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The Trojan-horse hypothesis for the genesis of invasive bacterial infection

Marco R. Oggioni

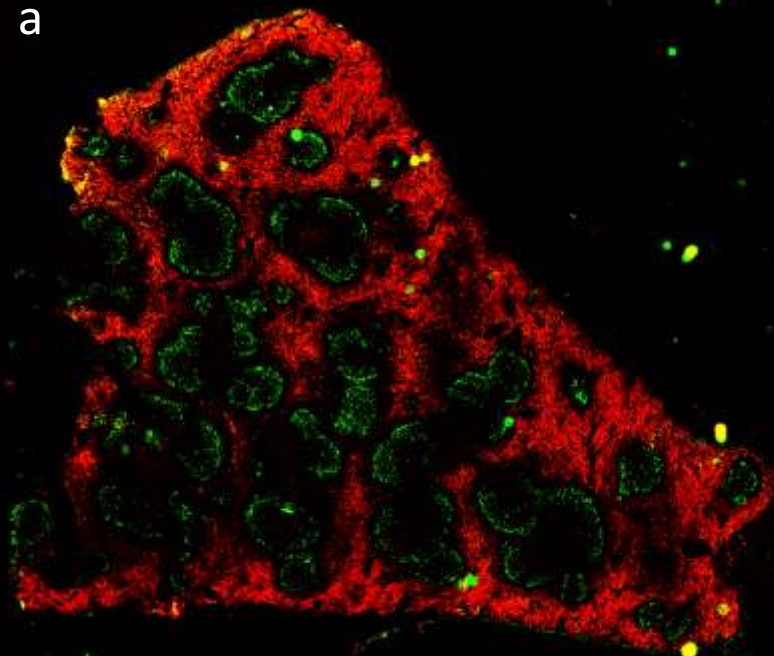
Professor of Microbial Genetics, Department of
Genetics, University of Leicester

