

The manifold nature of myeloid cells in tuberculosis

Mechanisms behind chronic infections

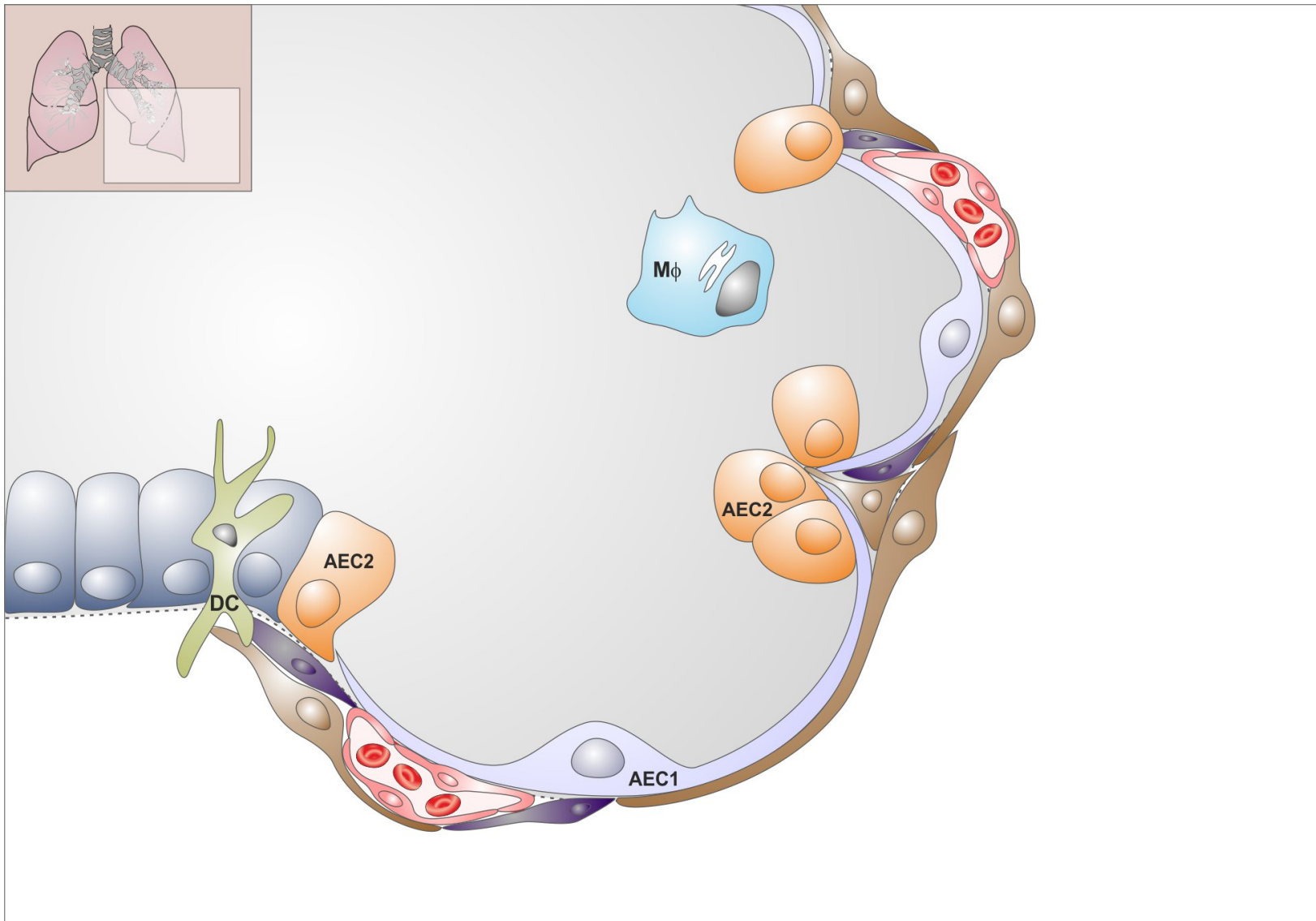
Les Pensières, Fondation Mérieux
Conference Center

