


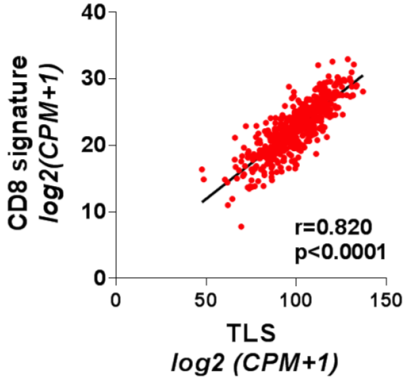


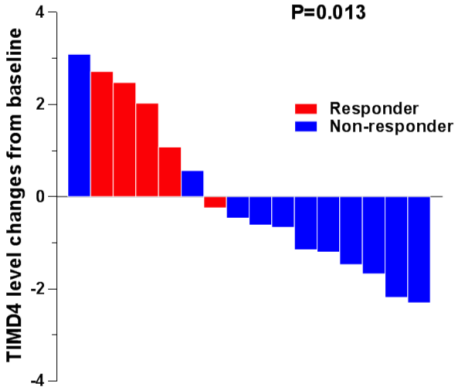


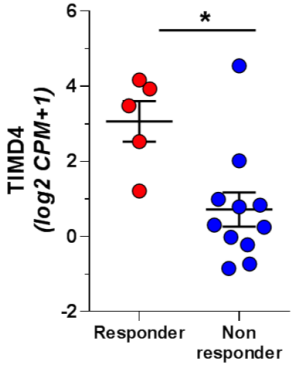
TIM4 is expressed on human cDC1 localized in tumor associated lymphoid structures and predicts responses to PD-1 therapy

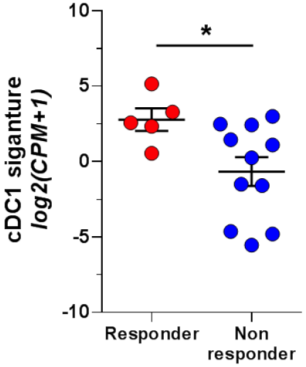


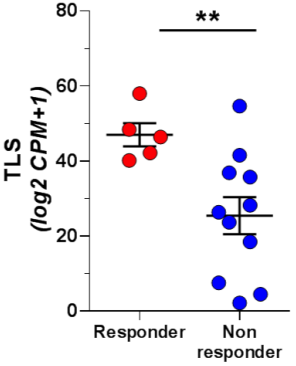


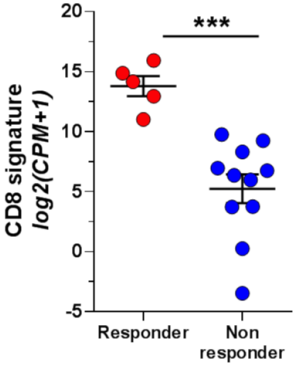




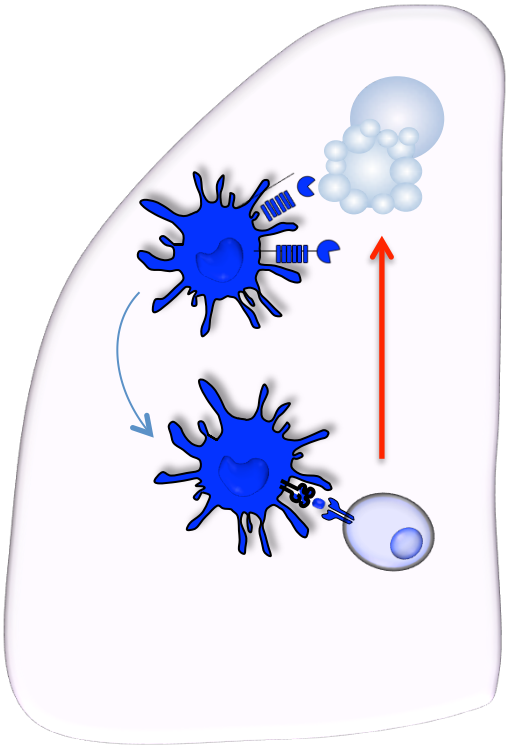




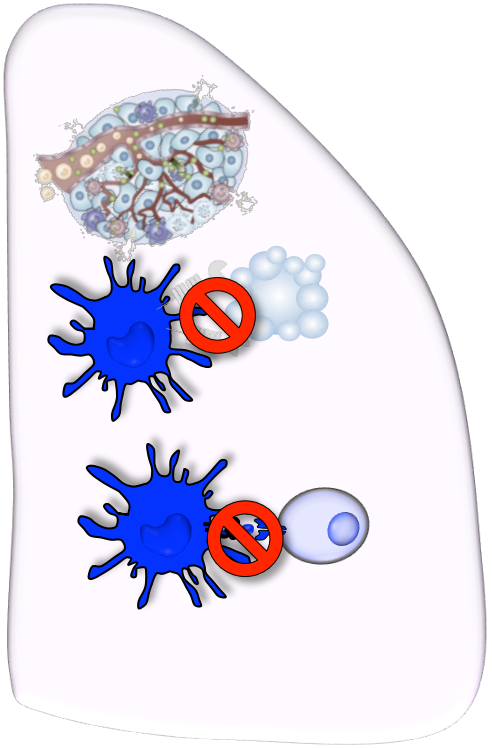




TIM4 downregulation is a novel mechanism of tumor immune evasion



Tissue surveillance by TIM4



TIM4 downregulation and tumor immune escape