Honorary Consultant Microbiologist, University
Hospitals of Leicester NHS Trust

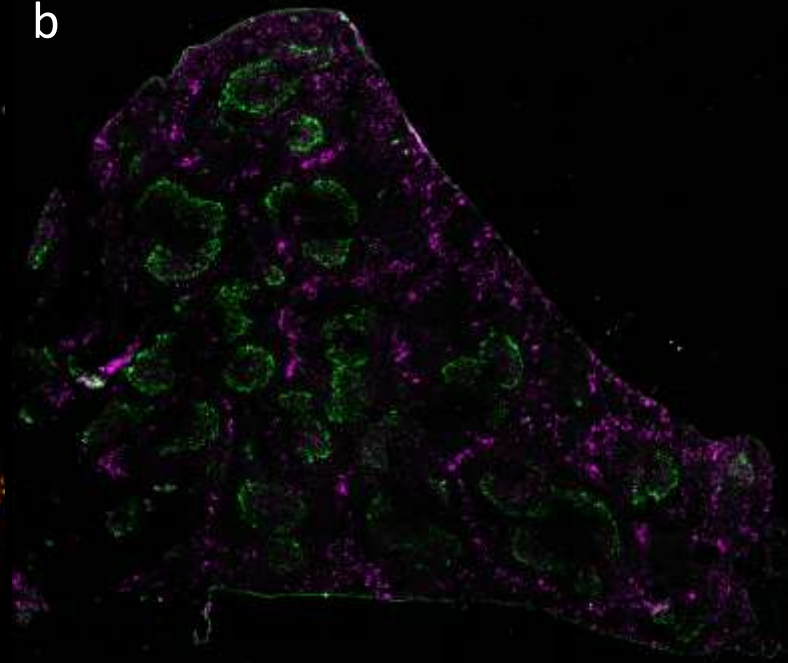
I have no conflicts of interest

... but I am looking for industrial collaborations

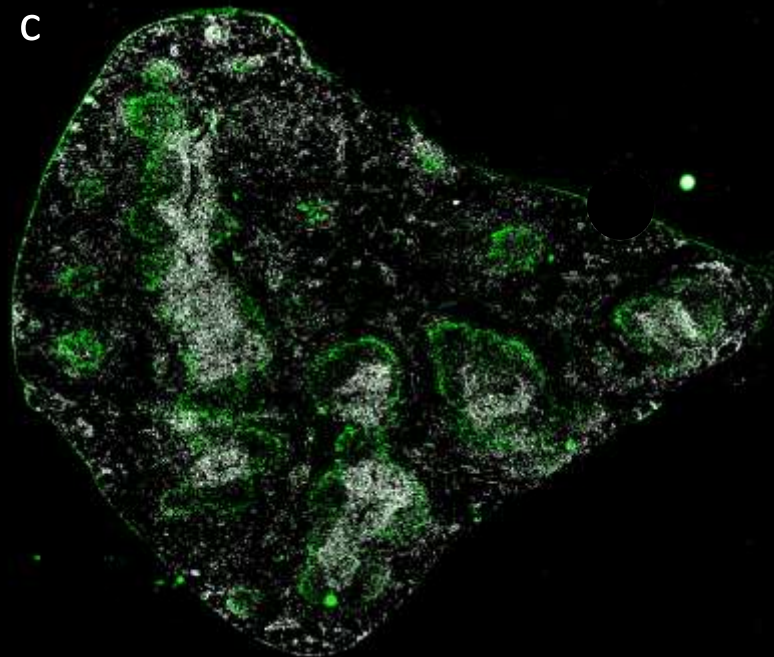
a



b



c



Mouse spleen (CD1)