May 4 2016

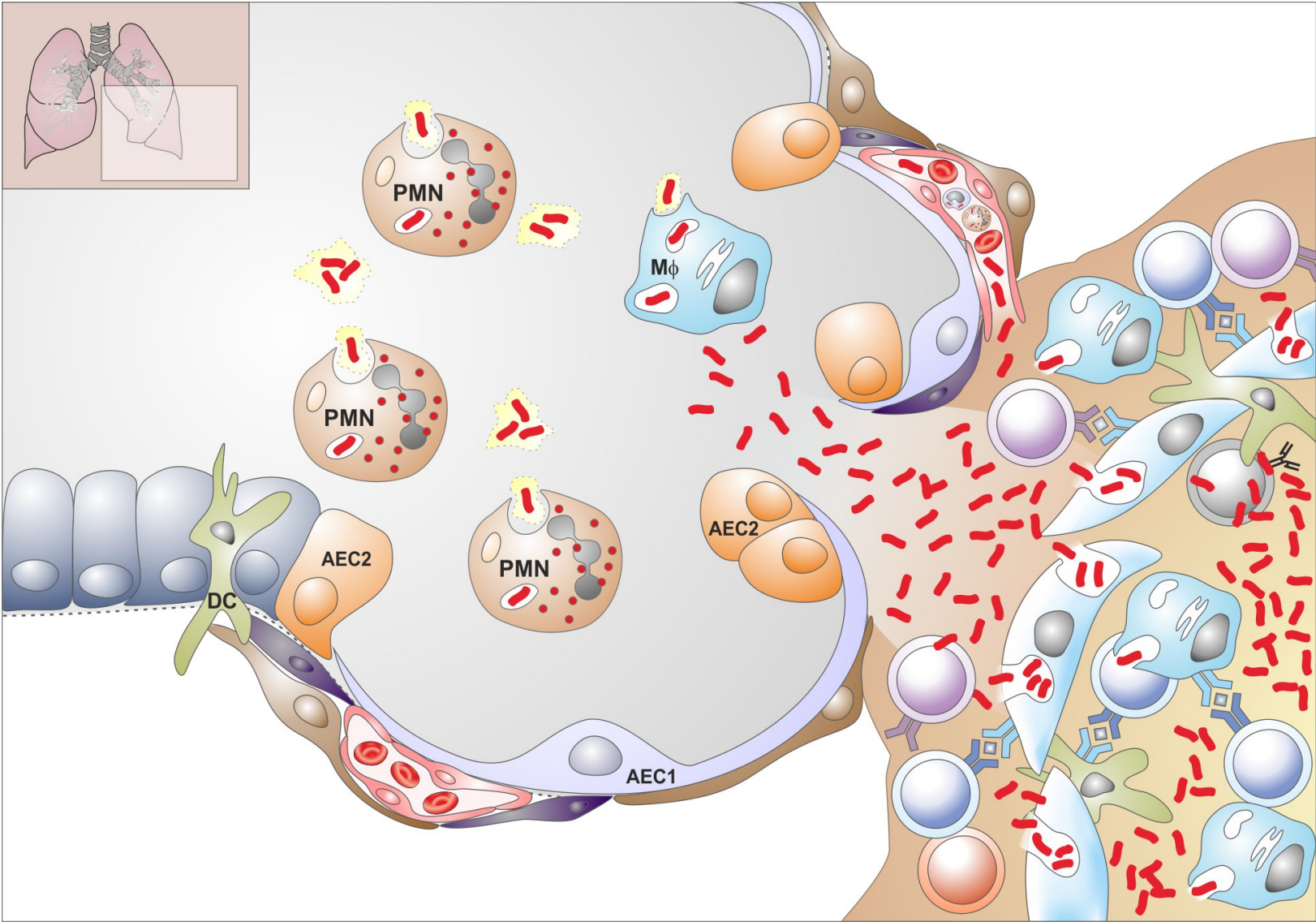
Anca Dorhoi



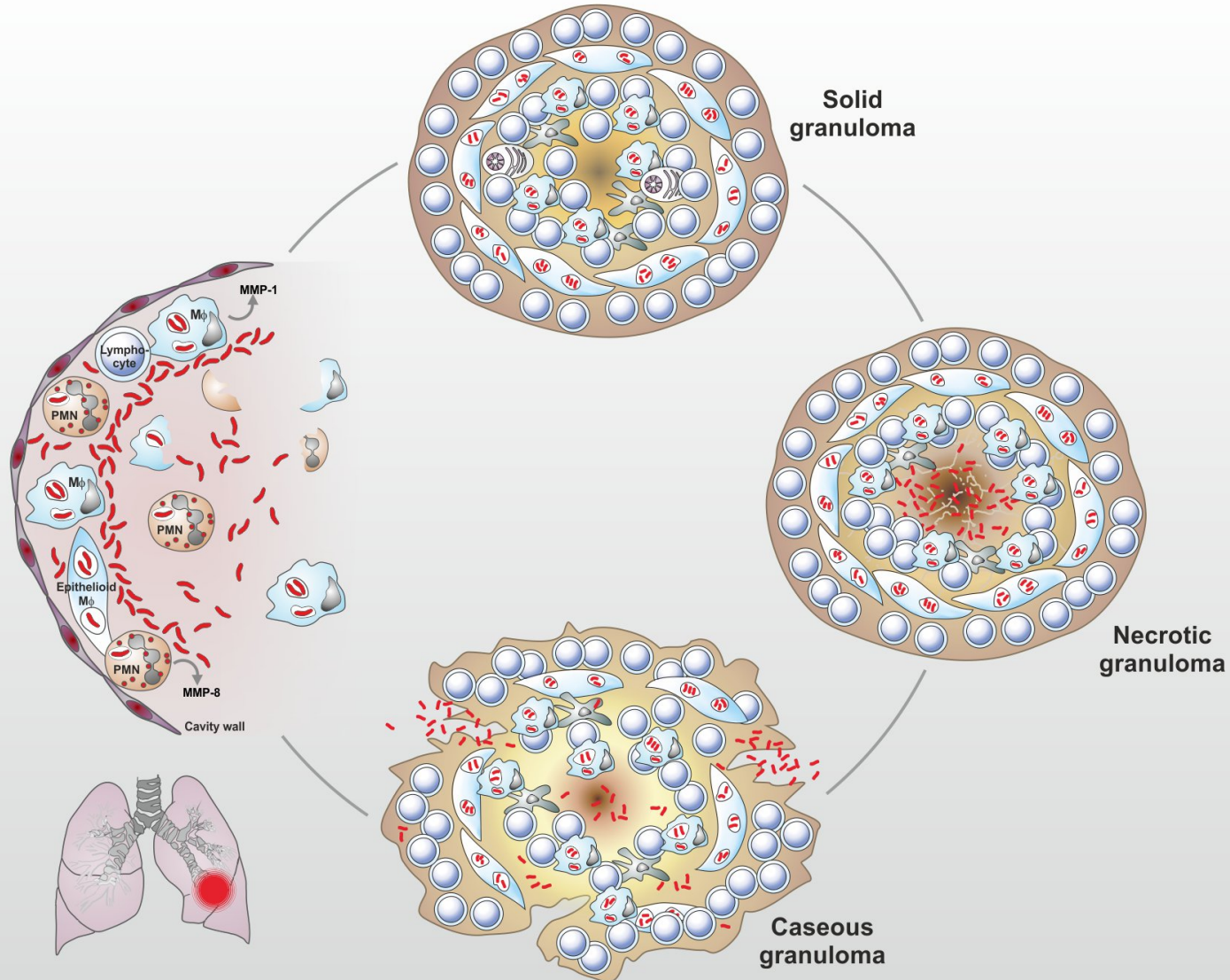
Pulmonary tuberculosis



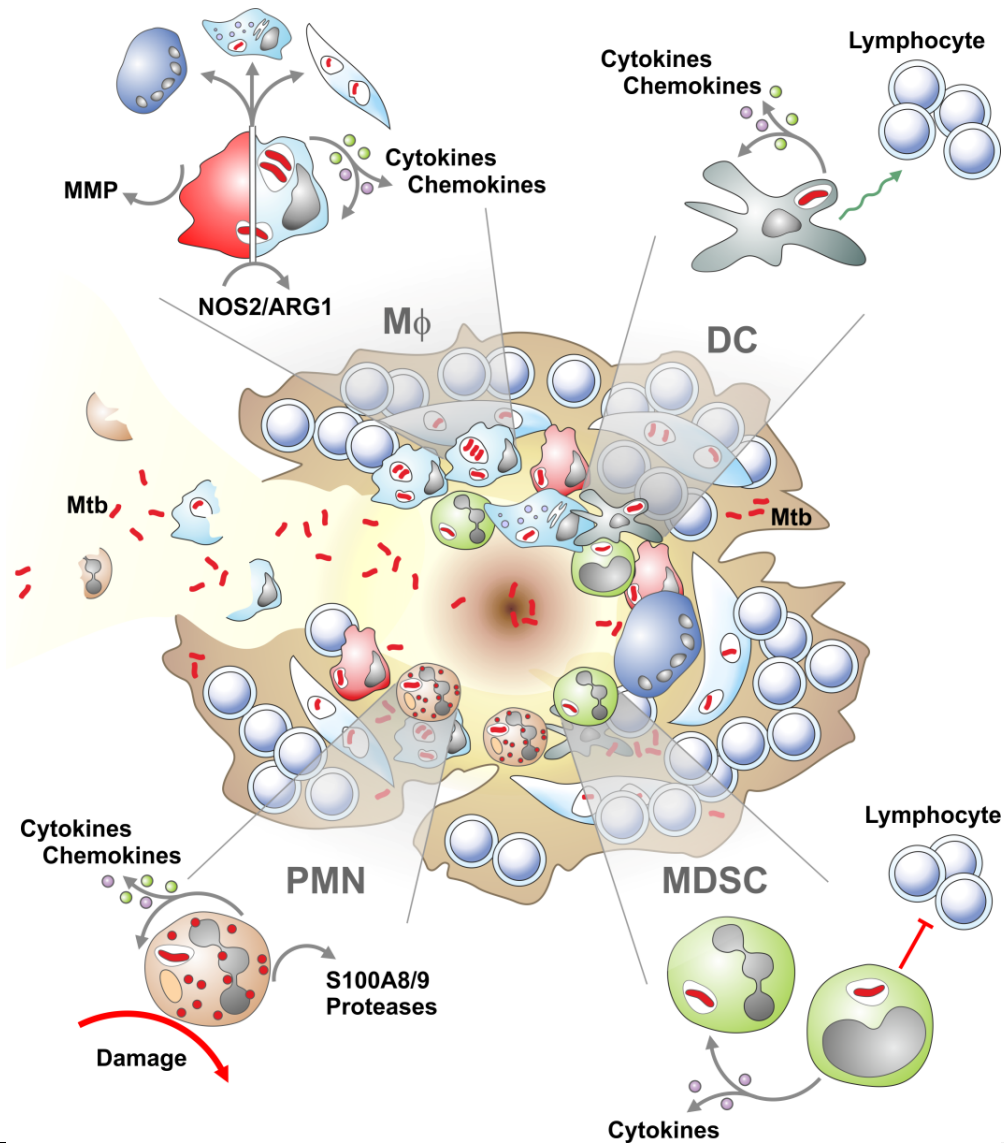
Immunopathology in tuberculosis



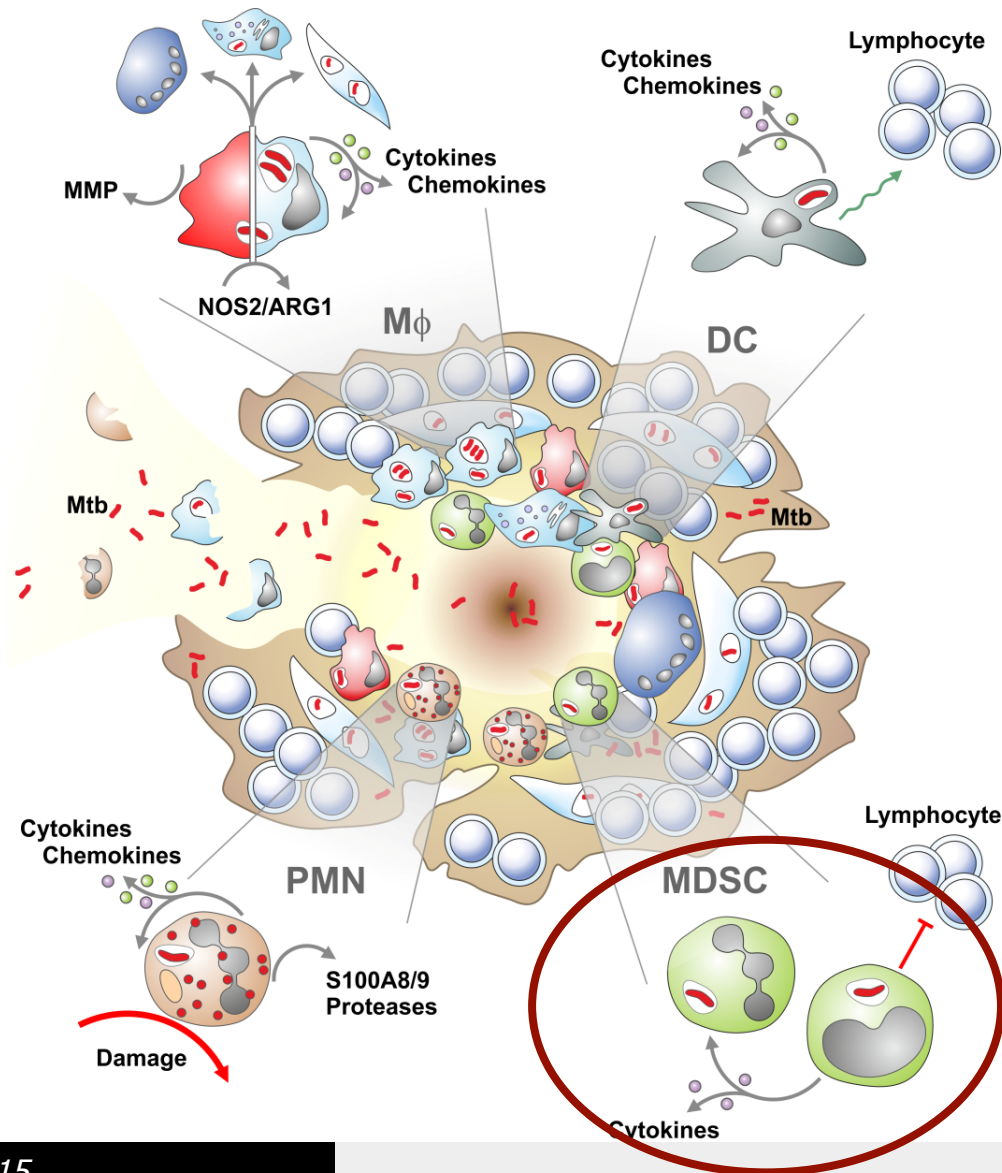
..... Diversity of granulomas



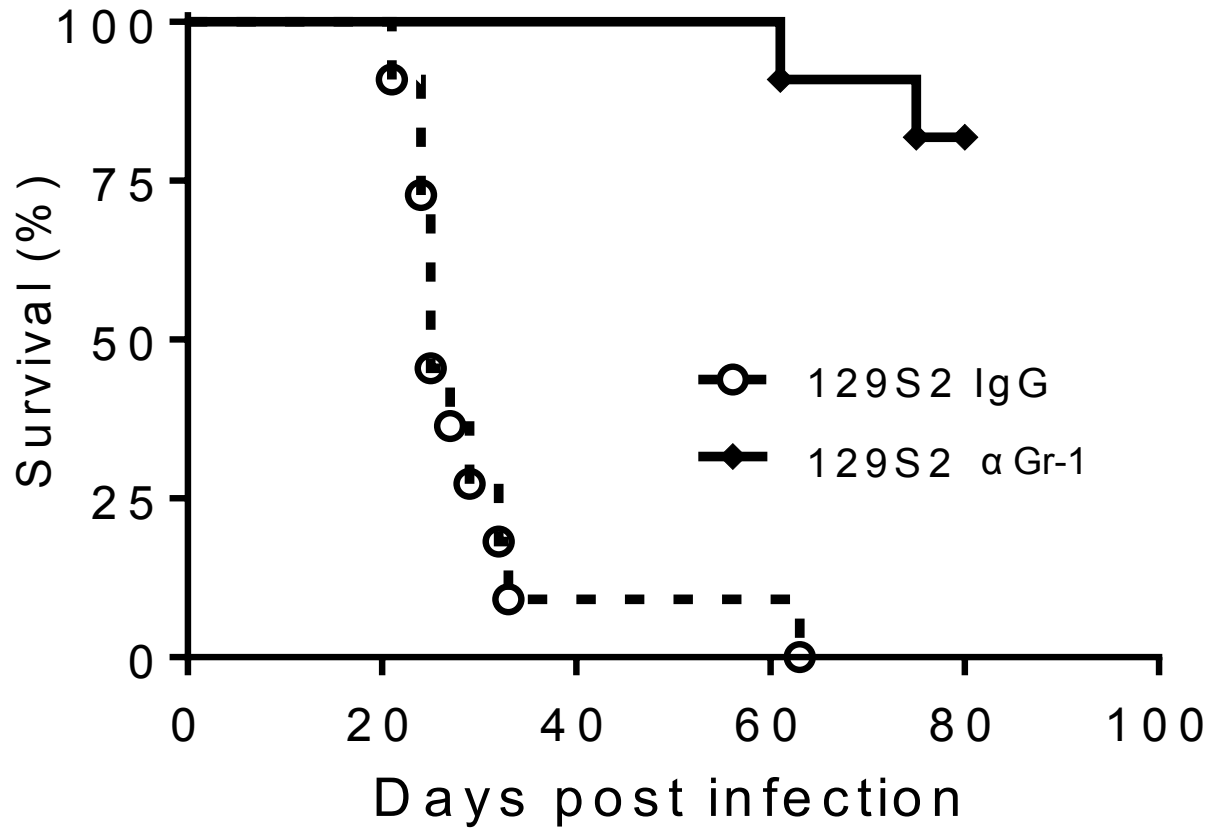
..... Cellular diversity within granulomas



..... Cellular diversity within granulomas



Depletion of Gr1⁺ cells rescues from lethal TB



Myeloid Regulatory Cells / Myeloid Derived Suppressor Cells

