Combining wet lab and computational simulations to predict optimal antibiotic drug regimens for *Mycobacterium tuberculosis*

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Problem: Tuberculosis is the number one cause of death due to infectious disease. Drug treatment is long (9 months), with multiple drugs and resistance is prevalent. No rational approach to drug regimen design exists.

How we approach it:

- We designed an integrated computational/experimental approach to optimizing drug regimen
- We developed an MSM of granuloma formation, antibiotic distribution, antibiotic treatment
- We predict optimal solutions for treatment that we will test in the non-human primate

Details:

- We utilize a cellular and tissue scale agent-based model to simulate immune cell and bacterial interactions on a two- or three-dimensional spatial grid to capture the emergent behavior of granuloma formation
- At the molecular scale, blood vessels in the agent-based model deliver antibiotics into lung tissue where antibiotics undergo diffusion, extracellular binding, and cellular partitioning
- We apply a surrogate-assisted optimization framework to predict optimal sterilizing regimens,
- providing an efficient way to identify optimal regimens
- We use sensitivity/uncertainty analysis to define parameters & predict factors driving outcomes
- We created a team with other MSM members for model credibility practices (see cartoon).