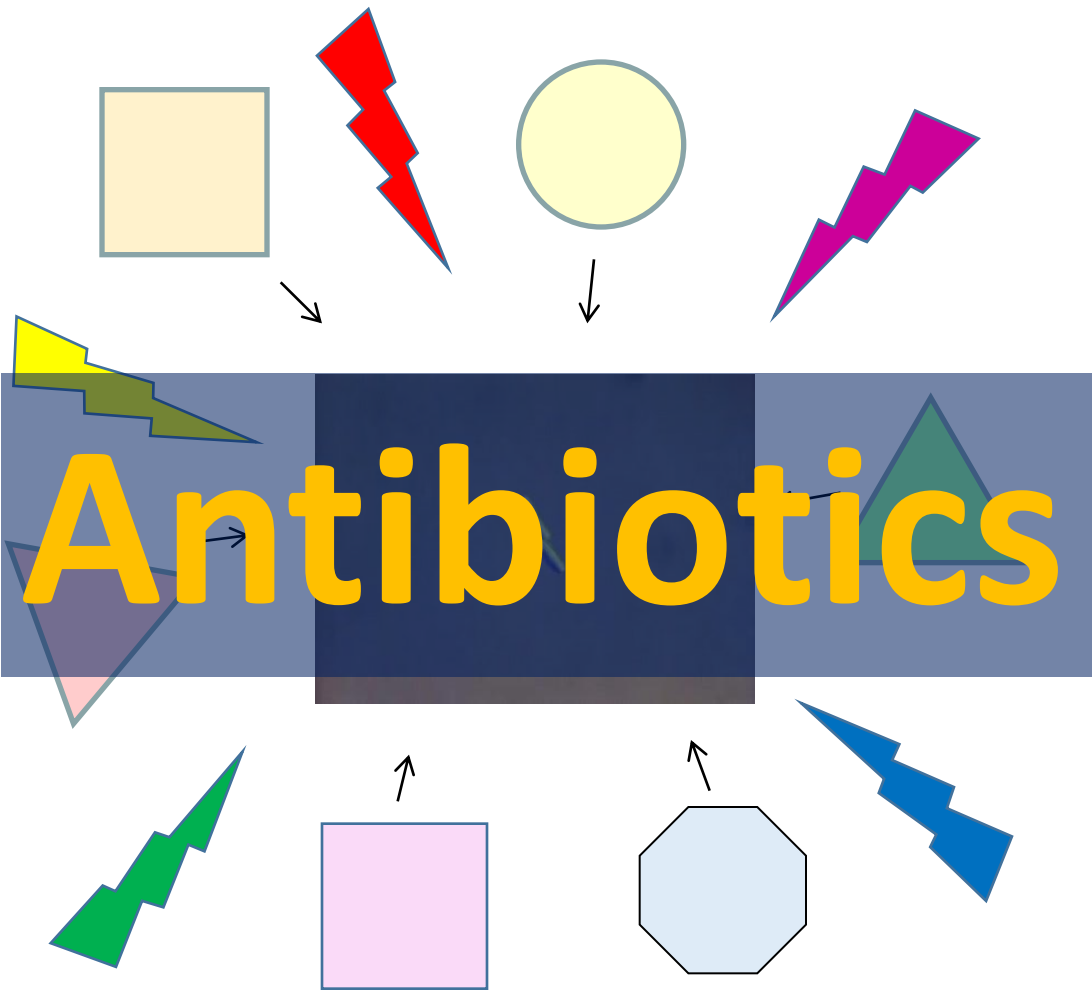
A fluorescence microscopy image of a tissue section, likely from a mouse model of Salmonella infection. The tissue is stained with a blue dye (likely DAPI) to highlight nuclei and a green/yellow dye to highlight Salmonella bacteria. The bacteria are visible as bright, irregular spots and clusters within the tissue structure. The overall appearance is dark with scattered bright spots and some blue-stained fibers.

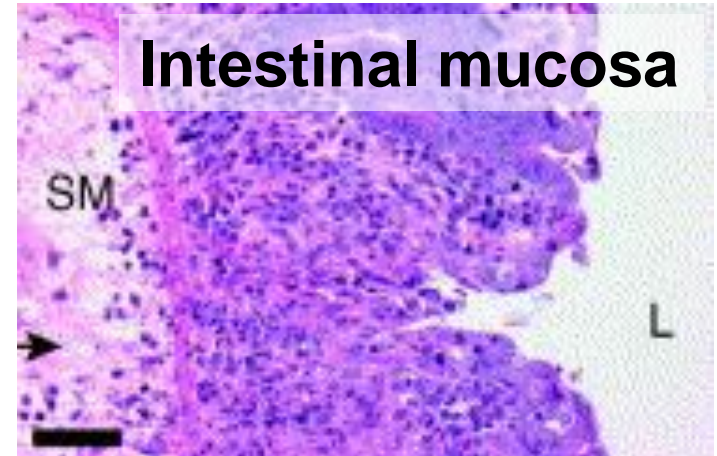
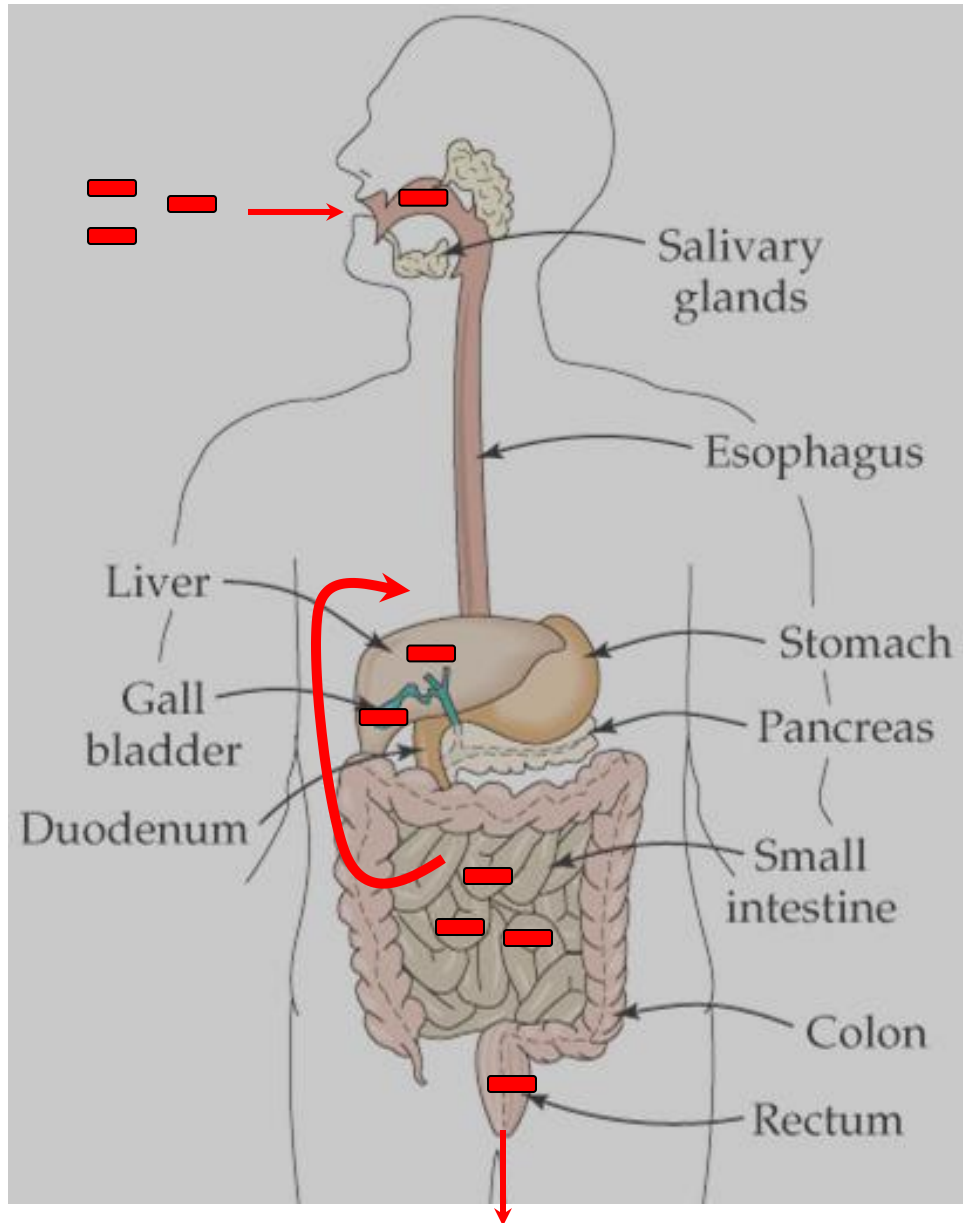
Salmonella single-cell dynamics
in complex tissues