Immature heterogeneous **myeloid** cell population: mononuclear and PMN-like subsets

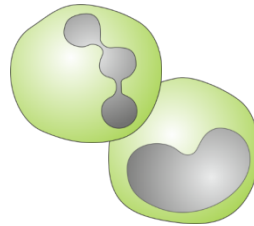
Suppressive under pathological conditions in mouse and man

Characterization:

1. Phenotype: **CD11b⁺ Gr1⁺**

Ly6G^{high} Ly6C^{int}

Ly6G^{low} Ly6C^{high}

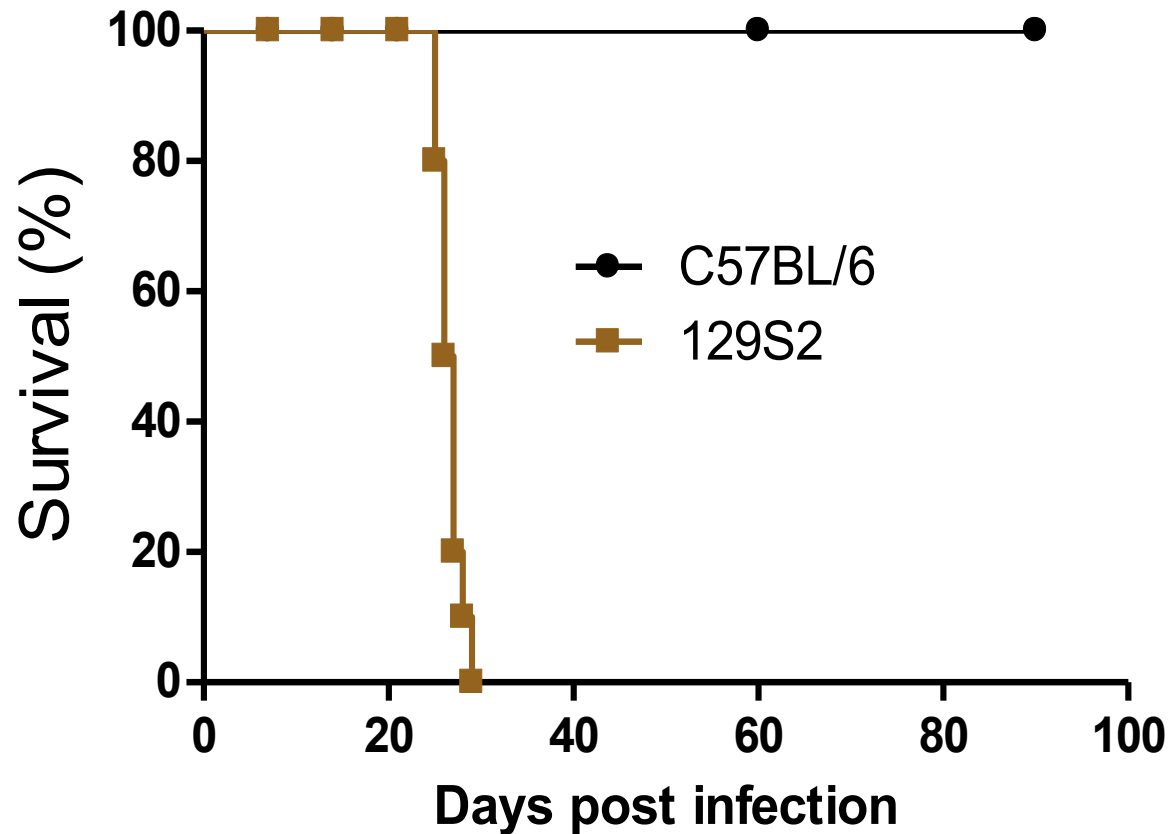


2. Morphology

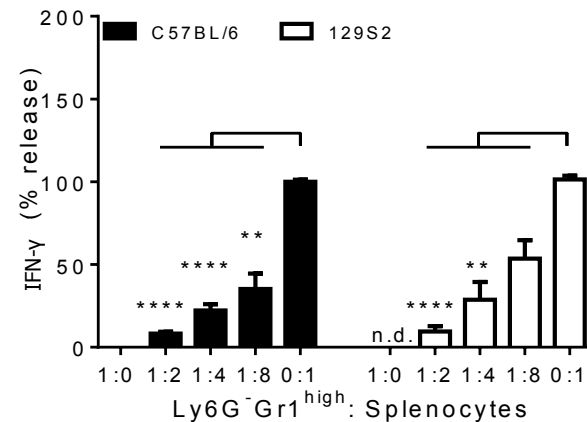
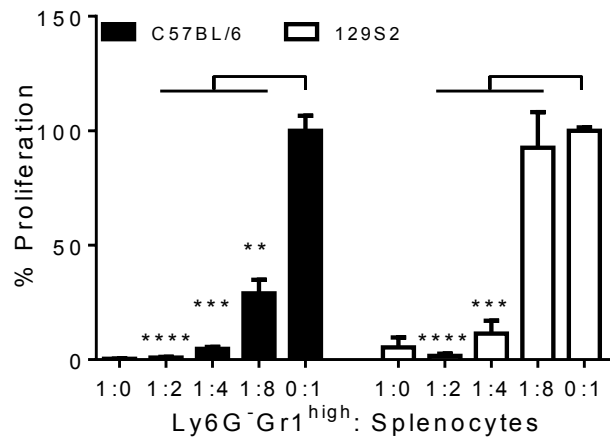
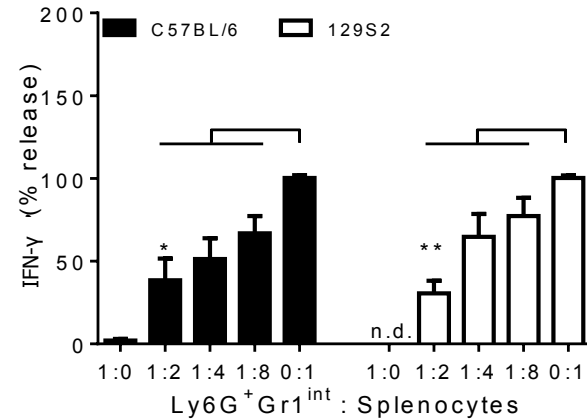
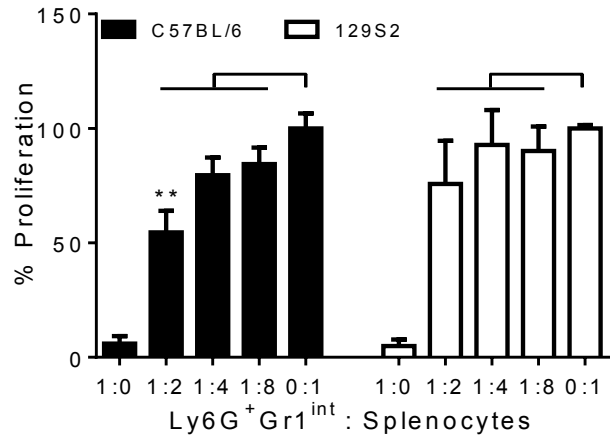
3. Function !!!

