

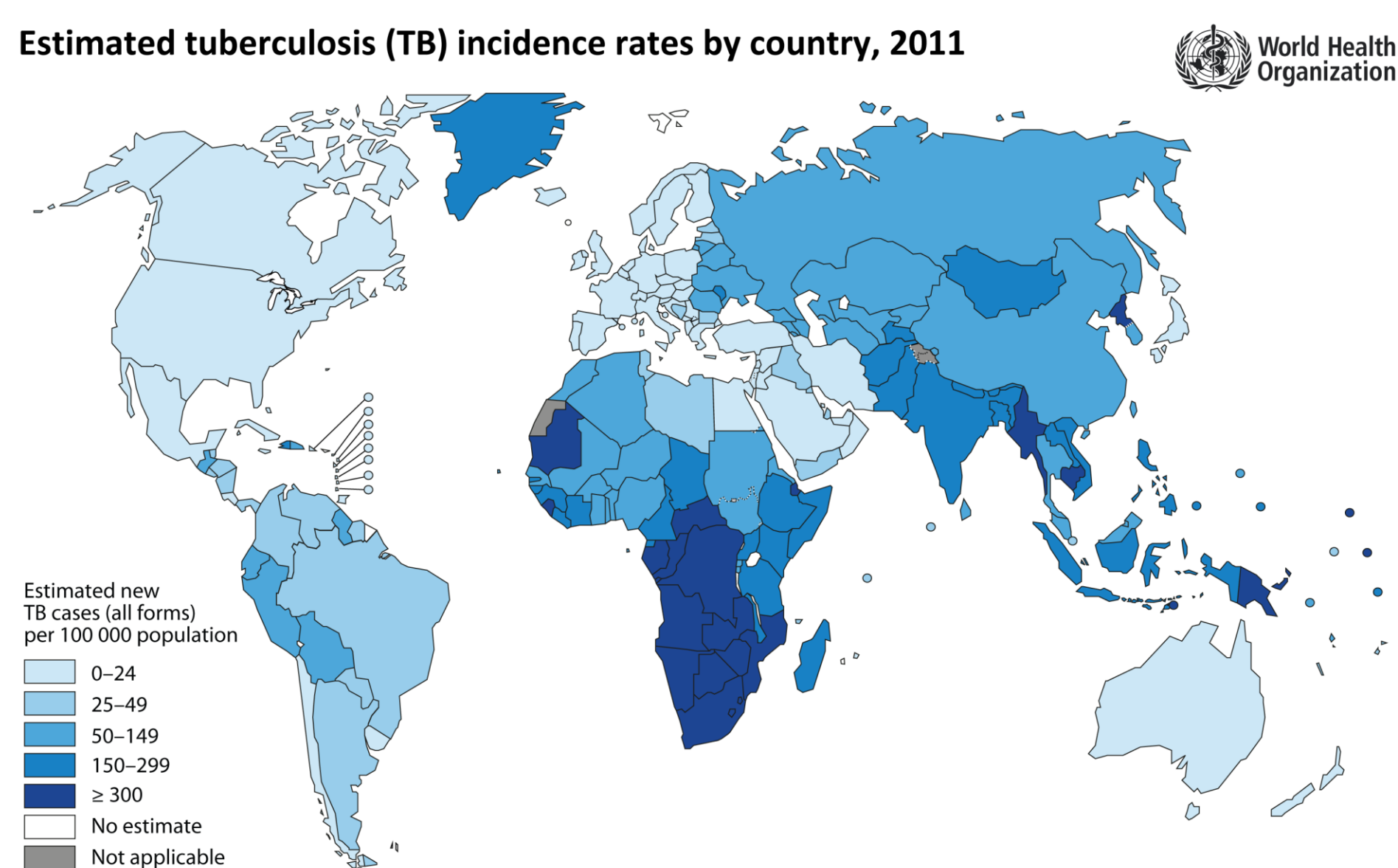
Development & Characterization of a BSL-2 Wistar Rat Model of Pulmonary Mycobacterial Infection