Dirk Bumann
Infection Biology
Biozentrum, Universität Basel

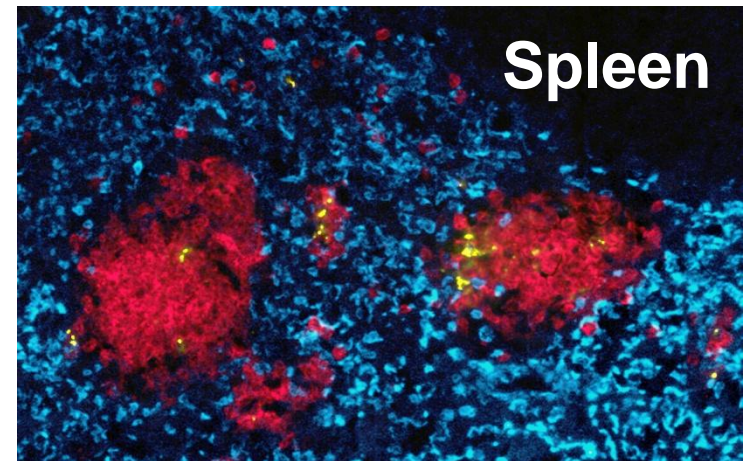
Pathogen growth as a function of nutrient access and host attacks



Course of salmonellosis



Diarrhea:
94 Mio cases, 80'000 deaths

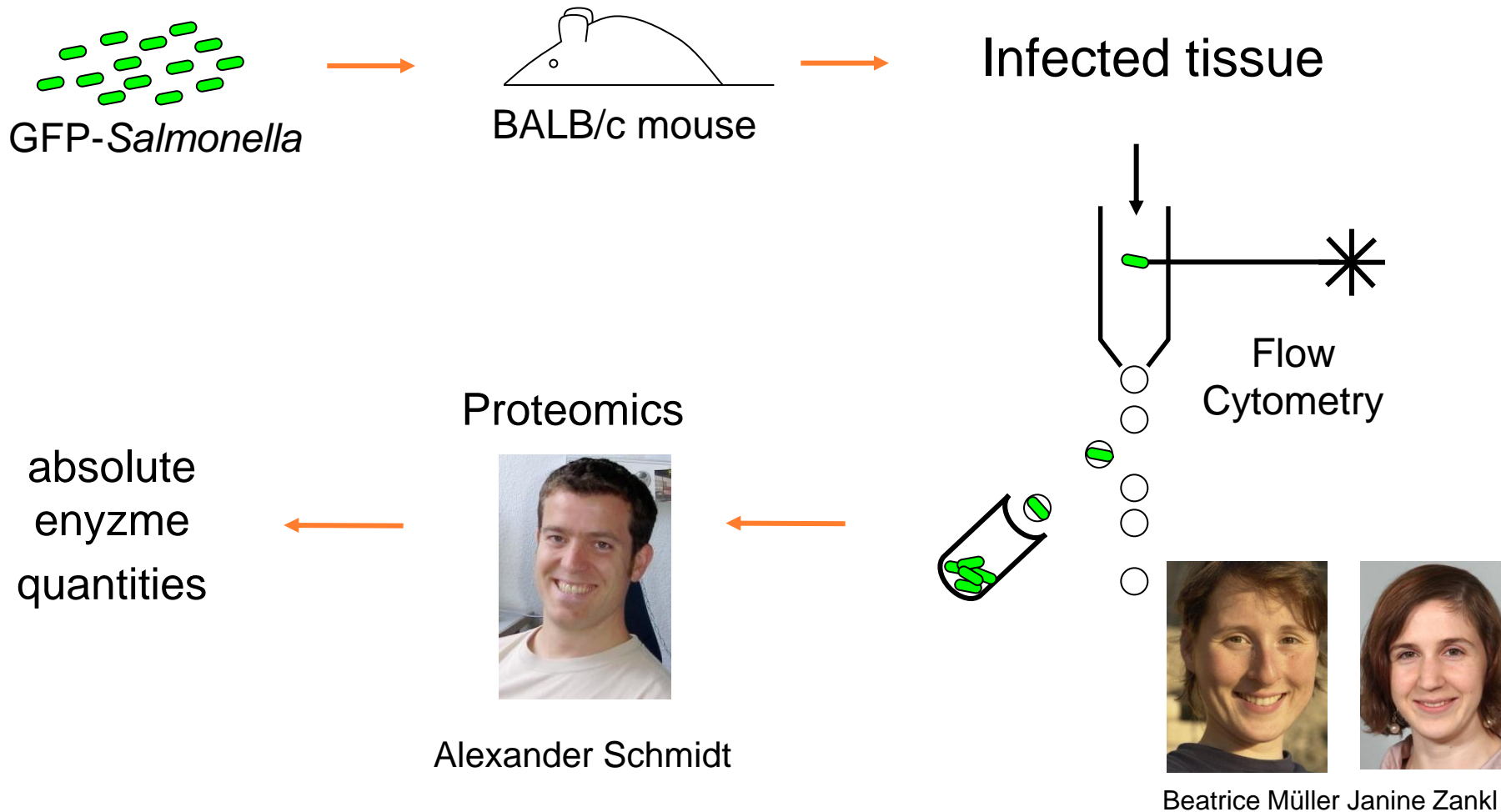


Typhoid fever:
16 Mio cases, 190'000 deaths

Ex vivo *Salmonella* proteomics



Neil Burton



GFP-*Salmonella*

BALB/c mouse

Infected tissue

Proteomics

absolute enzyme quantities

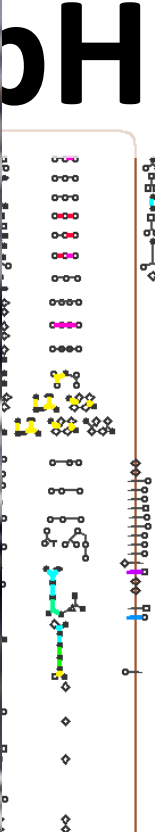
Flow Cytometry

Alexander Schmidt

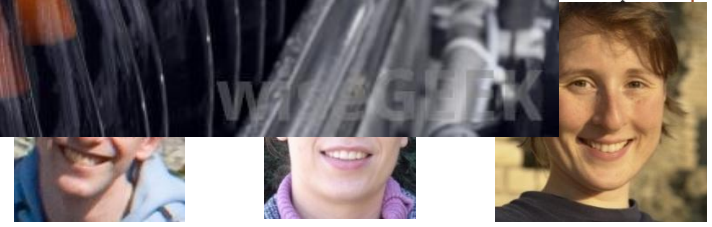
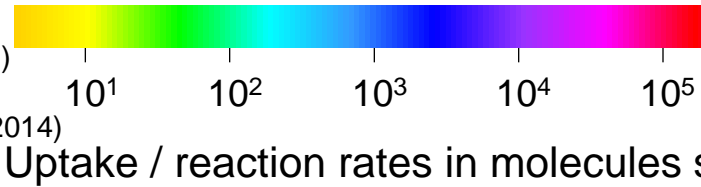
Beatrice Müller Janine Zankl

A quantitative model of *Salmonella* in vivo metabolism

The same drink for everybody ?