MDSC in TB – at the site of pathology

Survival post low dose aerosol infection (schematic)



Gr1⁺ cell subsets suppress proliferative responses



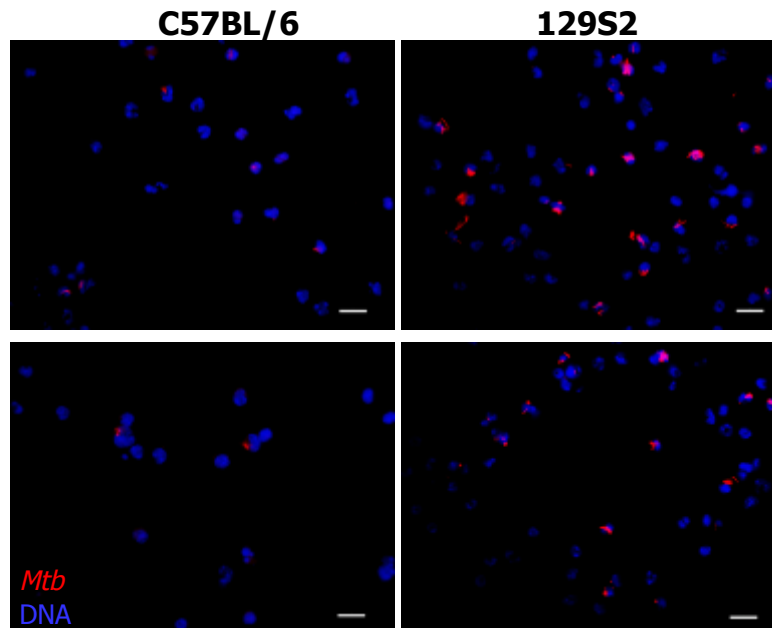
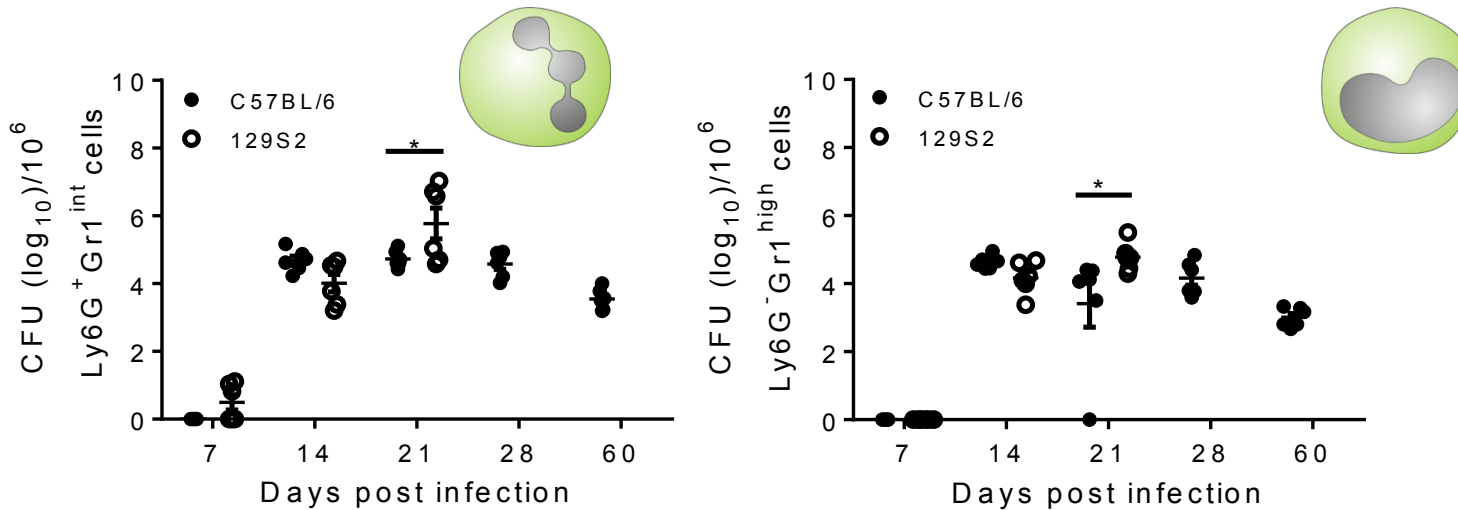
Phenotype

Morphology

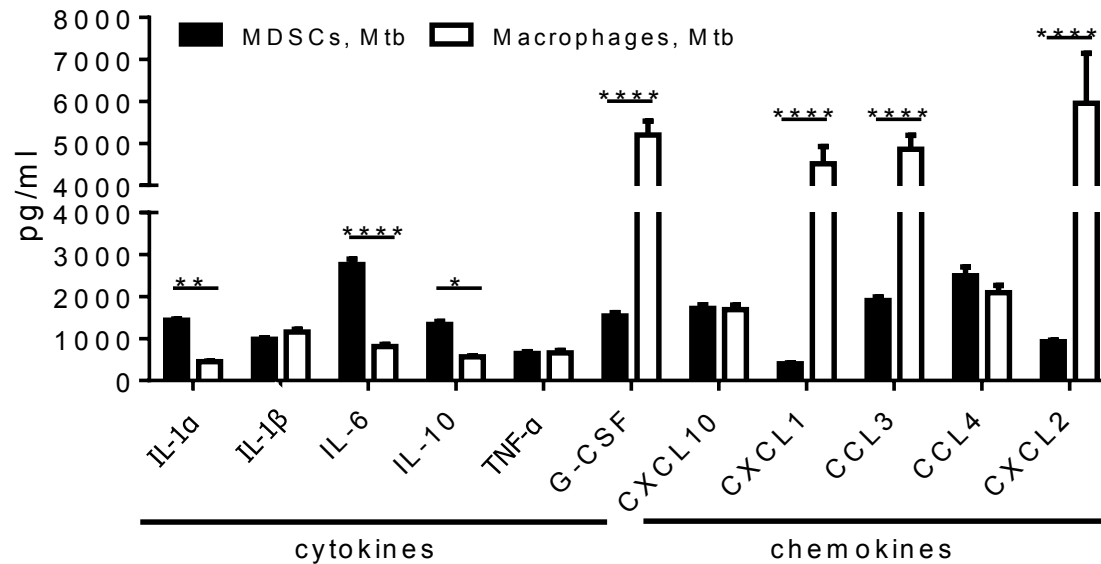
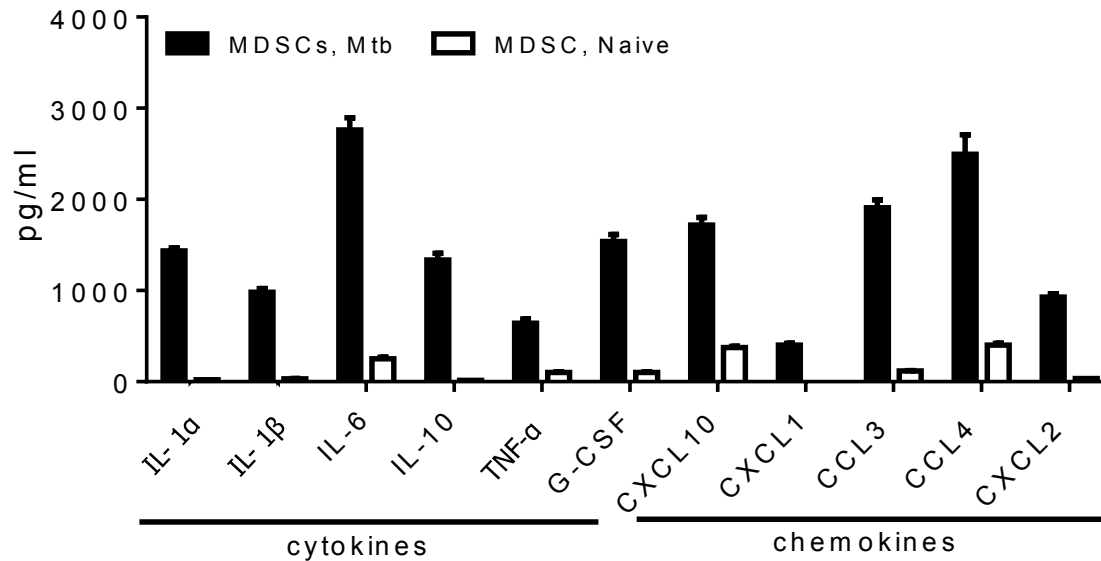
Function

