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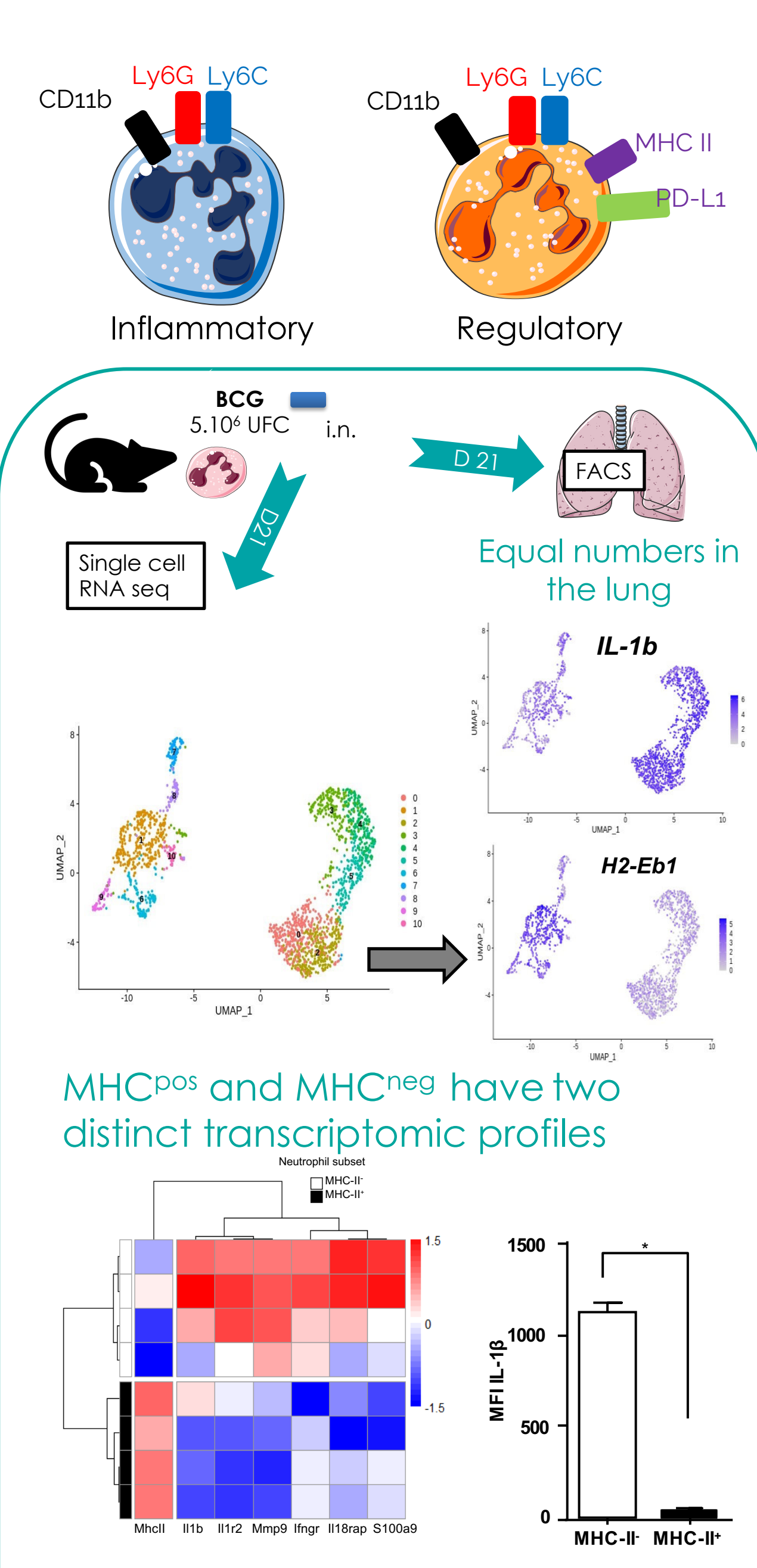