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Tuberculosis Health Burden



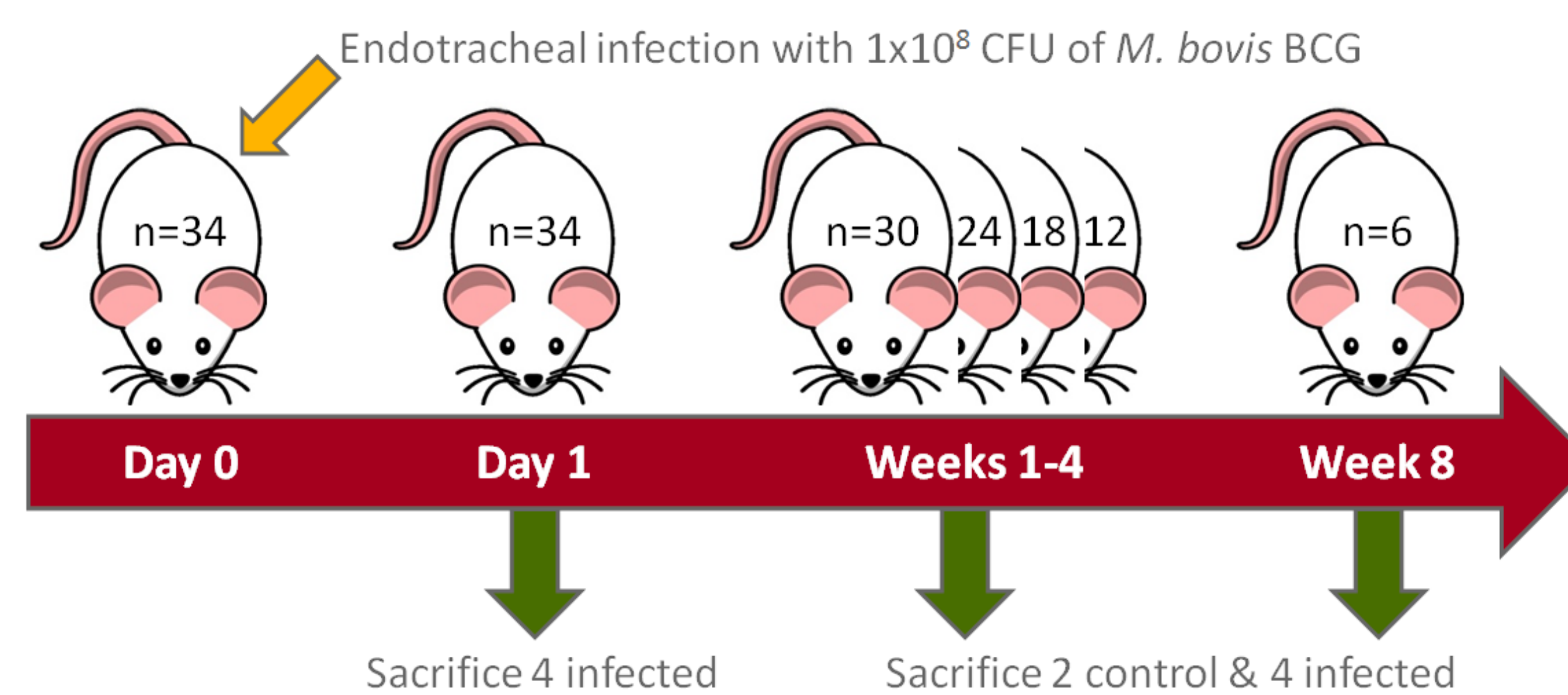
- *Mycobacterium tuberculosis* infects 33% of world
- 10 million new cases & 2 million deaths per year
- Widespread drug resistance; need new therapies

TB Animal Models Fall Short

Animal	Expense	Reagents	Mimics Human
Mouse	Low	Very many	Poorly
Guinea pig	Moderate	Few	Closely
Rabbit	Moderate	Few	Closely
Primate	Very high	Many	Very closely
Rat	Low	Many	Closely

- Many limitations with common animal models
- Easy-to-handle models poorly mimic human TB
- Cost & reagent availability hamper better models