MDSC in TB

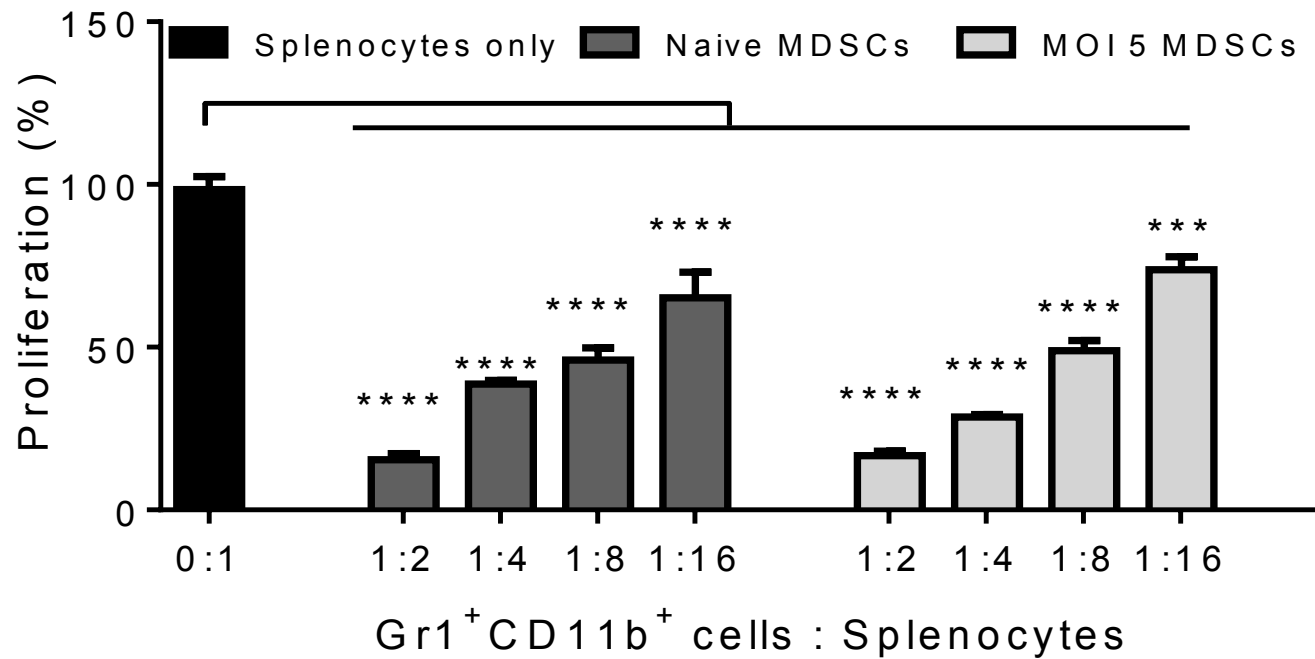
Lung MDSC harbor *Mycobacterium tuberculosis*



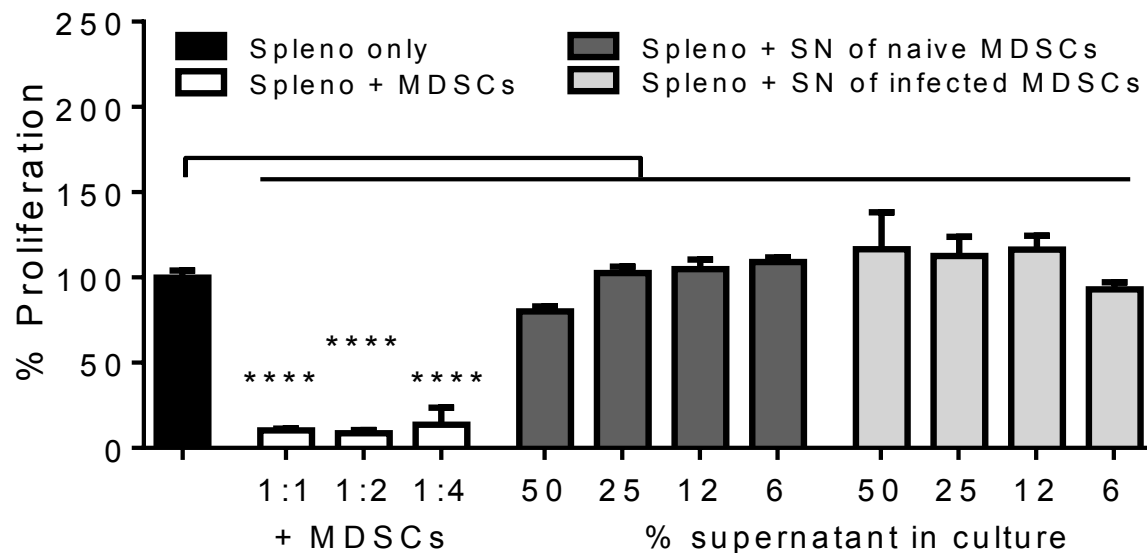
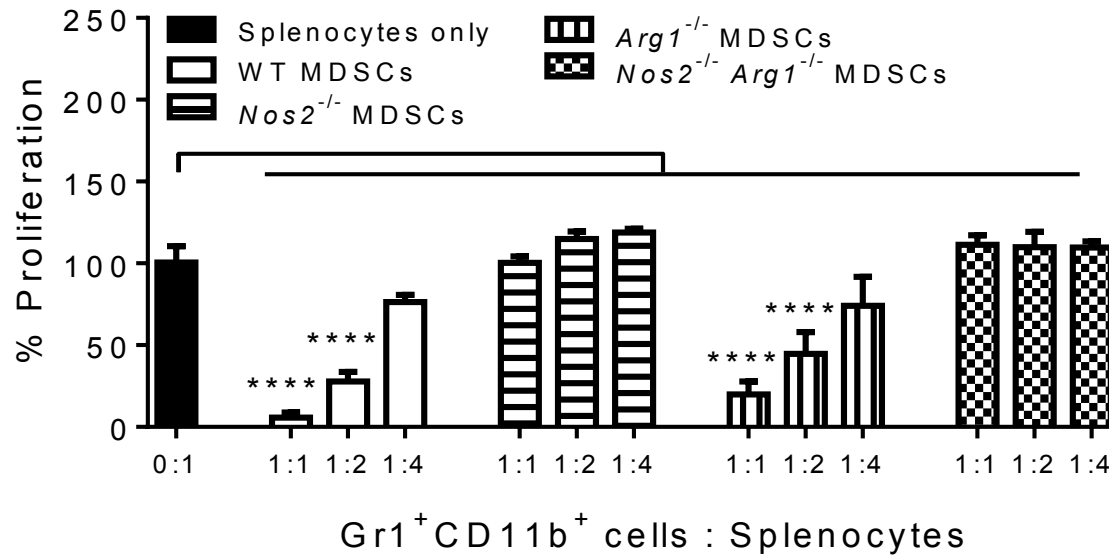
MDSC secrete discrete soluble mediators upon *Mtb* infection