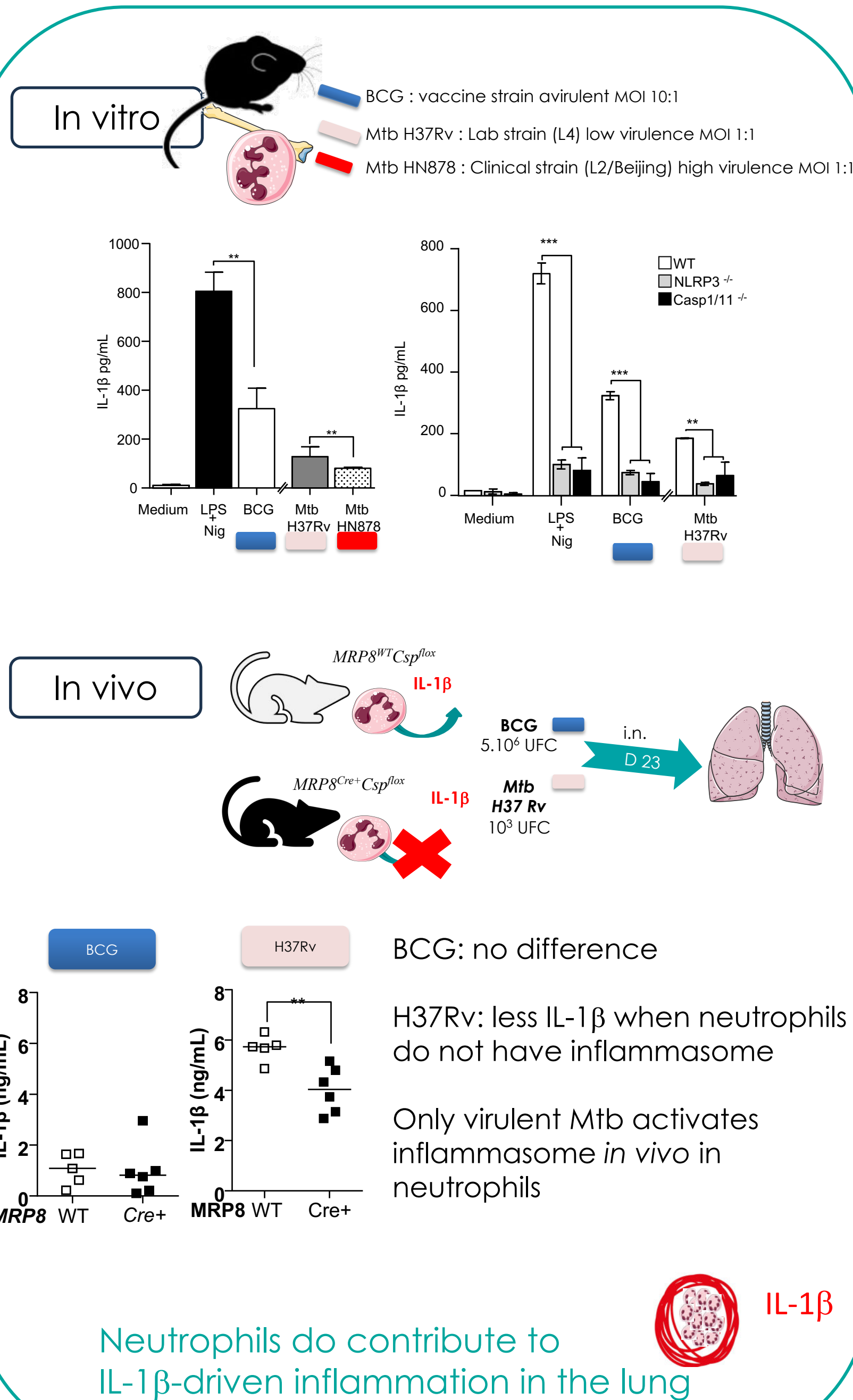
Dual neutrophil subsets accelerate or brake inflammation in tuberculosis.