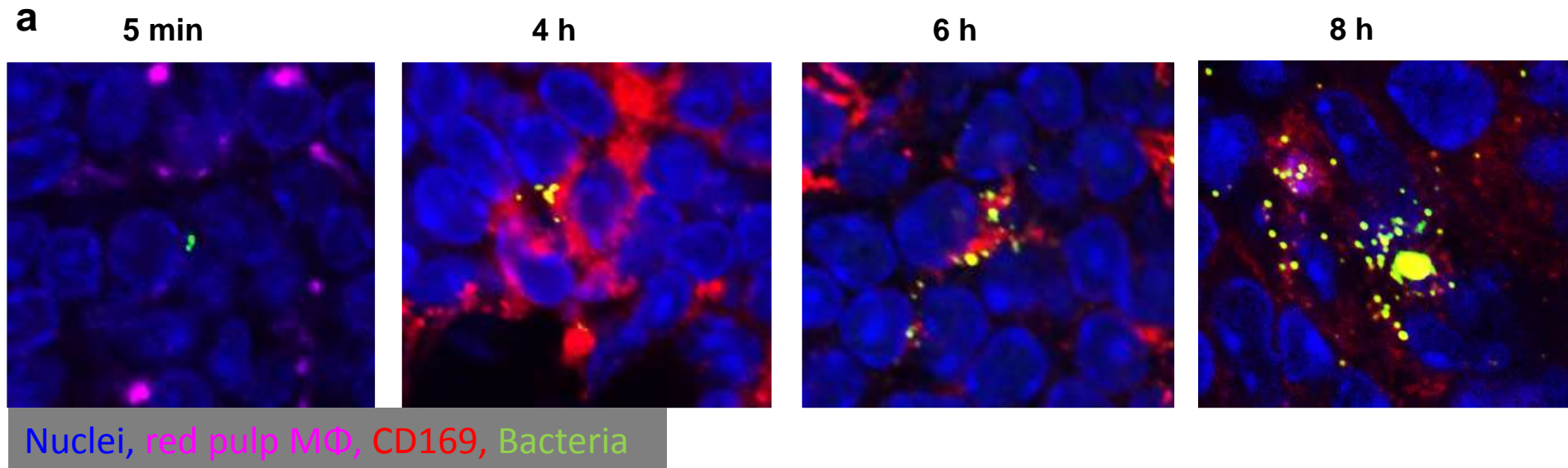
Red pulp macrophages

Marginal zone macrophages

Metallophilic macrophages

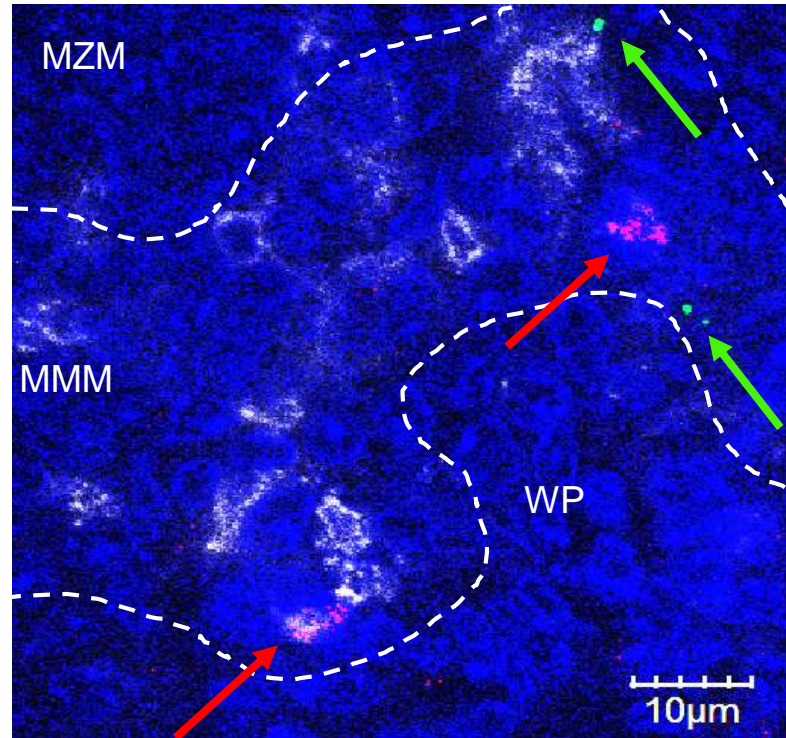
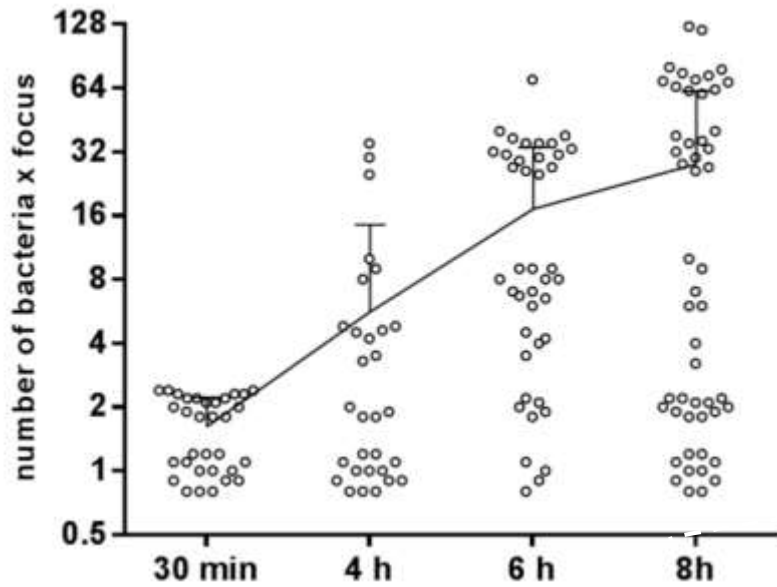
B and T cells

Can we see bacteria in the spleen ?