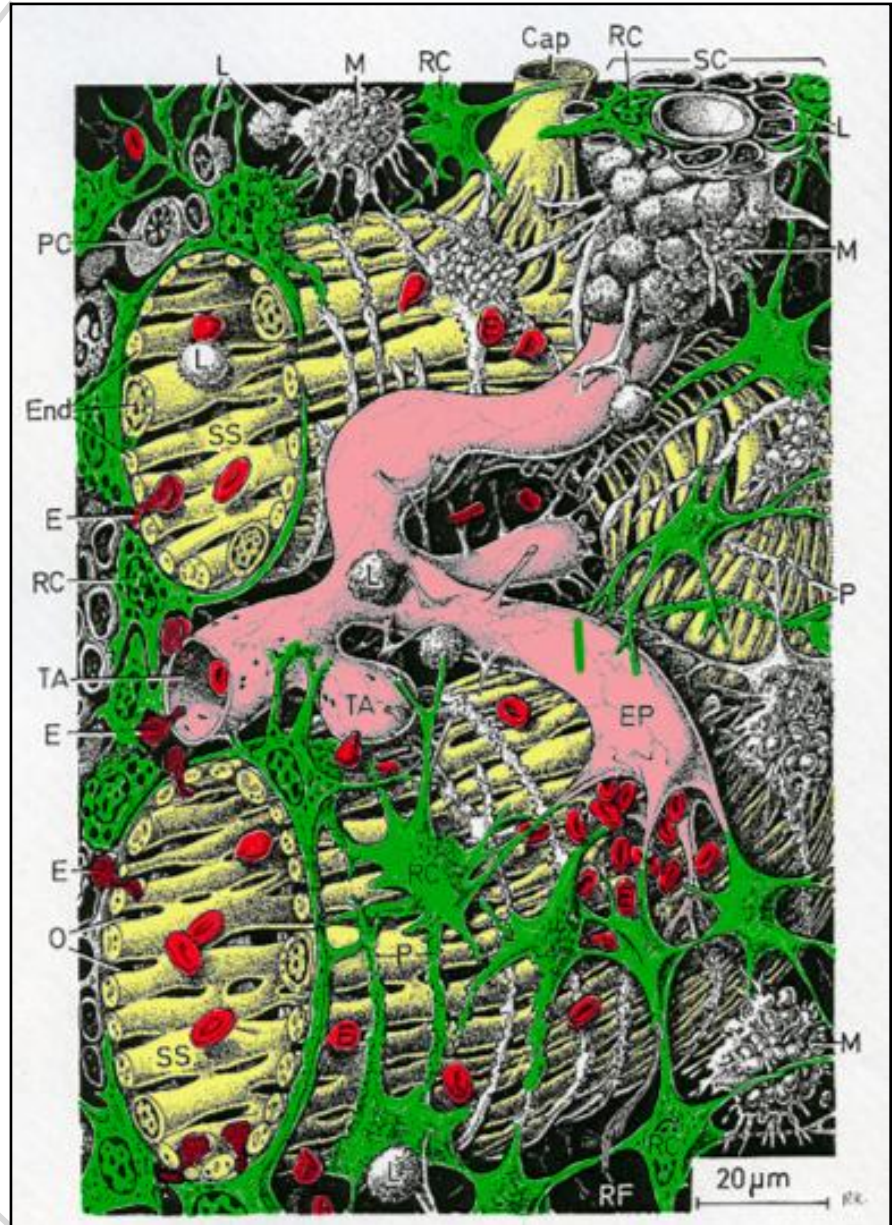
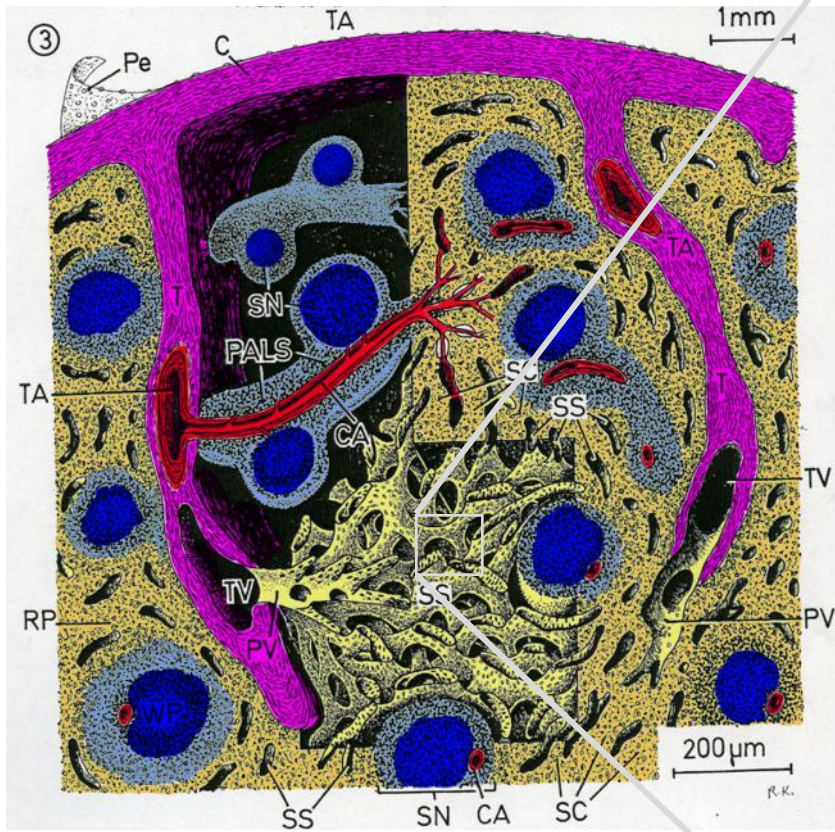


Becker et al Nature (2006)
 Thiele et al. BMS Syst Biol (2011)
 Steeb et al. PLoS Pathog (2013)
 Burton et al. Cell Host Microbe (2014)



Benjamin Steeb Ines Thiele Beatrice Müller

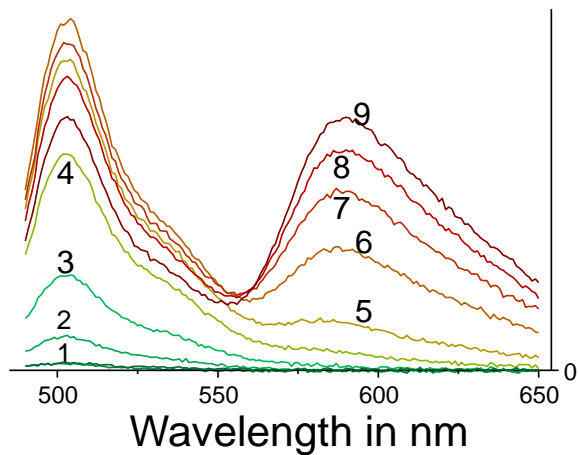
Complex anatomy of host organs



Adapted from:
Krstic, R.V. Human Microscopic Anatomy.
Springer Berlin Heidelberg (1991).