Emilie DOZ DEBLAUWE¹, Badreddine BOUNAB¹, Florence CARRERAS¹, Julia SIVEIRA FAHEL³, Sergio OLIVEIRA⁴, Mohamed LAMKANFI⁵, Yves LEVERN¹, Pierre GERMON¹, Julien PICHON¹, Christophe PAGET², Aude REMOT¹ and Nathalie WINTER¹

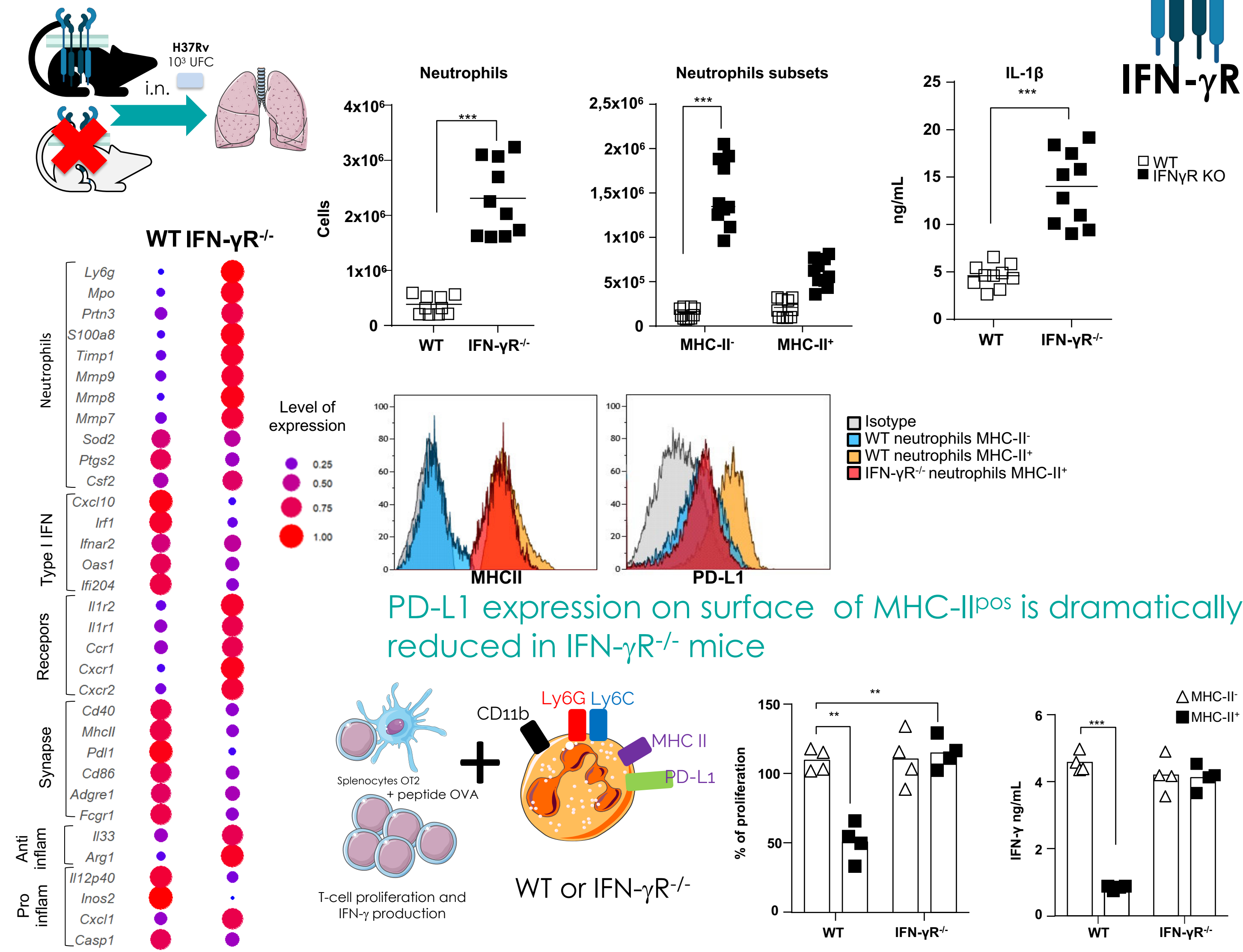
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Neutrophils can be beneficial or deleterious during tuberculosis (TB). Based on the expression of MHC-II and programmed death ligand 1 (PD-L1), we distinguished two functionally and transcriptionally distinct neutrophil subsets in the lungs of mice infected with mycobacteria. Inflammatory [MHC-II^{neg}, PD-L1^{lo}] neutrophils produced inflammasome-dependent IL-1 β in the lungs in response to virulent mycobacteria and "accelerated" deleterious inflammation, which was highly exacerbated in IFN- γ ^{-/-} mice. Regulatory [MHC-II^{pos}, PD-L1^{hi}] neutrophils "brake" inflammation by suppressing T-cell proliferation and IFN- γ production. Such beneficial regulation, which depends on PD-L1, is controlled by IFN- γ signaling in neutrophils. These findings add a layer of complexity to the roles played by neutrophils in TB and may explain the reactivation of this disease observed in cancer patients treated with anti-PD-L1.