Yes, they are in “foci” rapidly increasing in size

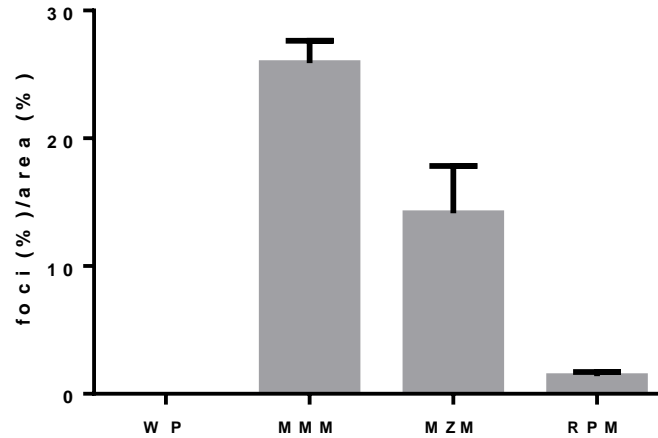
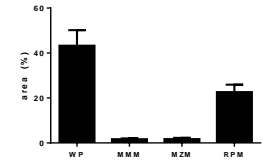
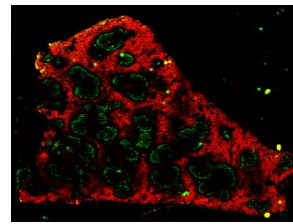
Are bacteria growing or is this a sequential uptake ?



GFP Bacteria
RFP Bacteria
CD169

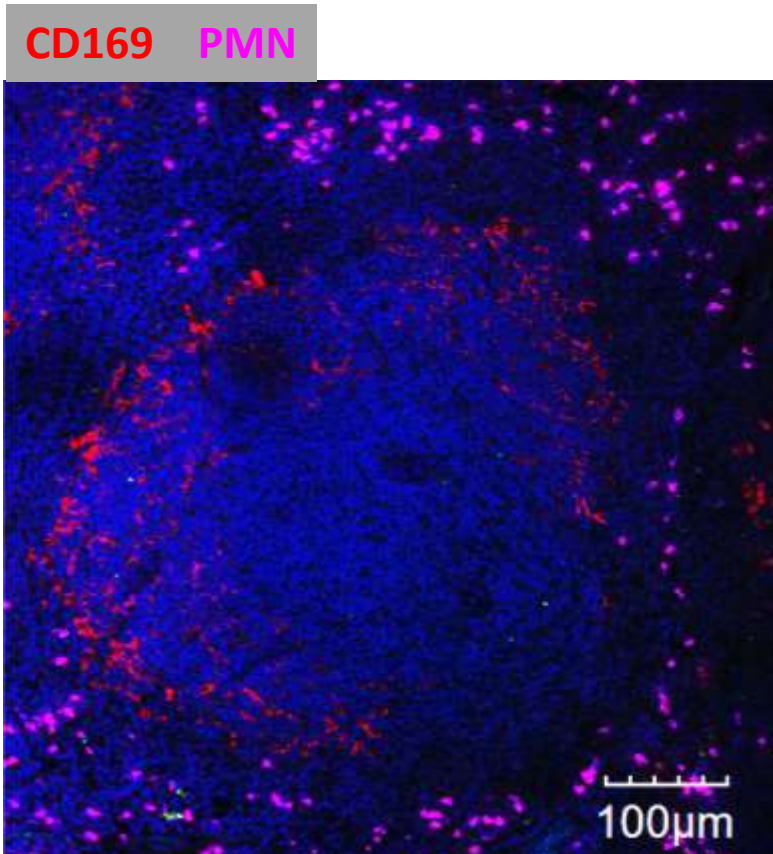
“Foci” derive from a single founder bacterium

Is a specific macrophage type involved ?