TIMER^{bac} as a growth rate reporter in vitro

Emission spectra

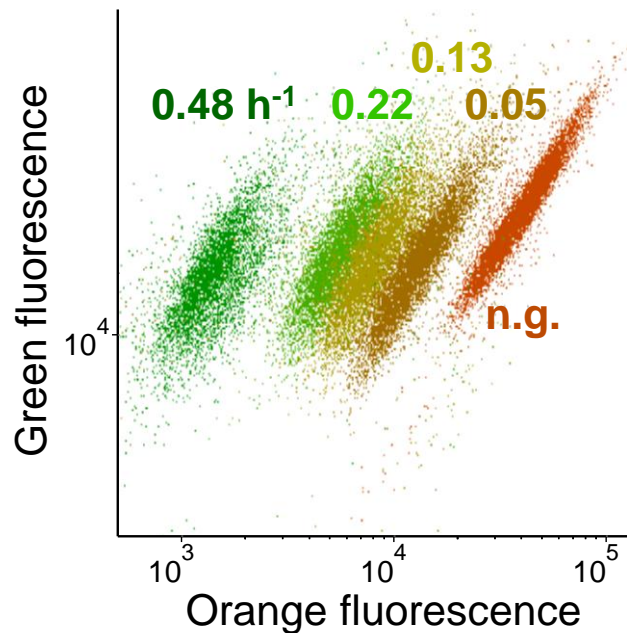


Petra Spröte

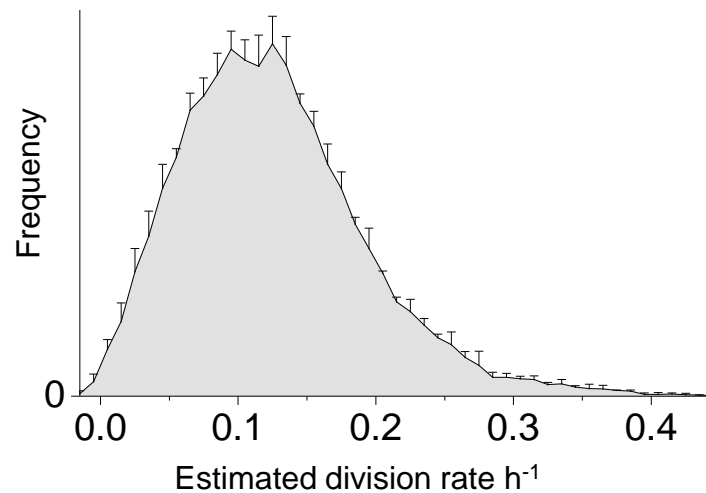


Beatrice Claudi

In vitro cultures



Mouse spleen



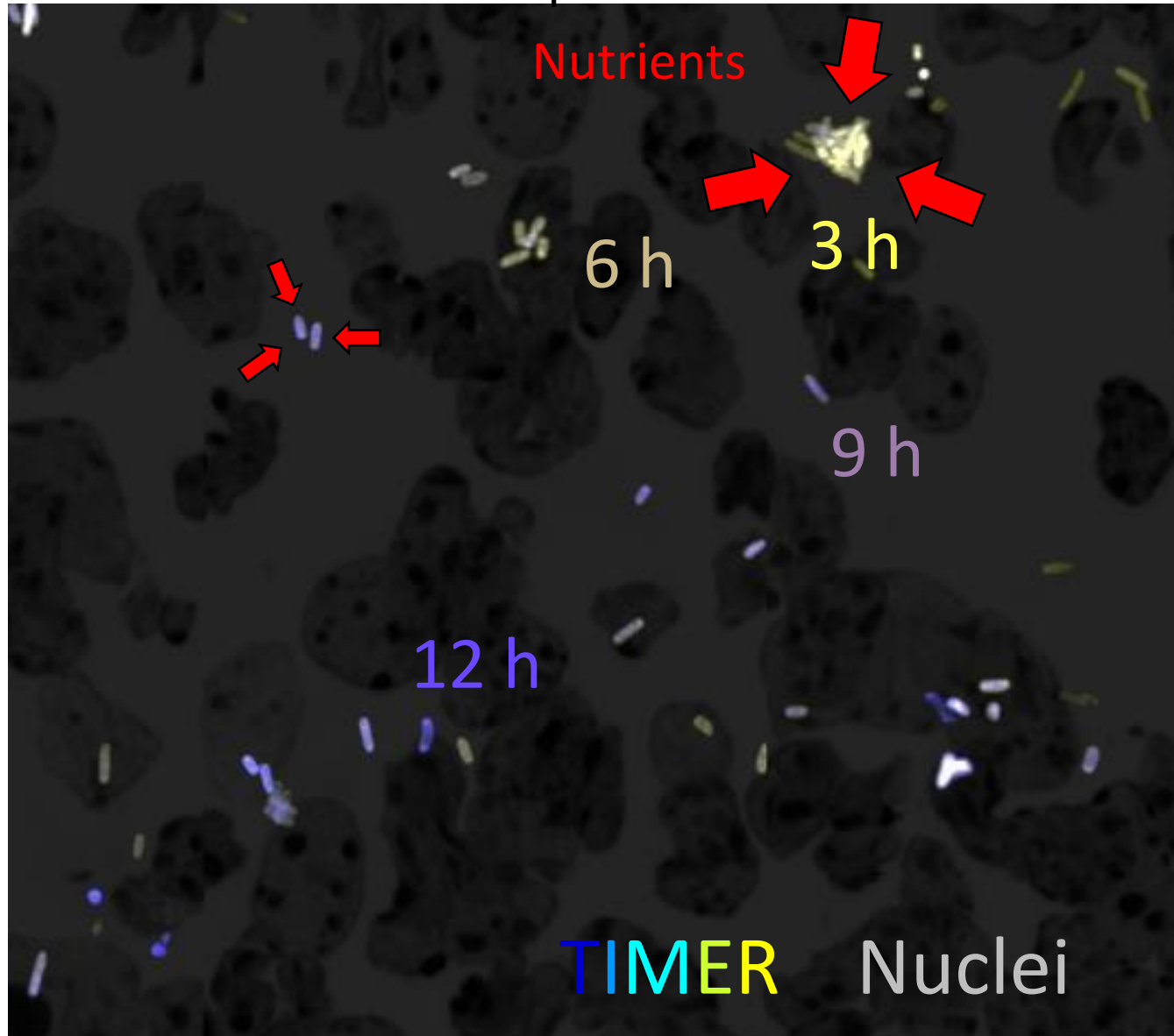
Janine Zankl



Anna Chirkova

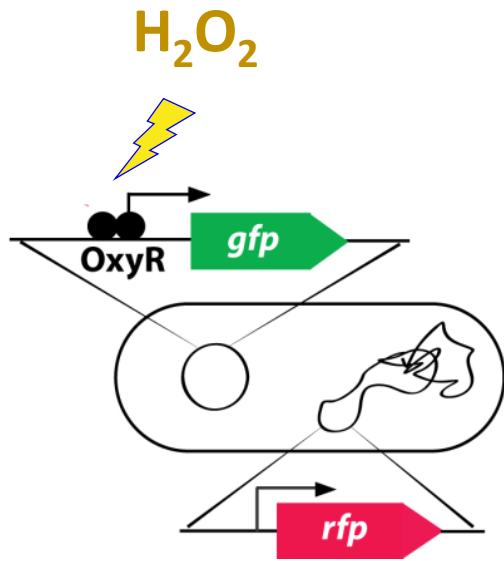
Heterogeneous growth of microcolonies

Infected spleen section

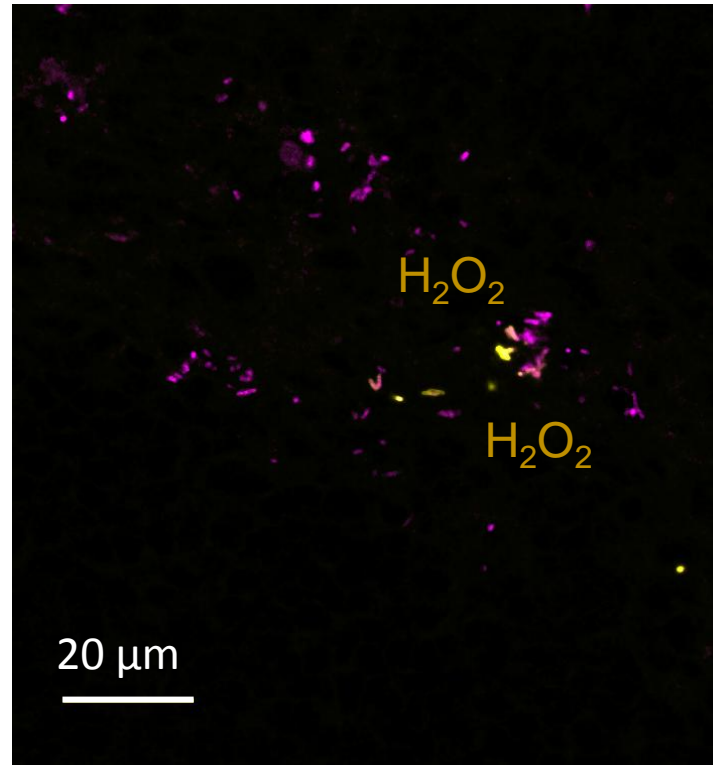


Beatrice Claudi

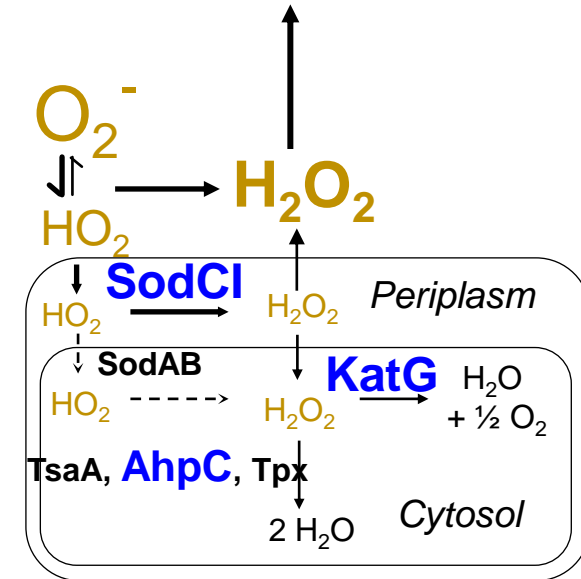
Heterogeneous stress in individual *Salmonella*