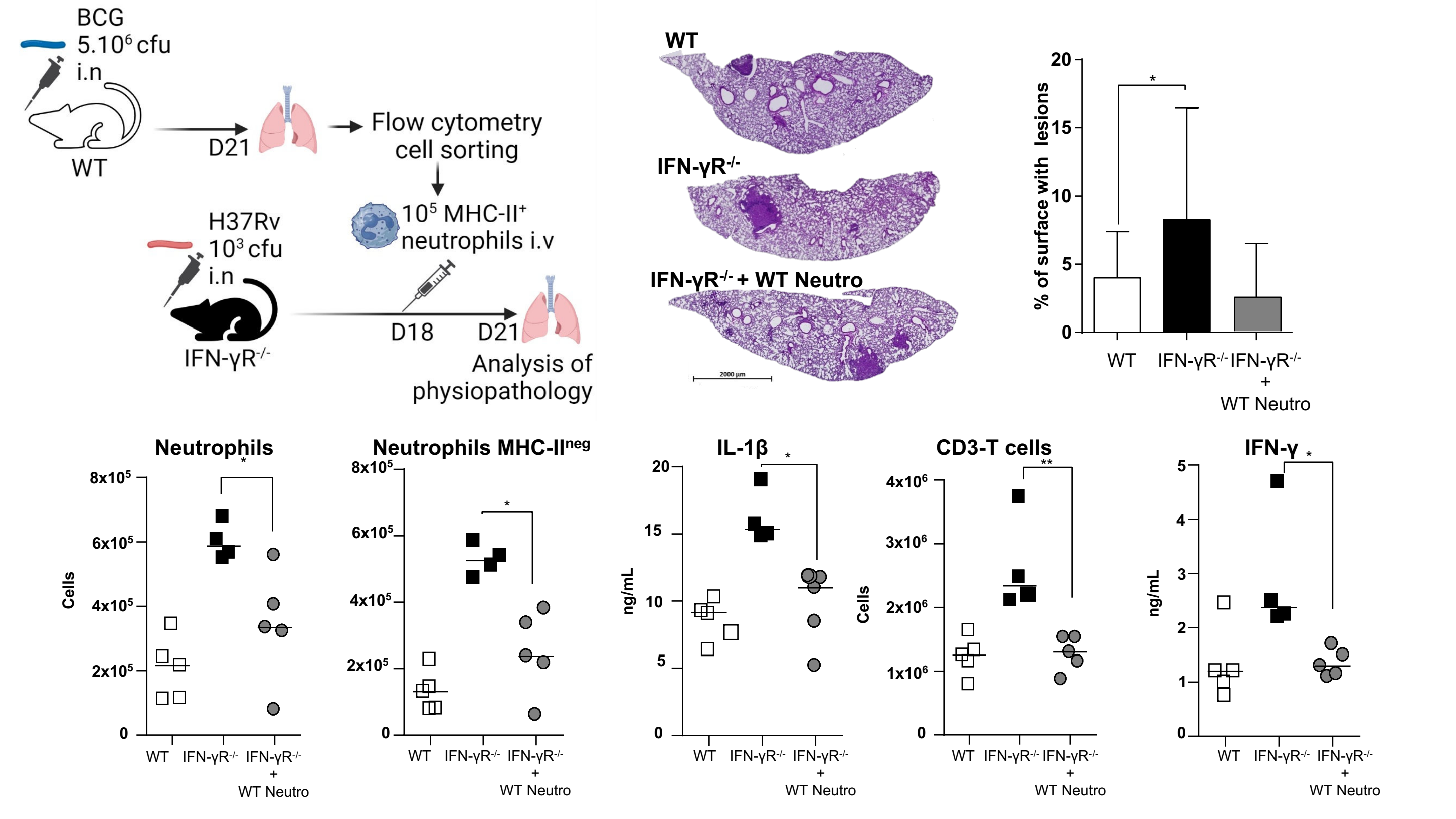
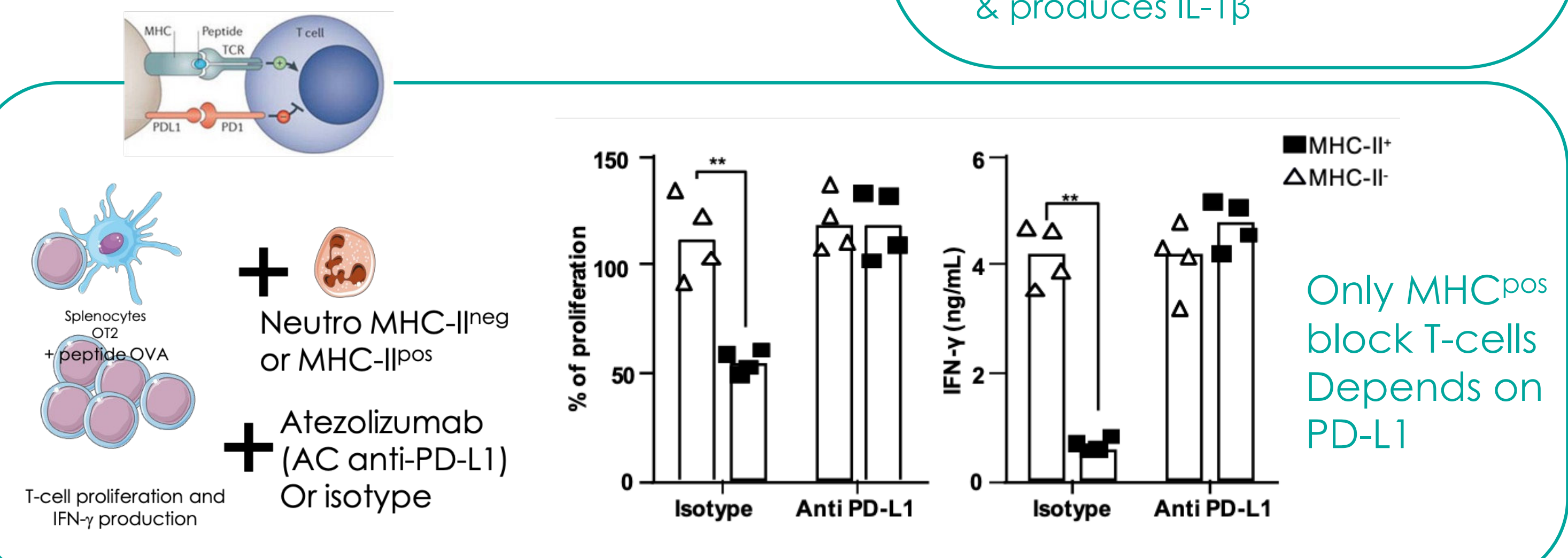
1- Two neutrophil subsets with two different functions