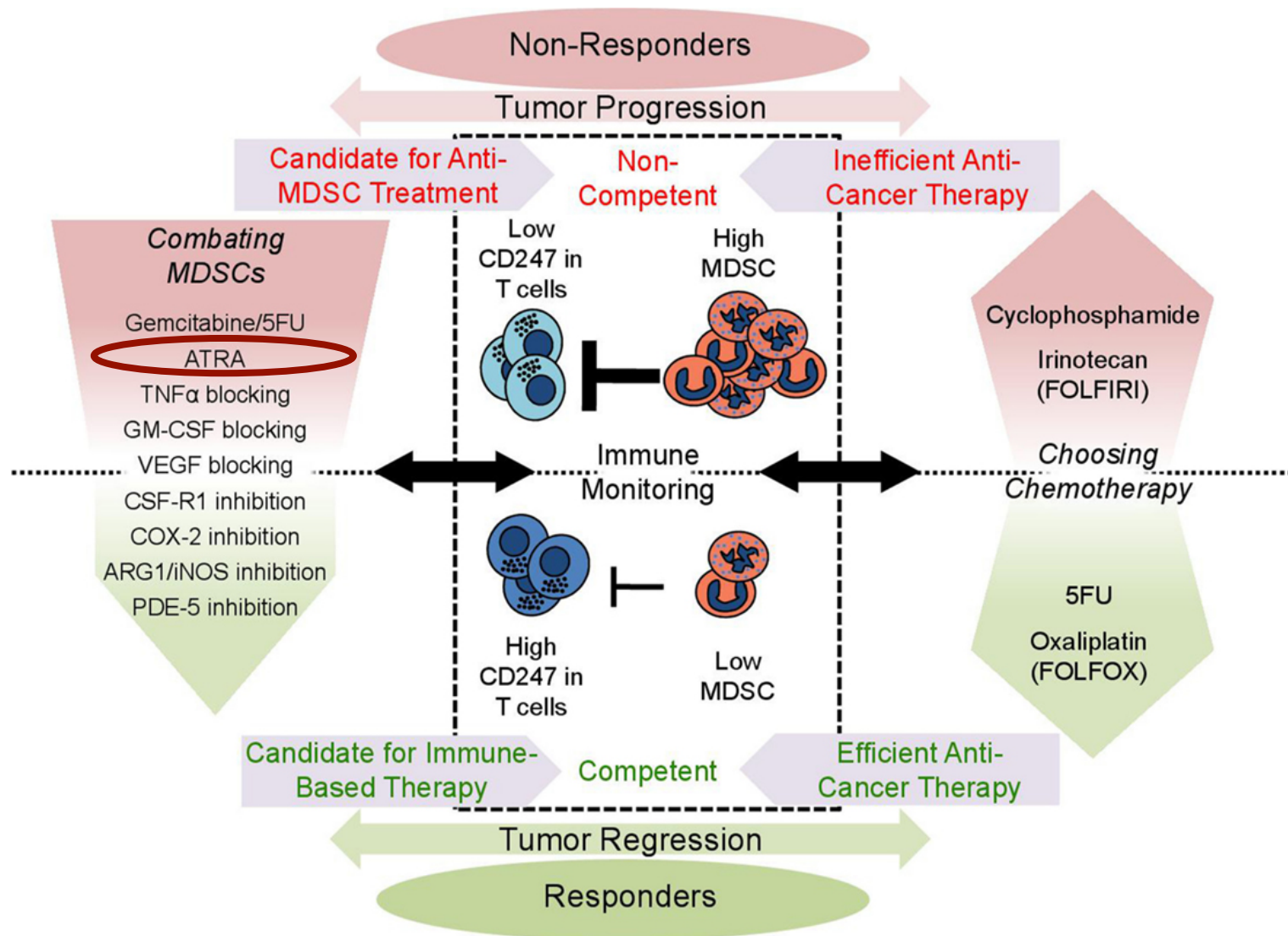
MDSC maintain suppressive activity upon *Mtb* infection



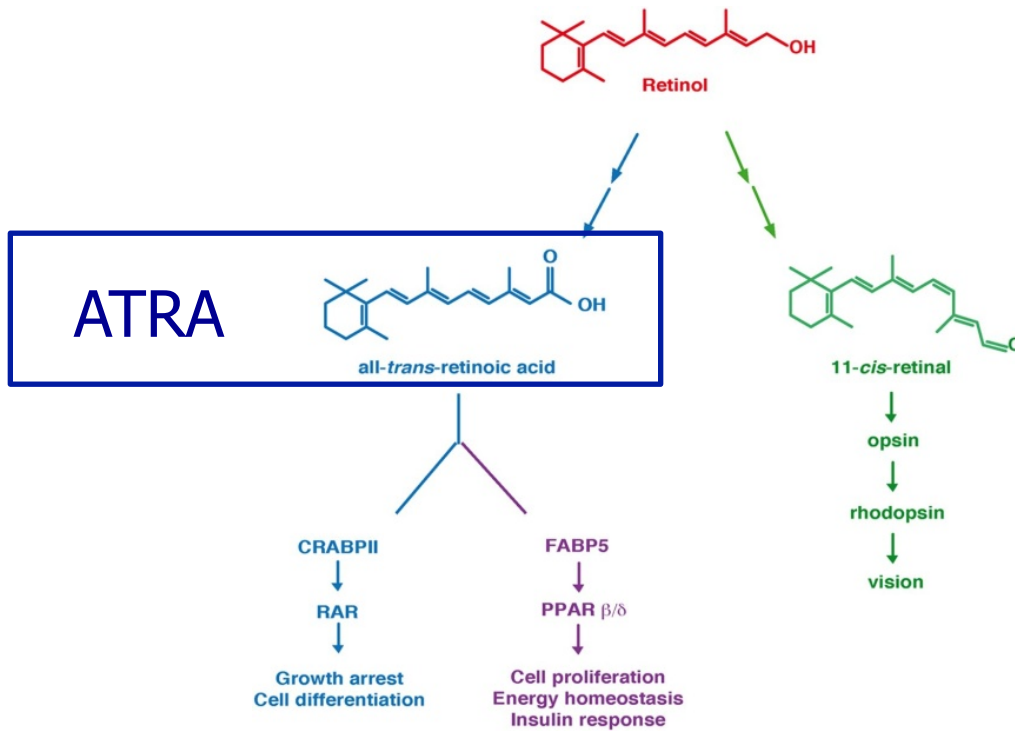
MDSC-derived soluble mediators do not confer suppression in absence of cell contact



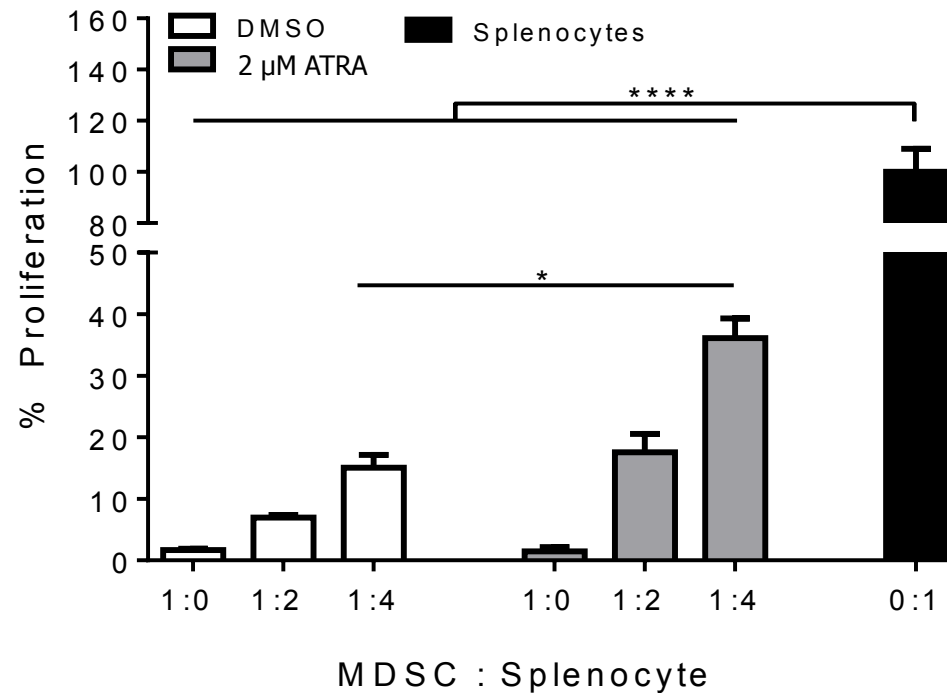
MDSC – targets for therapy of solid tumors