Infected spleen section



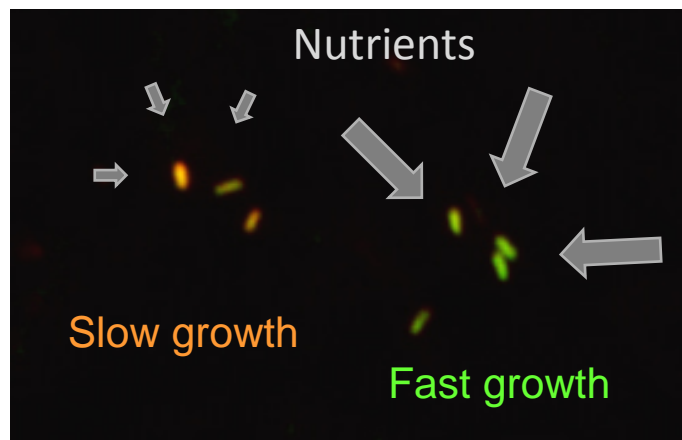
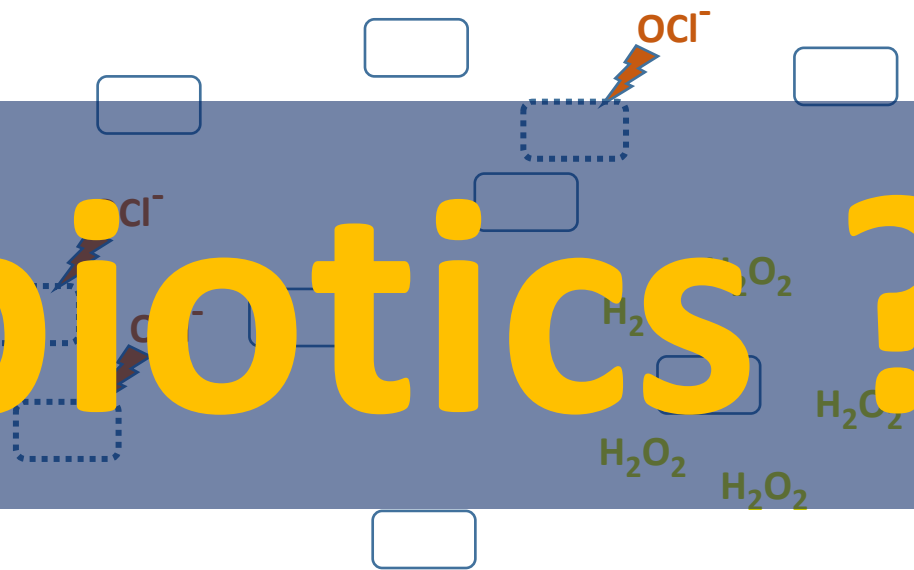
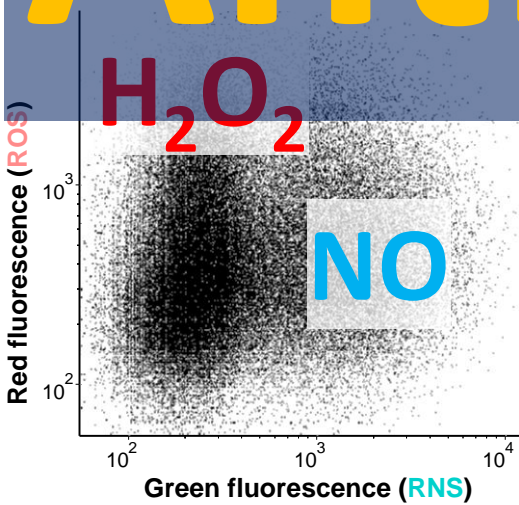
Salmonella defense



Neil Burton Nura Schürmann



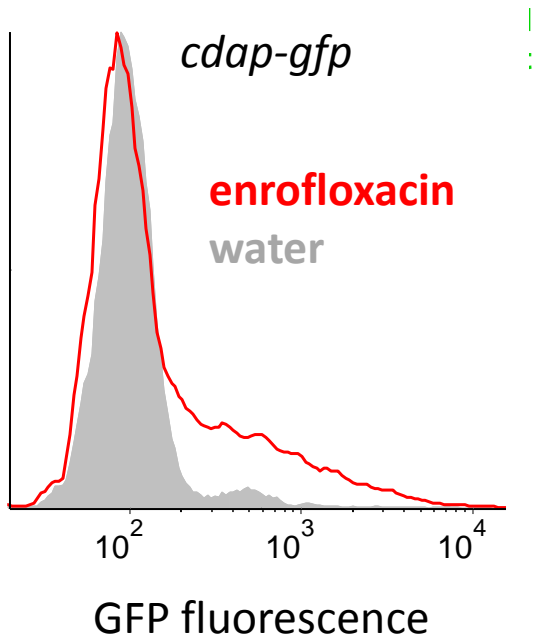
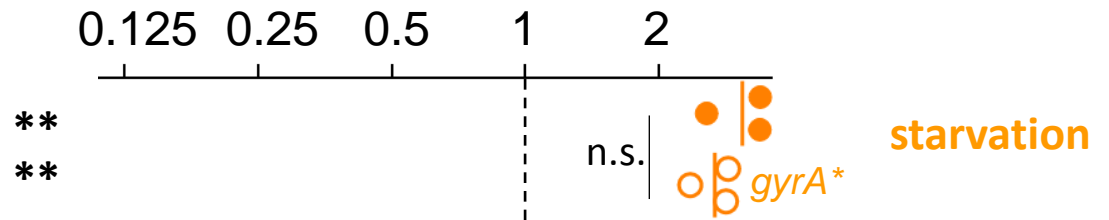
Antibiotics?



3. Impact of *Salmonella* heterogeneity on slow eradication ?

Relative survival of stressed subset

“Tolerance”



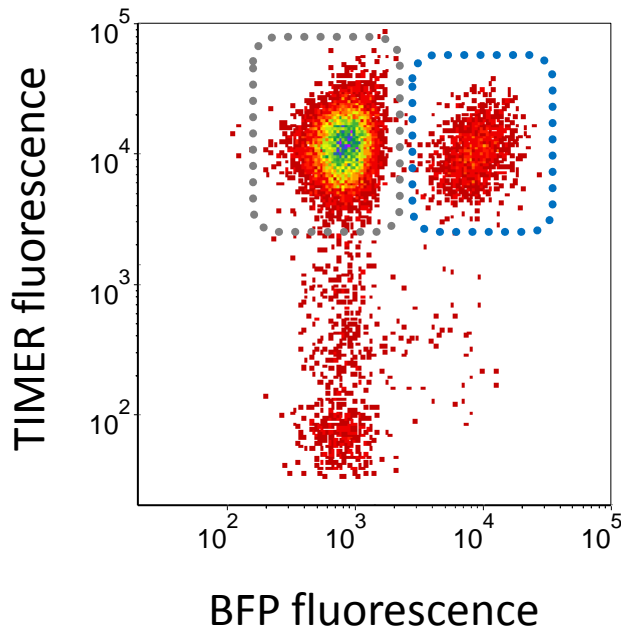
Strong antagonism / synergism of host attacks with antibiotic: Diverse levels of tolerance

Tolerance facilitates resistance?