2- Is PD-L1 regulated by other signals ?

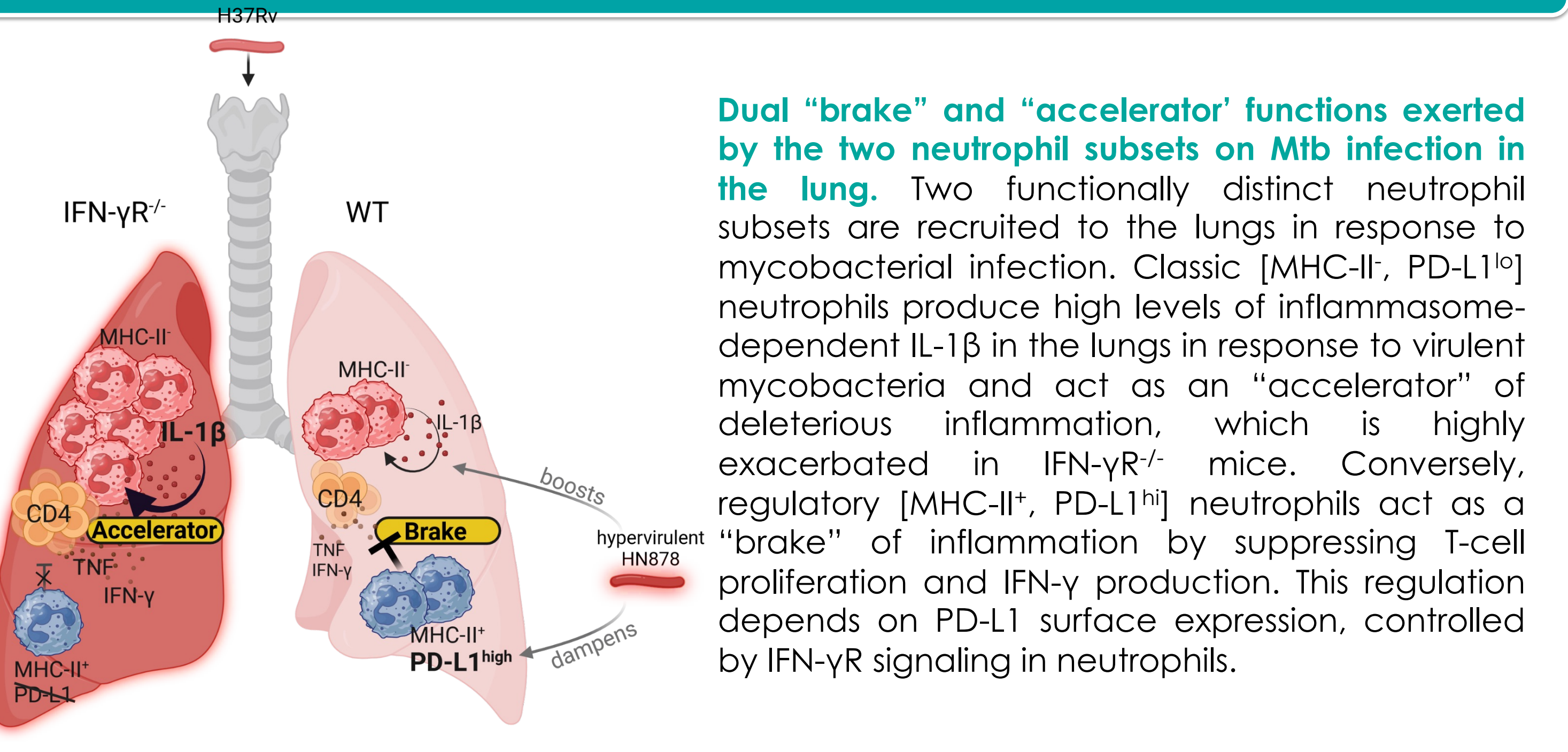


3- Can MHC-II^{pos} regulatory neutrophils dampen inflammation *in vivo*?



MHC-II^{neg} neutrophils produce IL-1 β and are inflammatory, MHC-II^{pos}; PD-L1^{pos} neutrophils are regulatory

IN SUMMARY



Many thanks to

The mouse team of the PFIE (INRAE, Nouzilly), especially **Corinne Beaug , J r me Pottier & Emilie Lortscher Val rie Quesniaux** (INEM, UMR7355 CNRS, Universit  d'Orl ans, France) *Aim2^{-/-}, Gsdmd^{-/-}, Nlrp3^{-/-}, Csp1/11^{-/-}* mice,
Alix Sausset and Christelle Rossignol, from the IMI team (ISP, INRAE, Nouzilly) neutrophil cell sorting and histology,
Sonia Lacroix-Lamand  and the AIM team (ISP, INRAE, Nouzilly) Fluidigm Biomark.
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MHC-II^{pos} neutrophils from WT mice transferred into Mtb-infected IFN- γ ^{-/-} mice dampen lung inflammation.

Next...

- C3HeB/FeJ mice : distribution of regulatory and inflammatory neutrophils in a model with "proper TB granuloma" (see poster by Doz-Deblauwe et al.)
- Examine these two neutrophil subsets in TB patients
- Understand their respective roles in inflammatory compounds production in the lung during TB