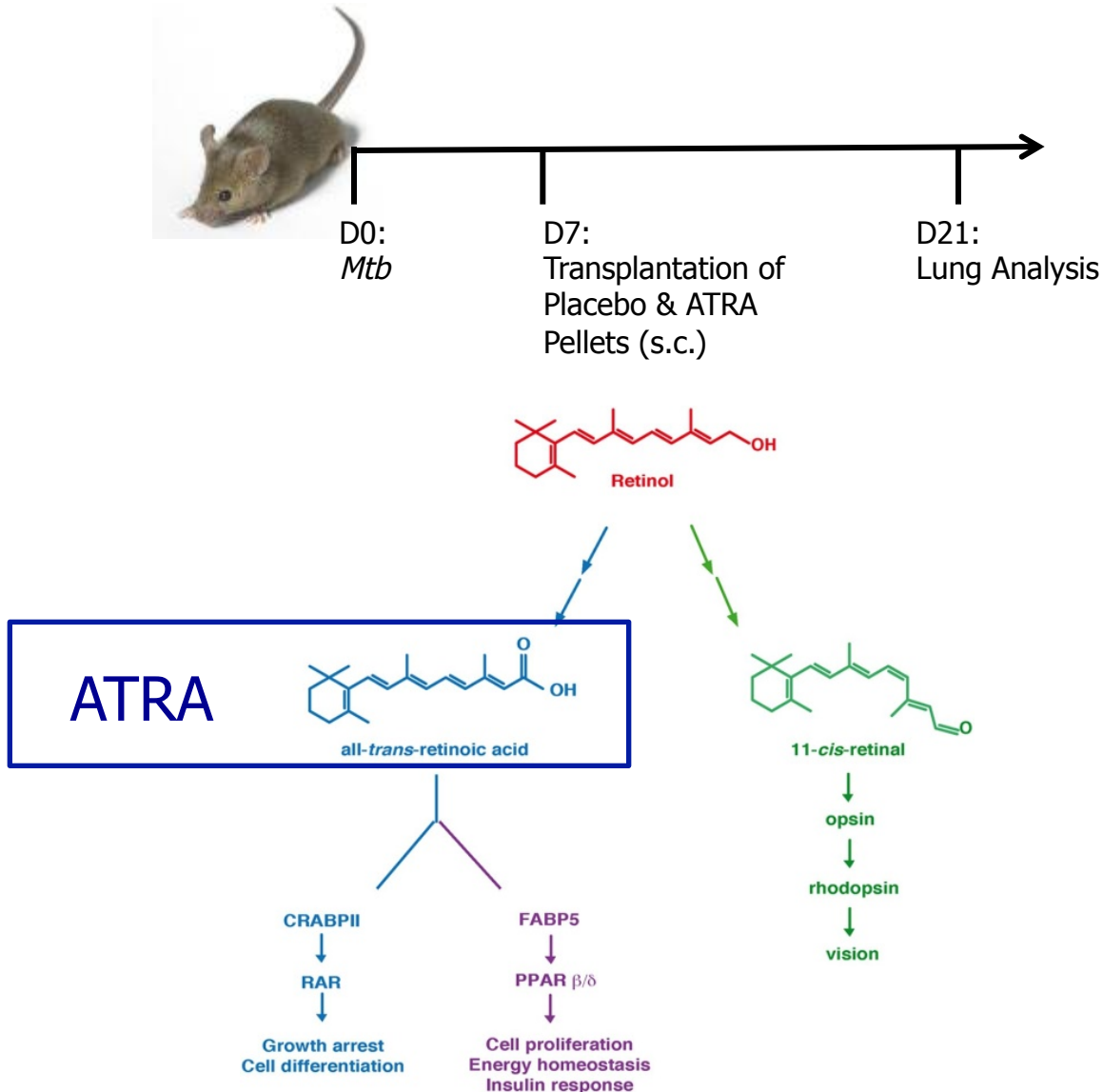
Maturation-induced MDSC ablation



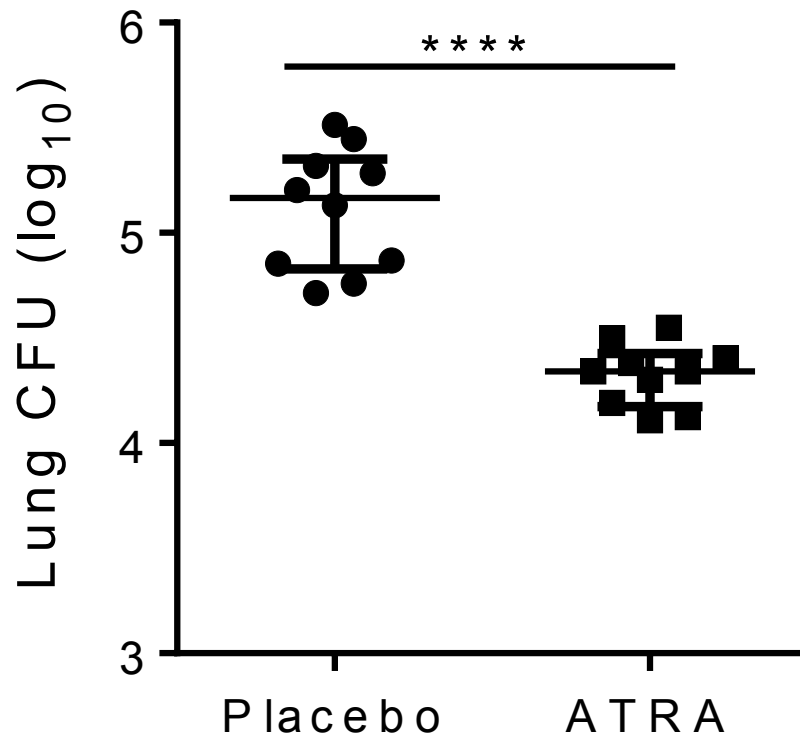
Maturation-induced MDSC ablation limits suppressive responses



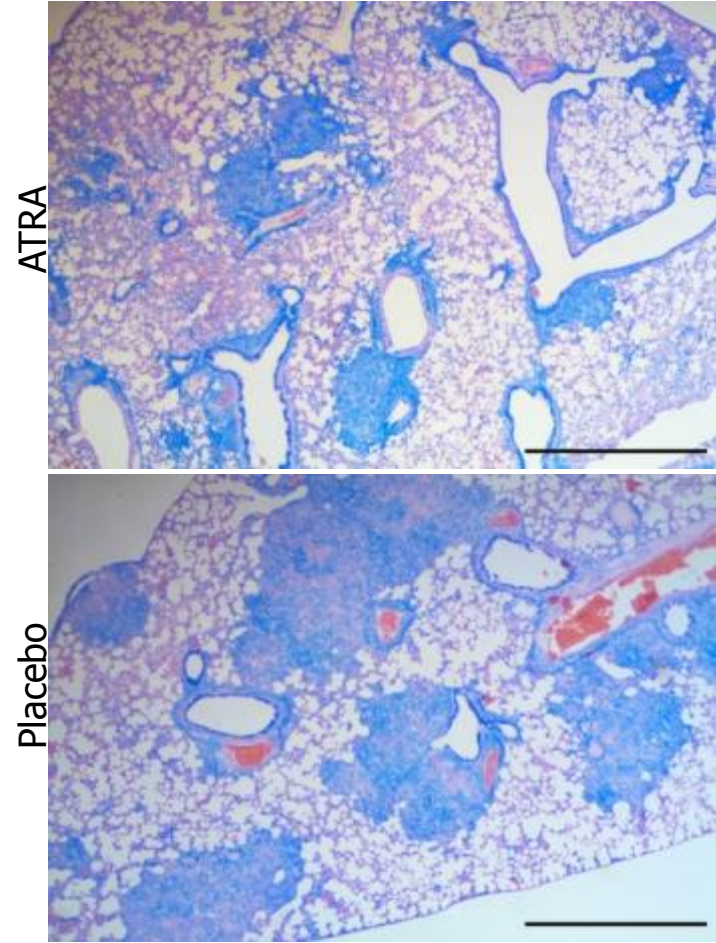
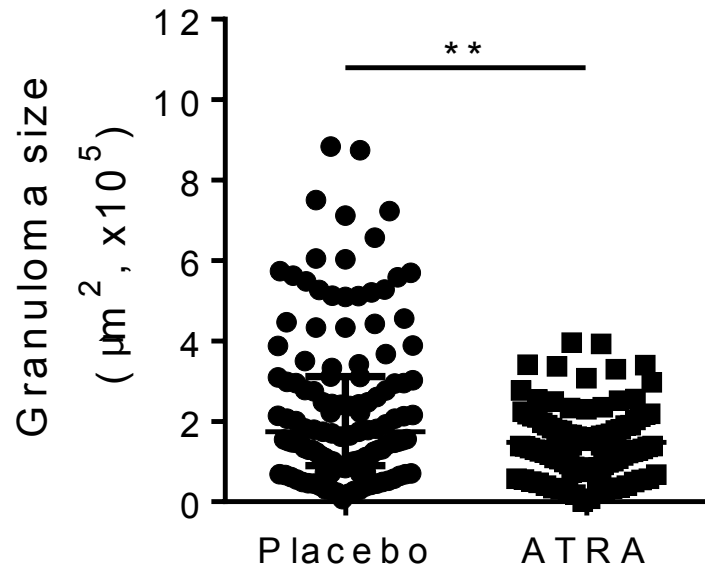
Maturation-induced MDSC ablation in TB



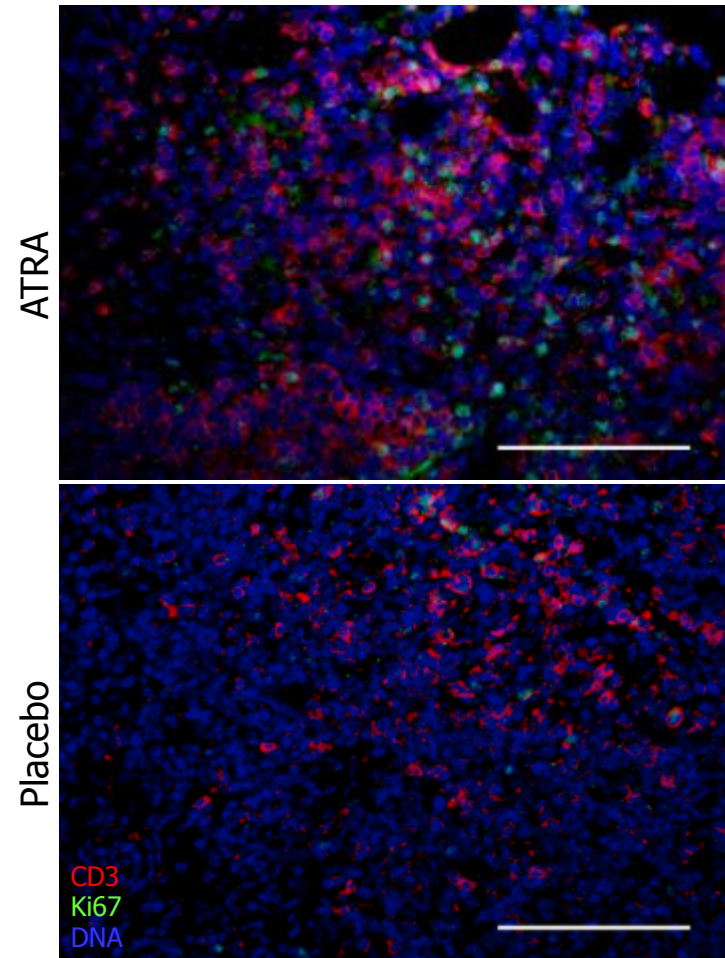
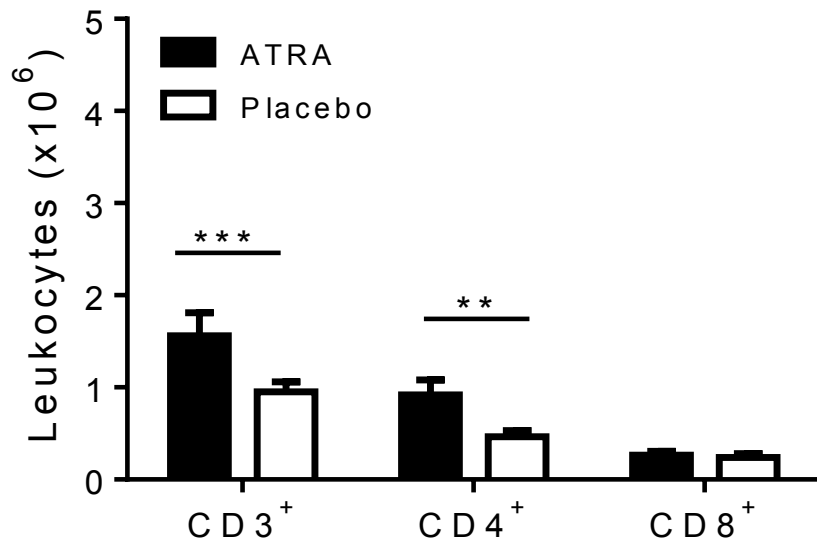
Maturation-induced MDSC ablation benefits the host