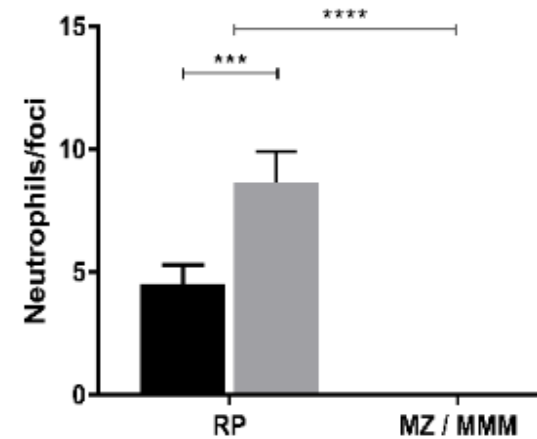
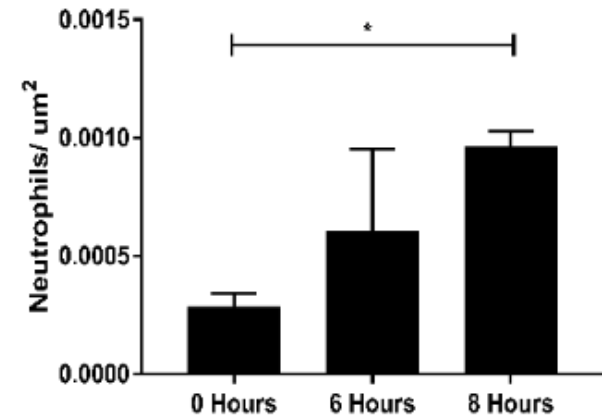


CD169+ macrophages are permissive to pneumococcal replication

How about immune surveillance ?



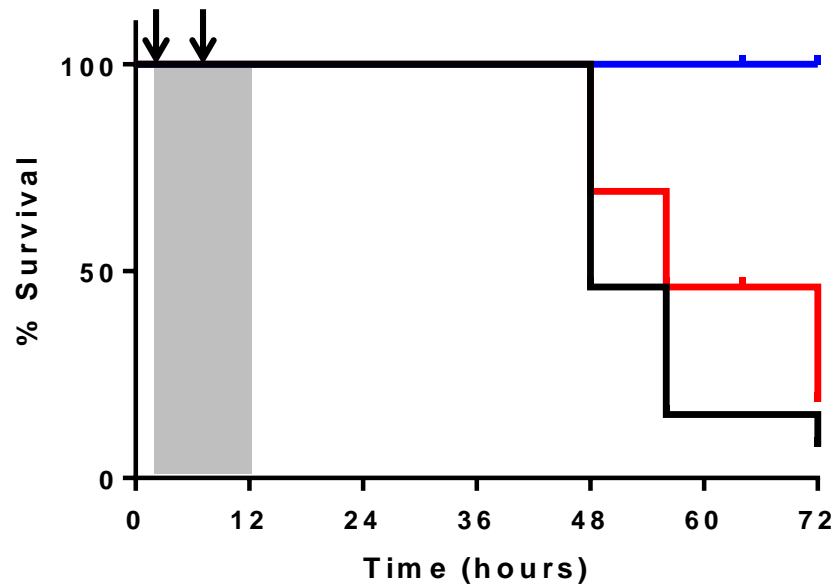
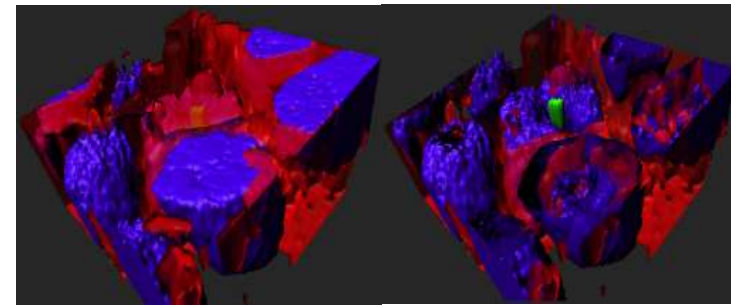
Neutrophils do not reach methallophilic macrophages



Splenic macrophages permissive for intracellular bacterial replication, a crucial phase in the early stages of septicaemia

Relevance of the finding ?

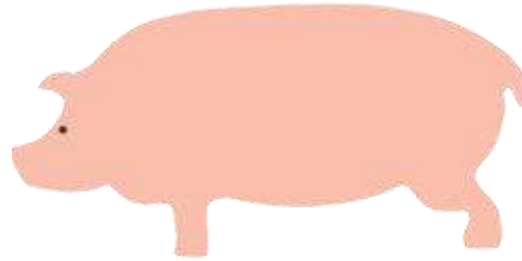
Any impact on therapy ?