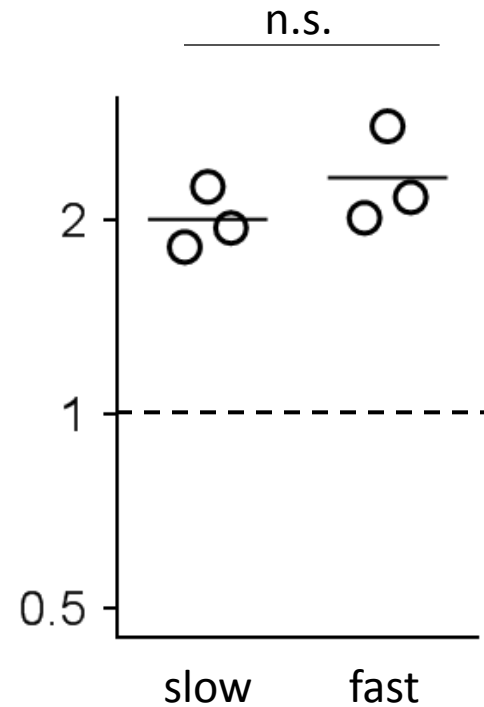


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WT-TIMER MIC 0.06 mg l⁻¹ (S) *gyrA** *bfp* -TIMER MIC 0.5 mg l⁻¹ (IR)

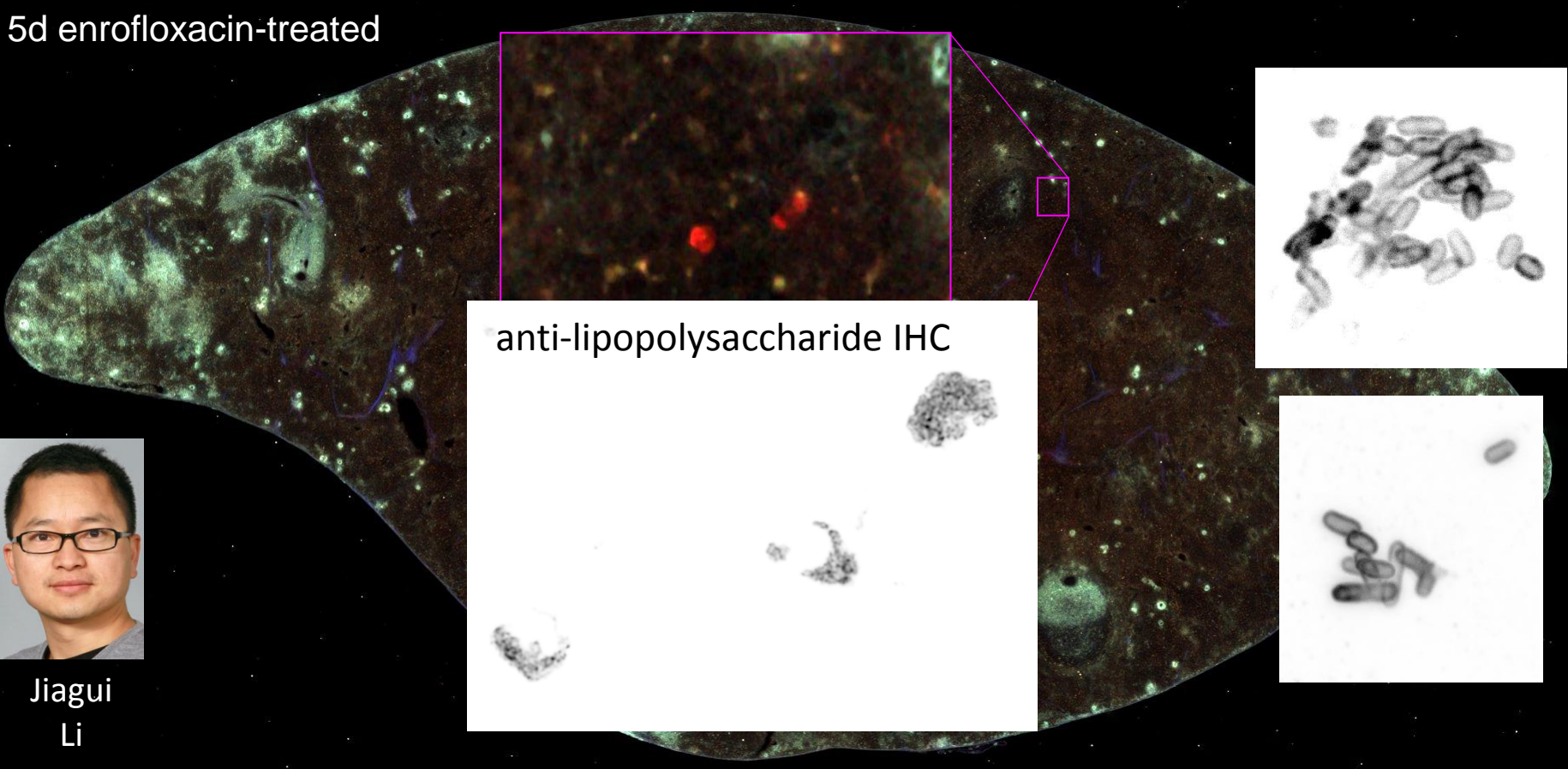


Relative survival of IR strain



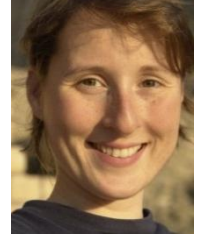
Finding rare live *Salmonella* in spleen: S2P tomography

5d enrofloxacin-treated



Jiagui
Li

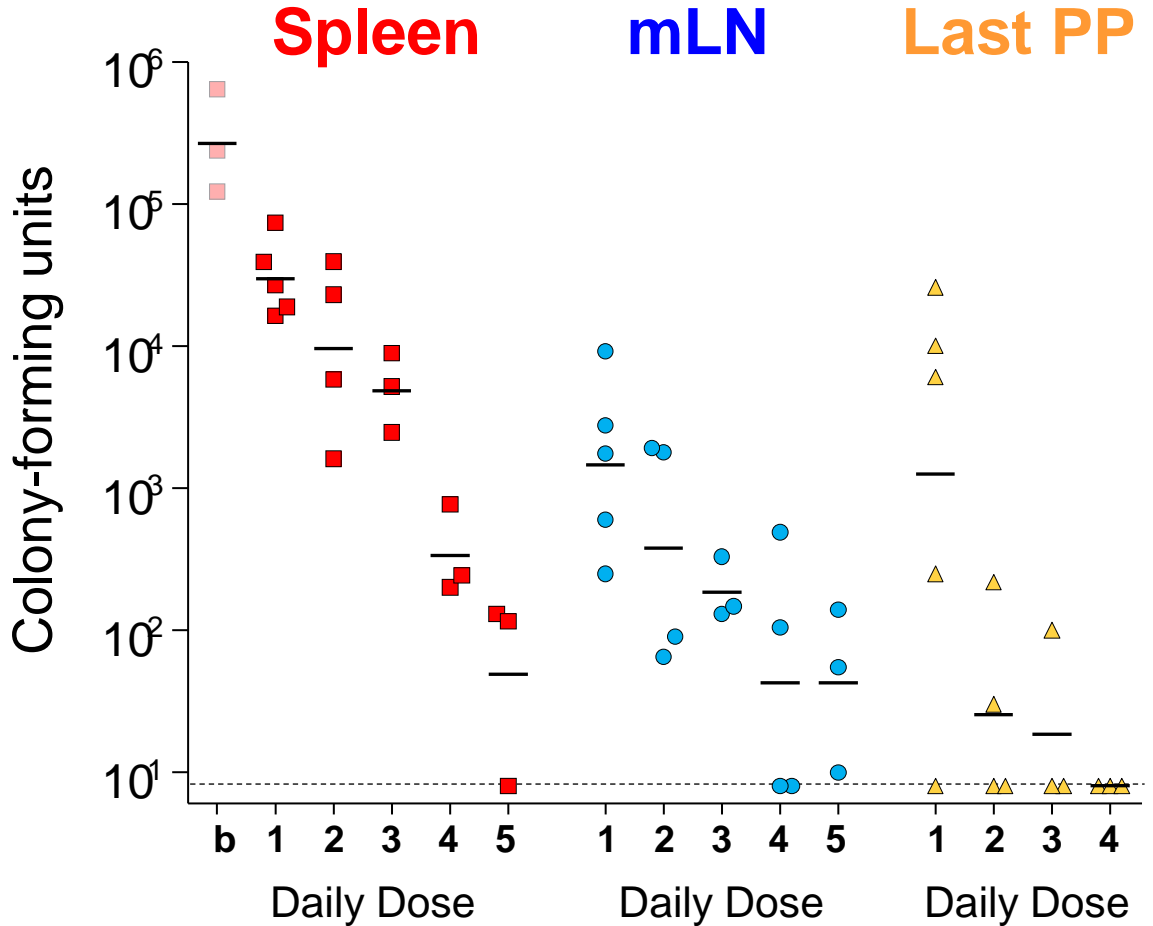
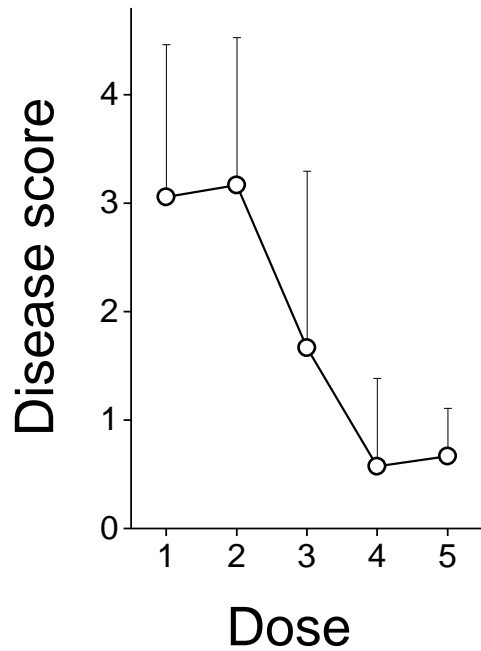