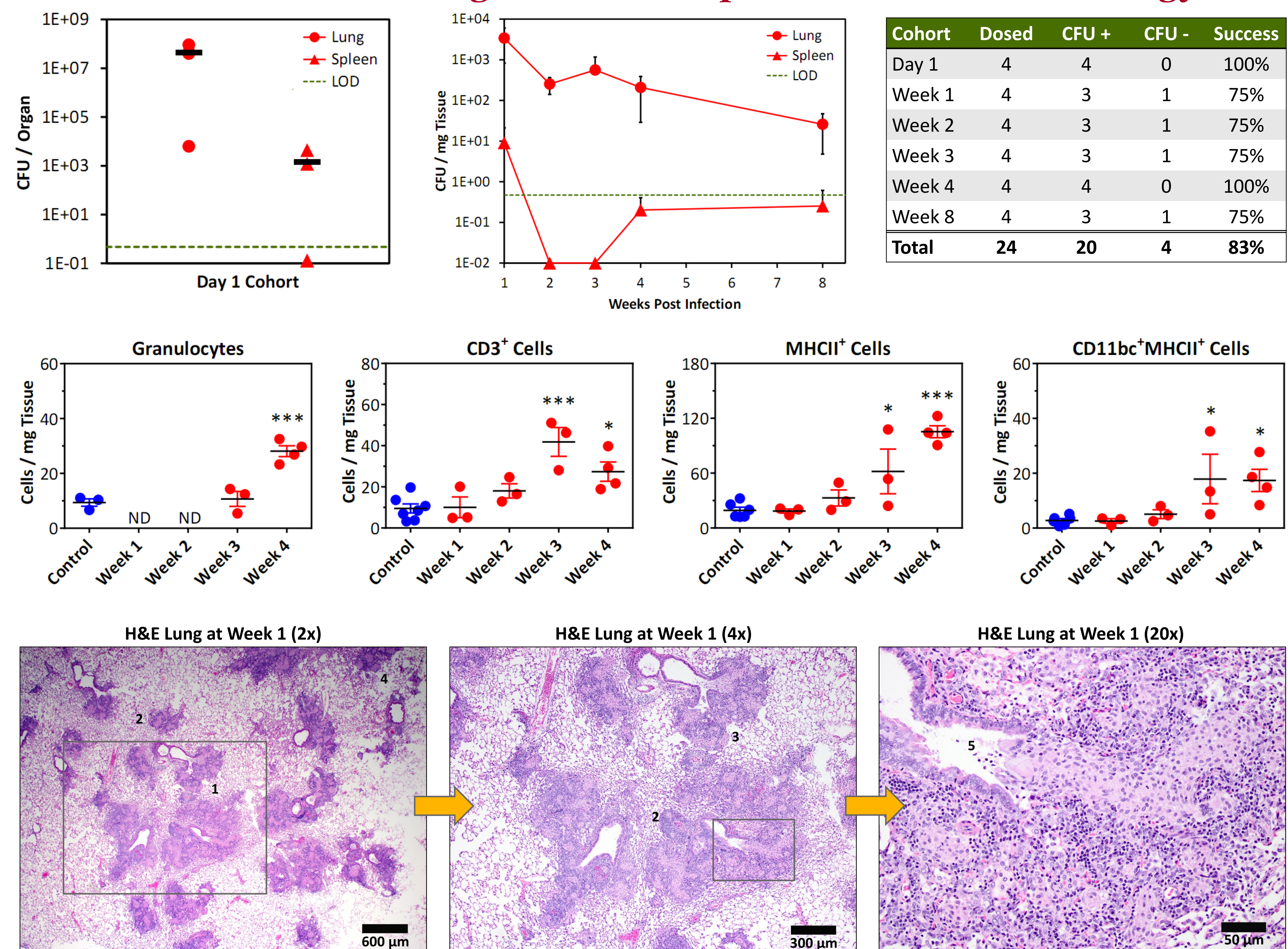
Model Details & Methods



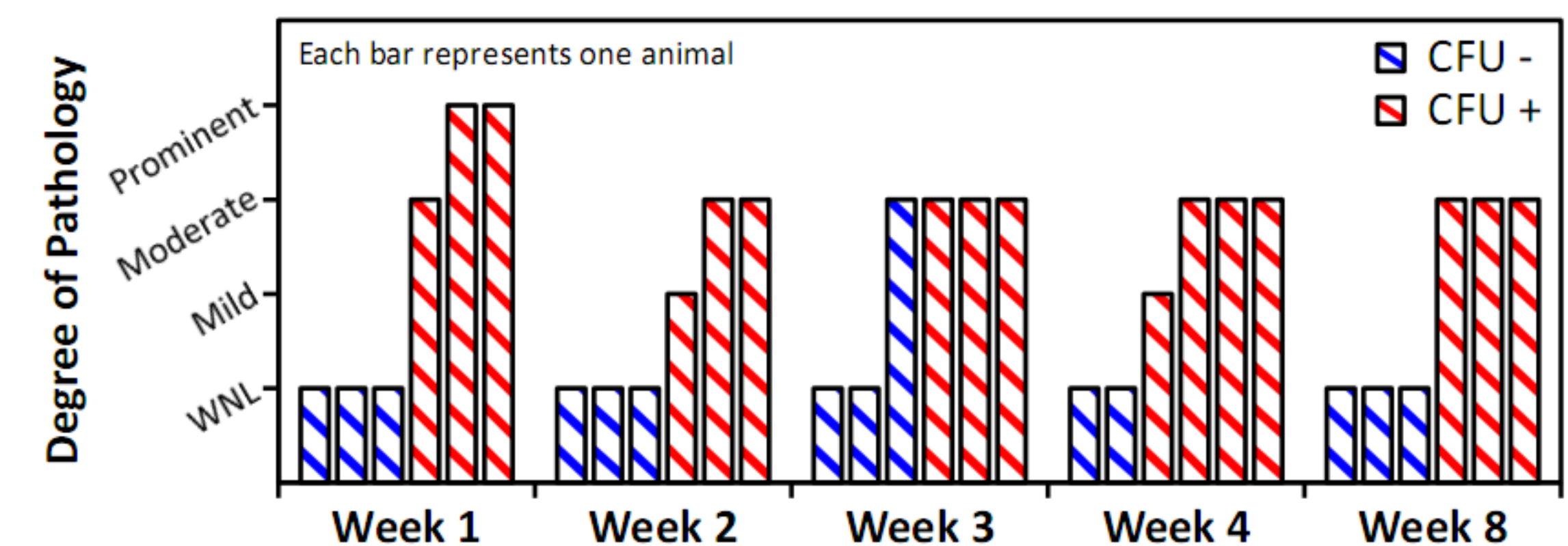
- *M. bovis* BCG as a BSL-2 analogue of *M. tb*
- 34 outbred female Wistar CRL rats at 6 weeks old

Tissue(s)	Assays Performed
Lung, Spleen	Homogenate plated for CFU counting
Lung	Flow cytometry for immune cell invasion
Lung	Formalin fixed for histopathology & IHC
Lung, Serum	Multiplex cytokine / chemokine panel
Lung, Liver, Spleen	Modified ribonucleoside analysis
Urine	LC-MS metabolomic profiling

Sustained Infection, Strong Immune Response, & Robust Pathology



Important Pathological Features	
1	Large regions of inflammation with increased cellularity
2	Coalescing granulomas of lymphocytes, macrophages, & MNCs
3	Frequent peribronchiolar localization of granulomas
4	Scattered smaller granulomas throughout the parenchyma
5	Attenuation of bronchiolar epithelium by impinging granulomas



Ongoing Work & Concluding Remarks

We have developed a new BSL-2 rat model of pulmonary mycobacterial infection. This model is affordable, easy to use, and displays persistent infection, significant immune infiltration, and robust pathology with granuloma-like structures. We are undertaking IHC, qPCR, & cytokine profiling to finish characterization.

This model will be useful for future drug development & metabolomic studies