Erythromycin
Ampicillin
PBS

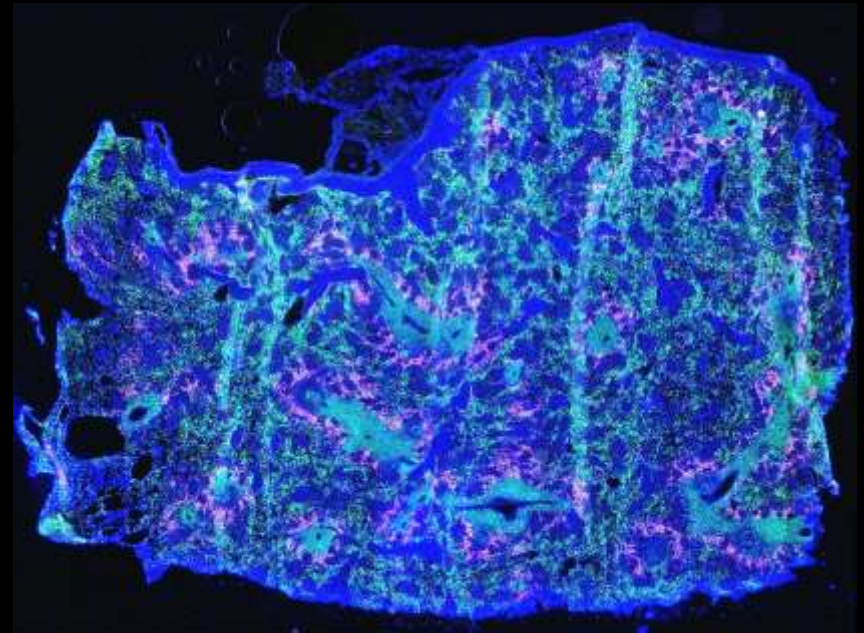
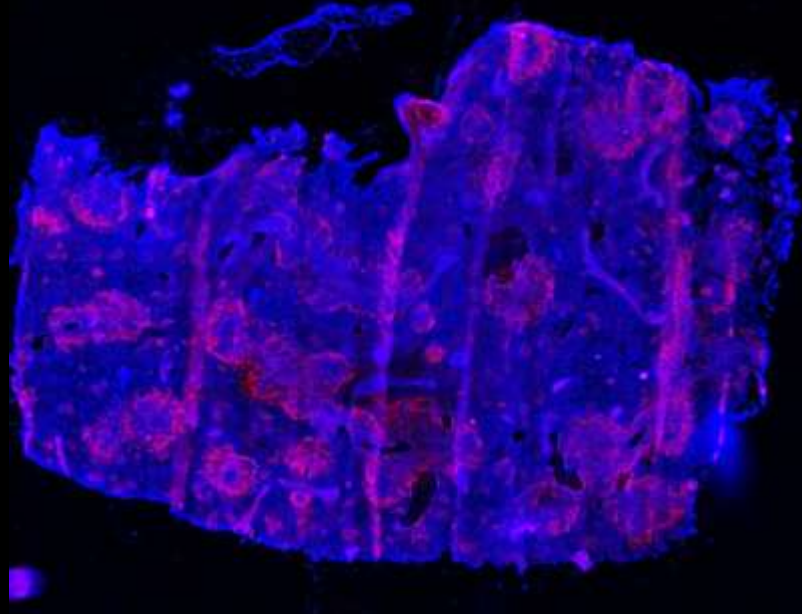
Antibiotics targeting extracellular bacteria fail to prevent sepsis