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Slow eradication of *Salmonella* in vivo

BALB/c mice, oral infection day 5, treatment with 5 mg kg⁻¹ enrofloxacin

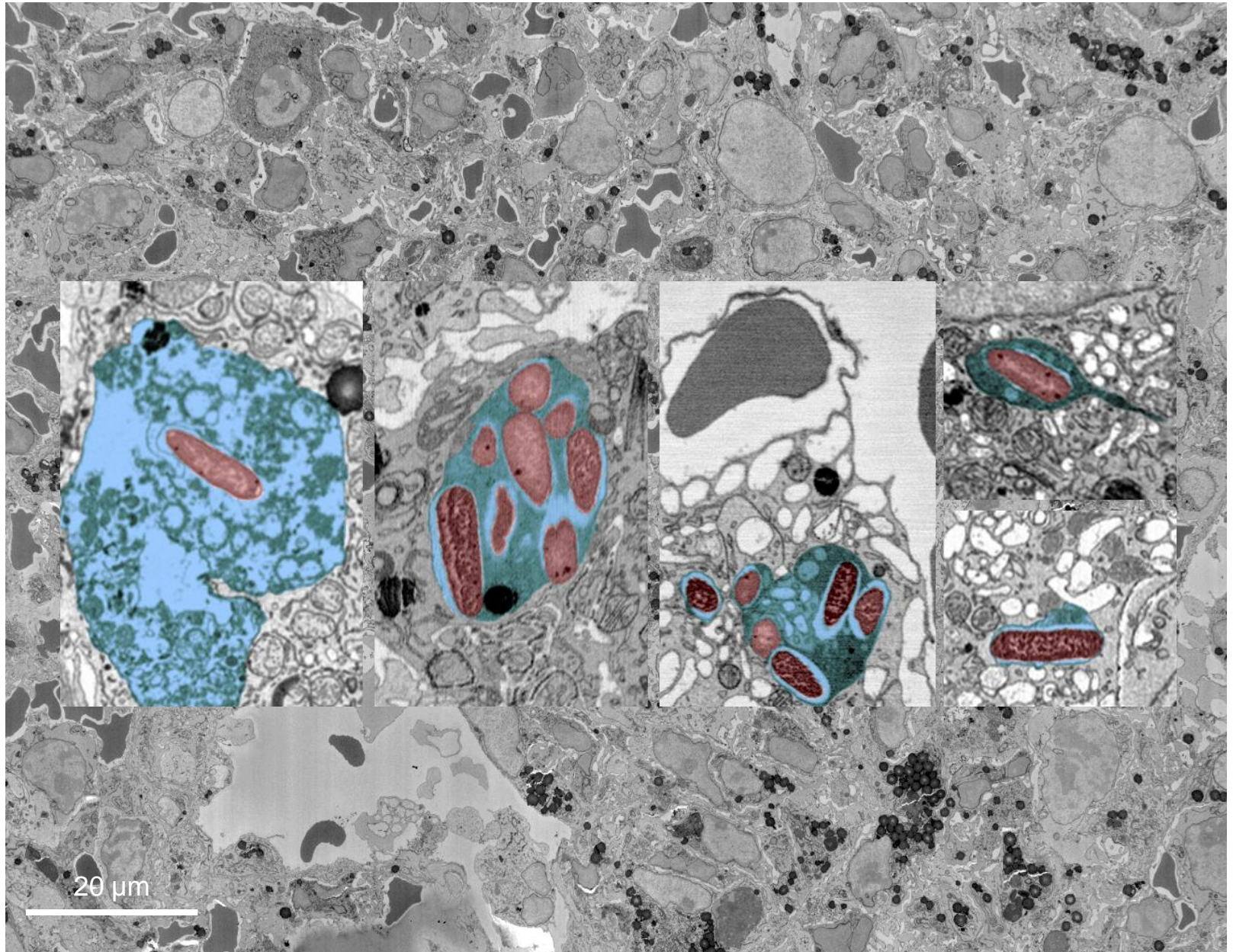


Similar in human enteric fever patients:
Travel Med Infect Dis 9, 263-277 (2011)

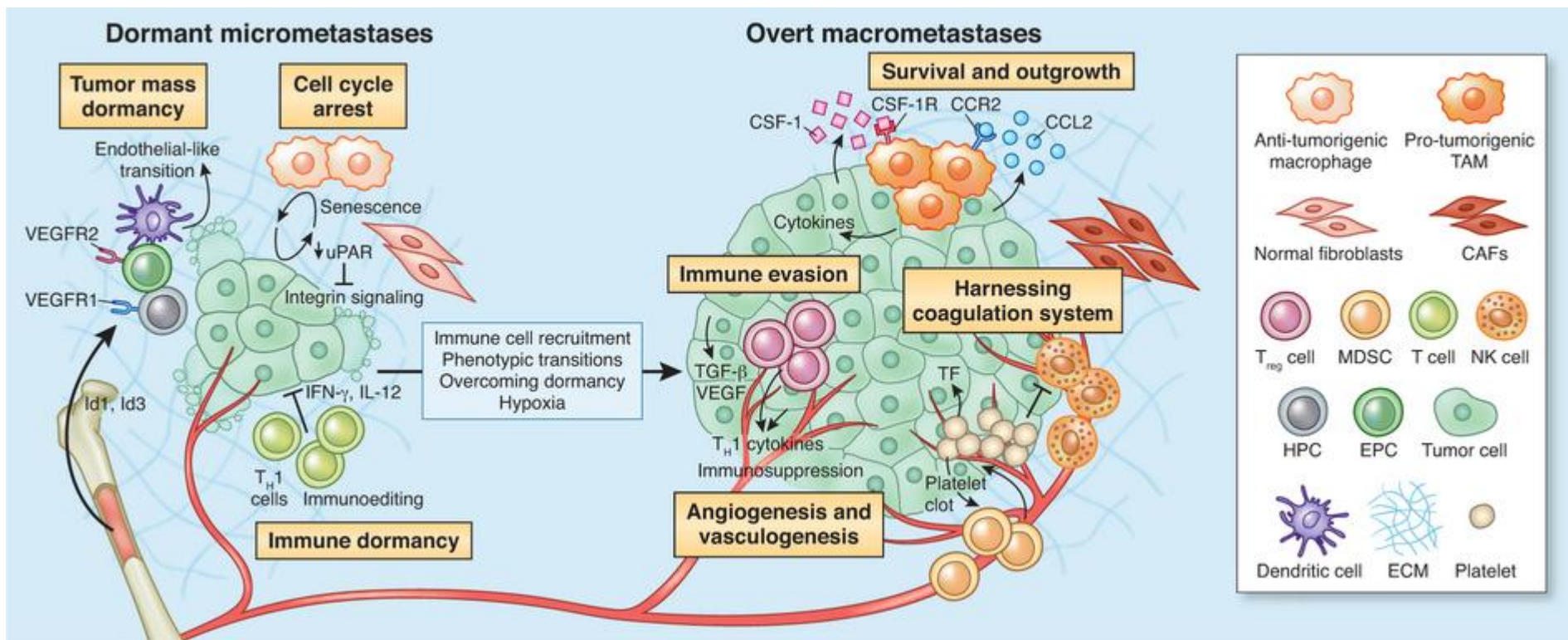
Summary



Mapping *Salmonella* microenvironments – SBF-SEM



Tumor microenvironments determine cancer outcome



Science 352, DOI: 10.1126/science.aad3018 (2016)