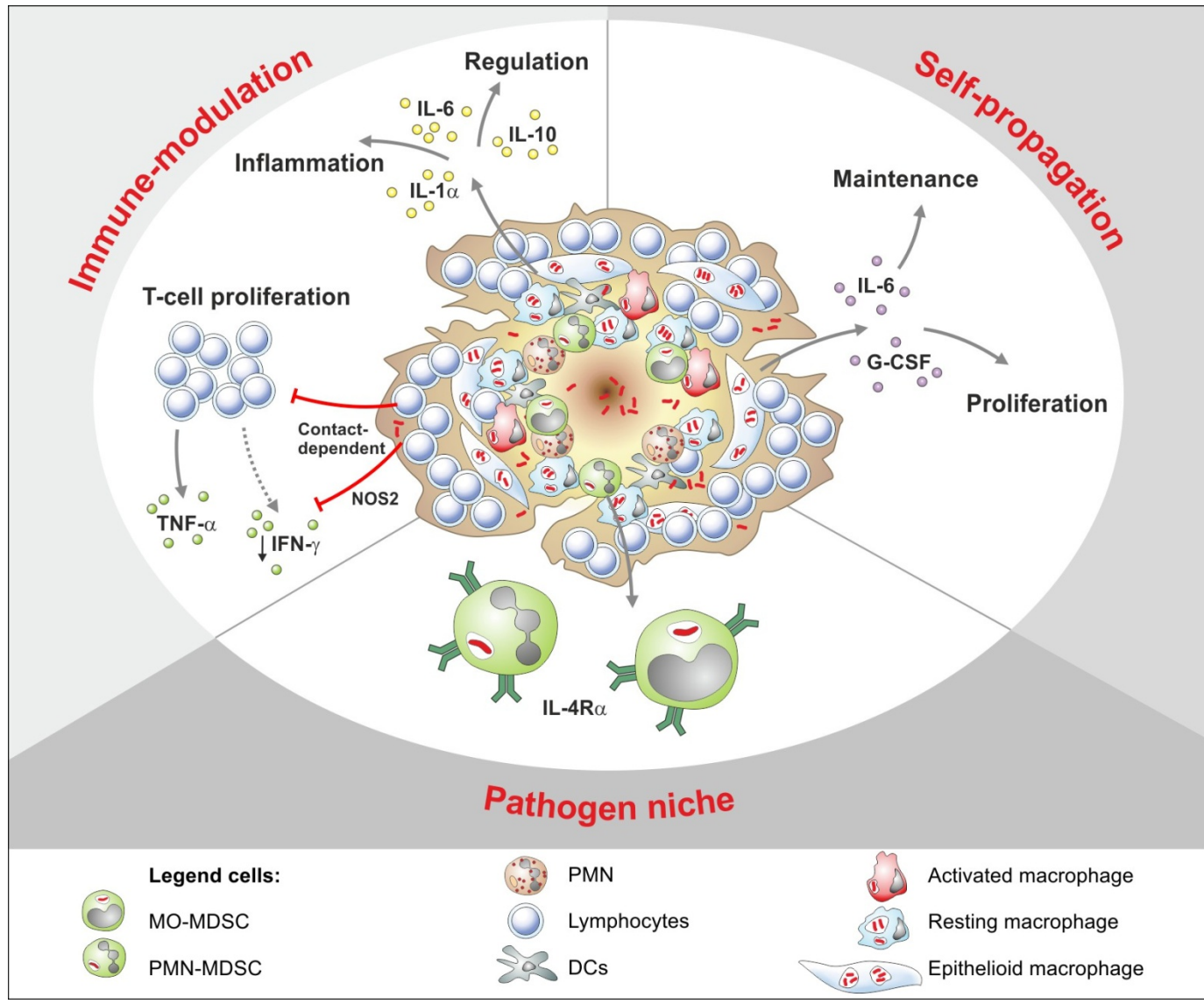
Maturation-induced MDSC ablation ameliorates pathology



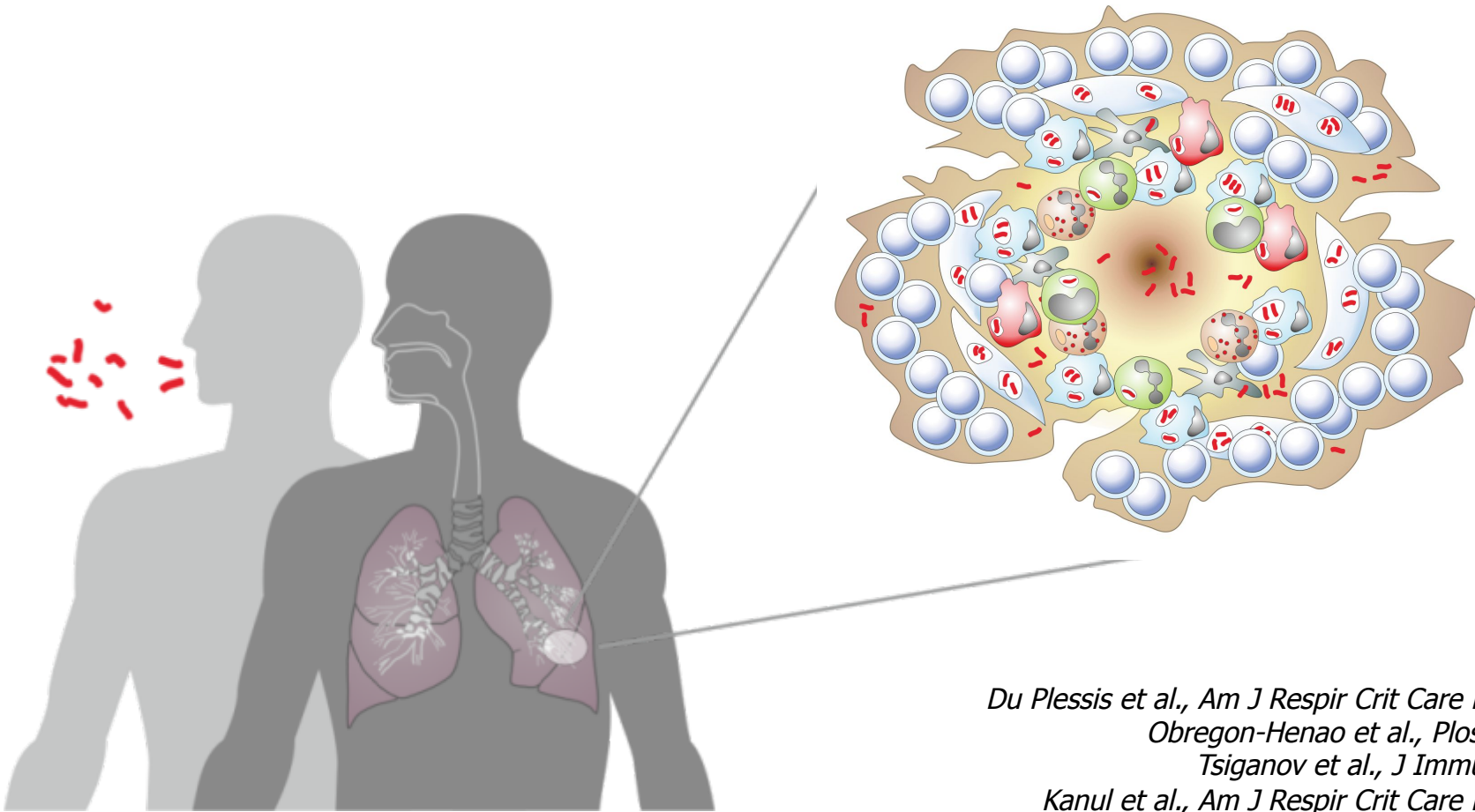
Maturation-induced MDSC ablation favors T-cell expansion



MRC / MDSC have multiple roles in TB and can be targeted within HDT



The manifold nature of myeloid cells drives TB immunopathology



Du Plessis et al., Am J Respir Crit Care Med, 2013
Obregon-Henao et al., PlosOne 2013
Tsiganov et al., J Immunol, 2014
Kanul et al., Am J Respir Crit Care Med, 2014
Yang et al., Immunol. Lett. 2014
El Daker et al., PlosOne 2015

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ELSE KRÖNER-FRESENIUS-STIFTUNG

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