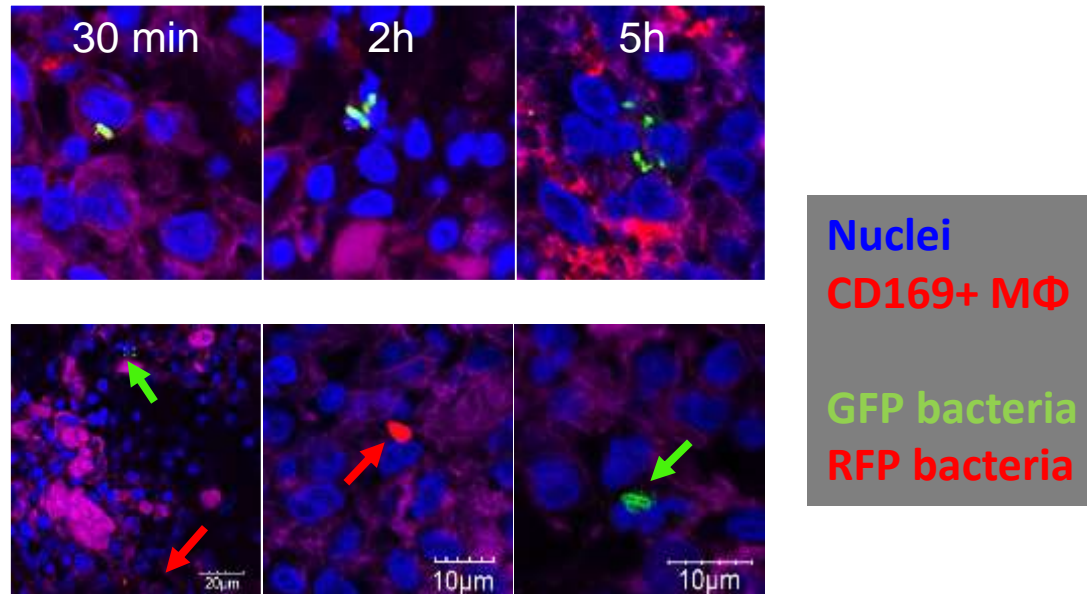
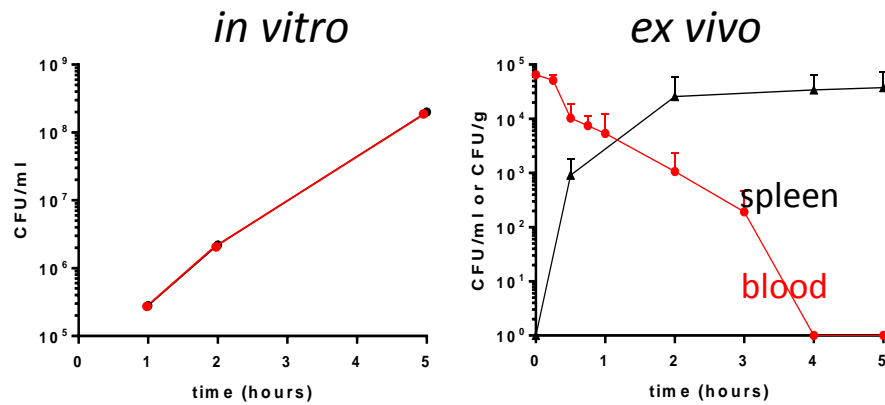
Events early after challenge shape the outcome of infection and have relevance for therapeutic strategies



Relevance of the model ?

CD169+ MΦ T-cells PMN Nuclei





In pigs, like in mice, bacteria replicate in splenic macrophages

summary

- pneumococci replicate in CD169+ splenic macrophages before bacteraemia and sepsis
- An intracellular phase preceding bacteraemia may have impact on treatment outcome
- This is valid in mouse and pig models, can it hold true also for humans?

- Giuseppe Ercoli, Joseph Wanford, Kees Straatman, Chris Bayliss, Dept. Genetics,
- Vitor Fernandes, Peter W. Andrew, Dept. Infect. Immun. Inflamm., Univ. Leicester
- Wen Chung, Ashley Dennison, HPB unit, Leicester General Hospital
- Luisa Martinez-Pomares, Univ. Nottingham
- Richard Moxon, Univ. Oxford



One Day Without Us 2017
Department of Genetics, University of Leicester