Nature Rev Immunol 15, 669–82 (2015)

Nature Rev Cancer 15, 409–25 (2015)

Nature 501, 346–54 (2013)

Nat Med 19, 1423–37 (2013)



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Cristela Oliveira Cravo
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Gerardine Suter-Cremin

Alain Brühlhardt



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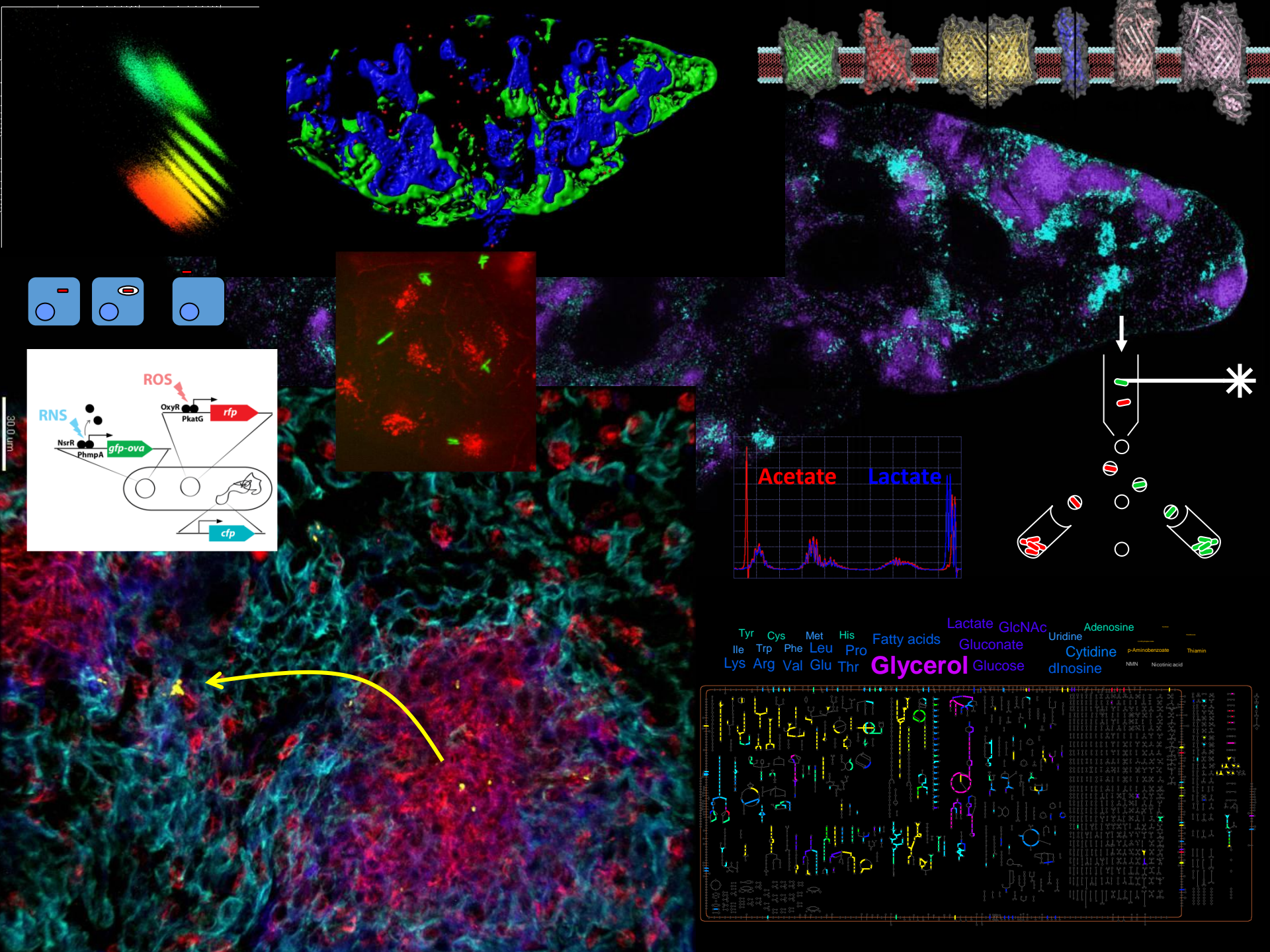


HUMAN FRONTIER SCIENCE PROGRAM
FUNDING FRONTIER RESEARCH INTO COMPLEX BIOLOGICAL SYSTEM

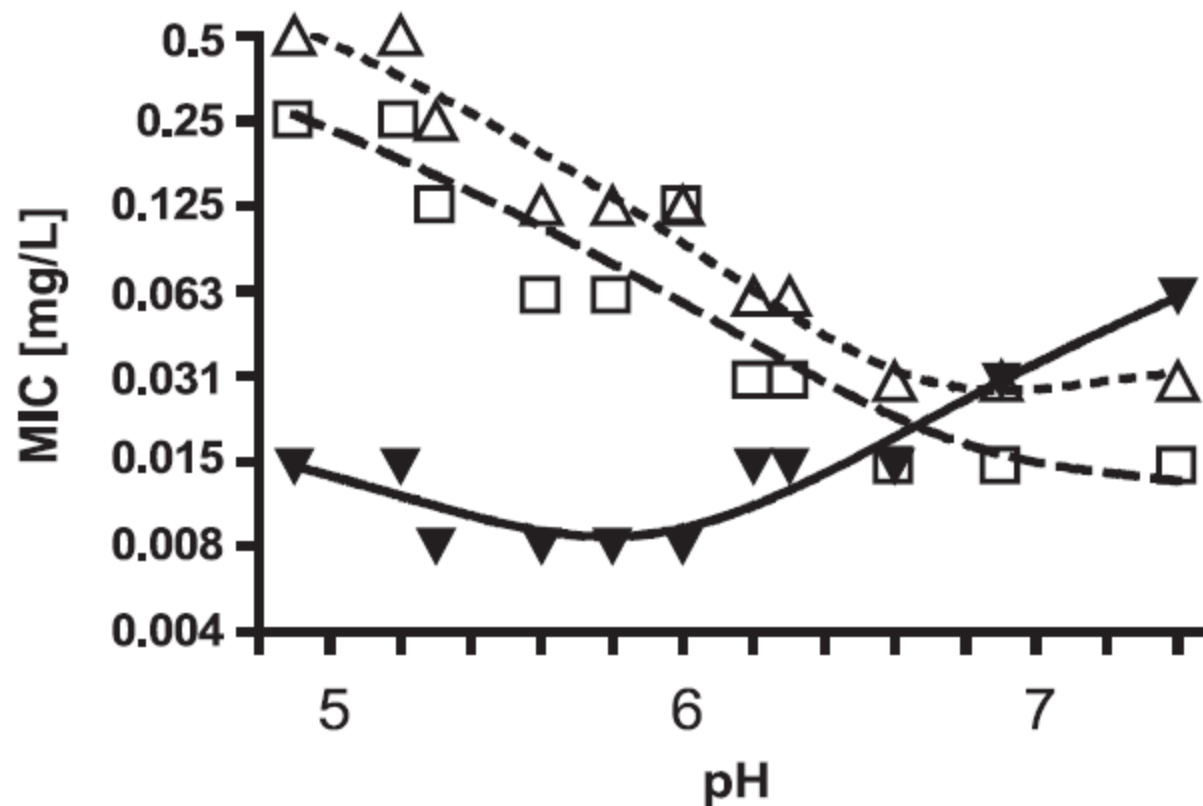


Innovative Medicines Initiative

SystemsX.ch
The Swiss Initiative in Systems Biology



E. coli ATCC 25922



Salmonella Polymorphonuclear Neutrophils Erythrocytes

Salmonella enterica ser. Typhimurium
in mouse spleen

Nutrients, *Salmonella* metabolic pathways, stresses?

Ex vivo proteomics, metabolic mutants, in silico