

3D Granuloma Organ on a Chip

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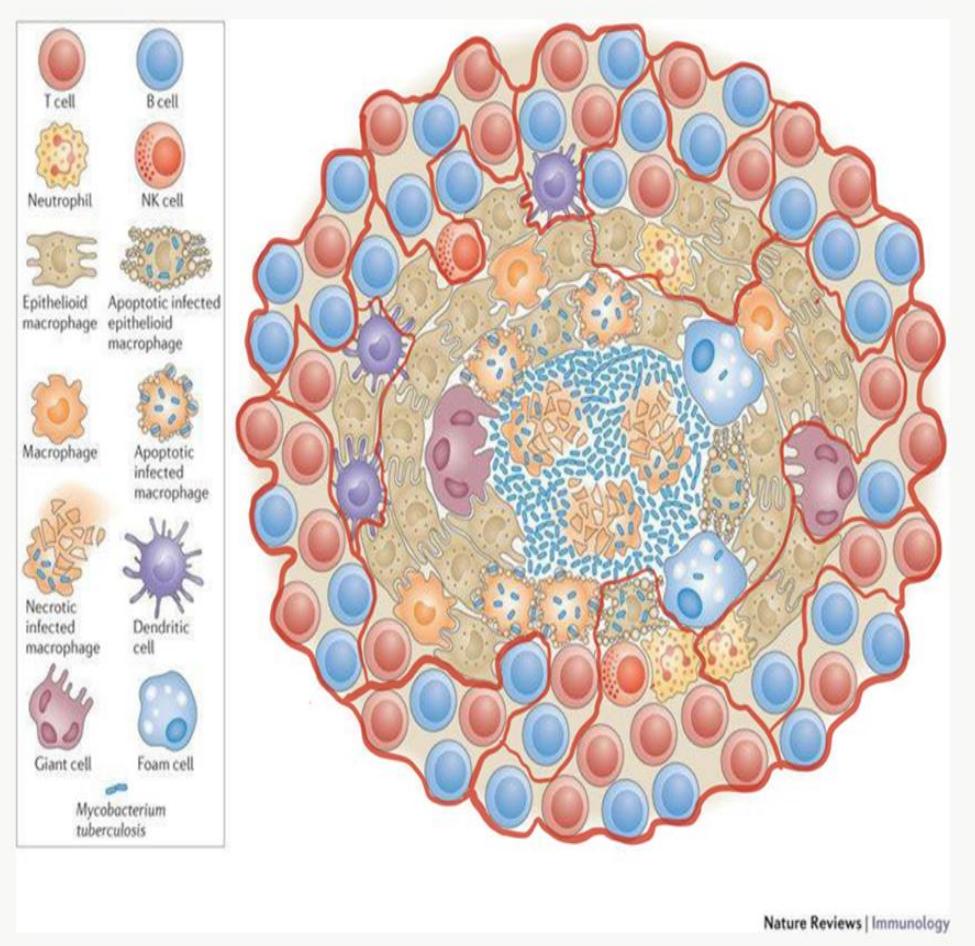
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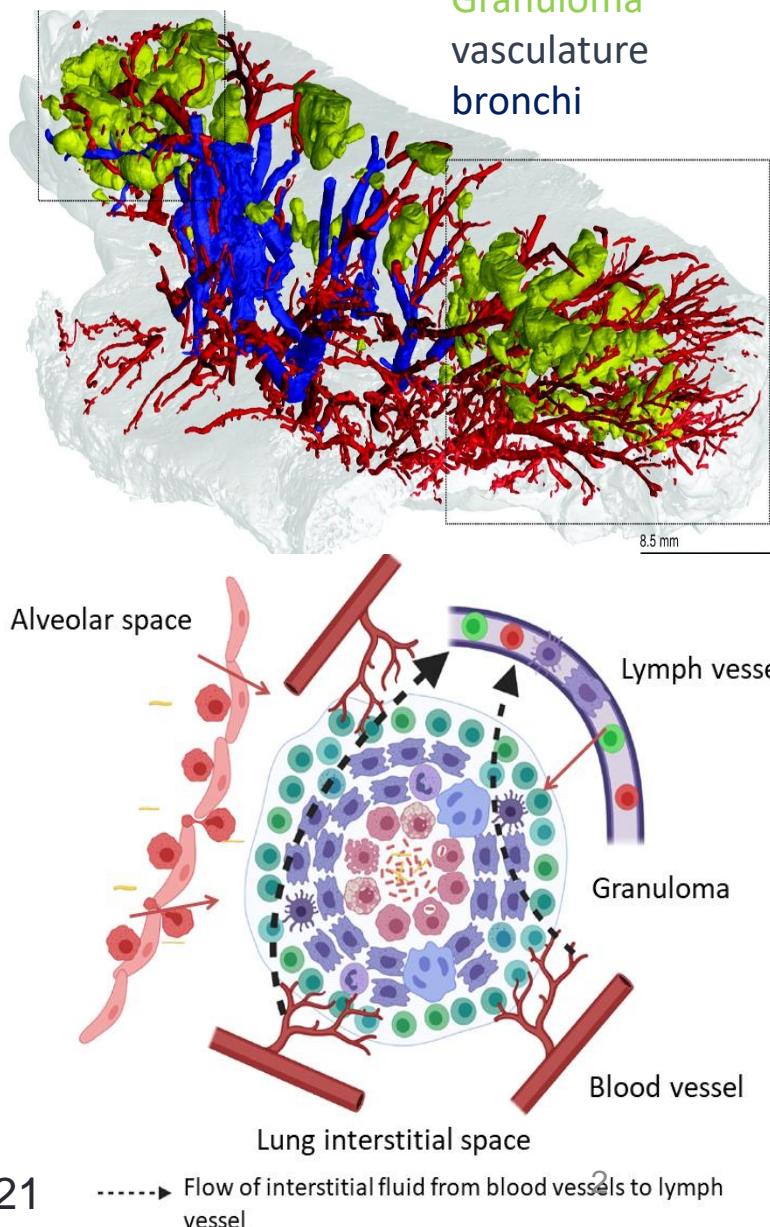
The tuberculosis granuloma



Collagen matrix

- The granuloma is the pathological hallmark of tuberculosis
- Organized 3D aggregate of immune cells
- Dynamic structure of cells
- Necrotic when size $> 3\text{mm}$
- Can develop a caseous hypoxic core

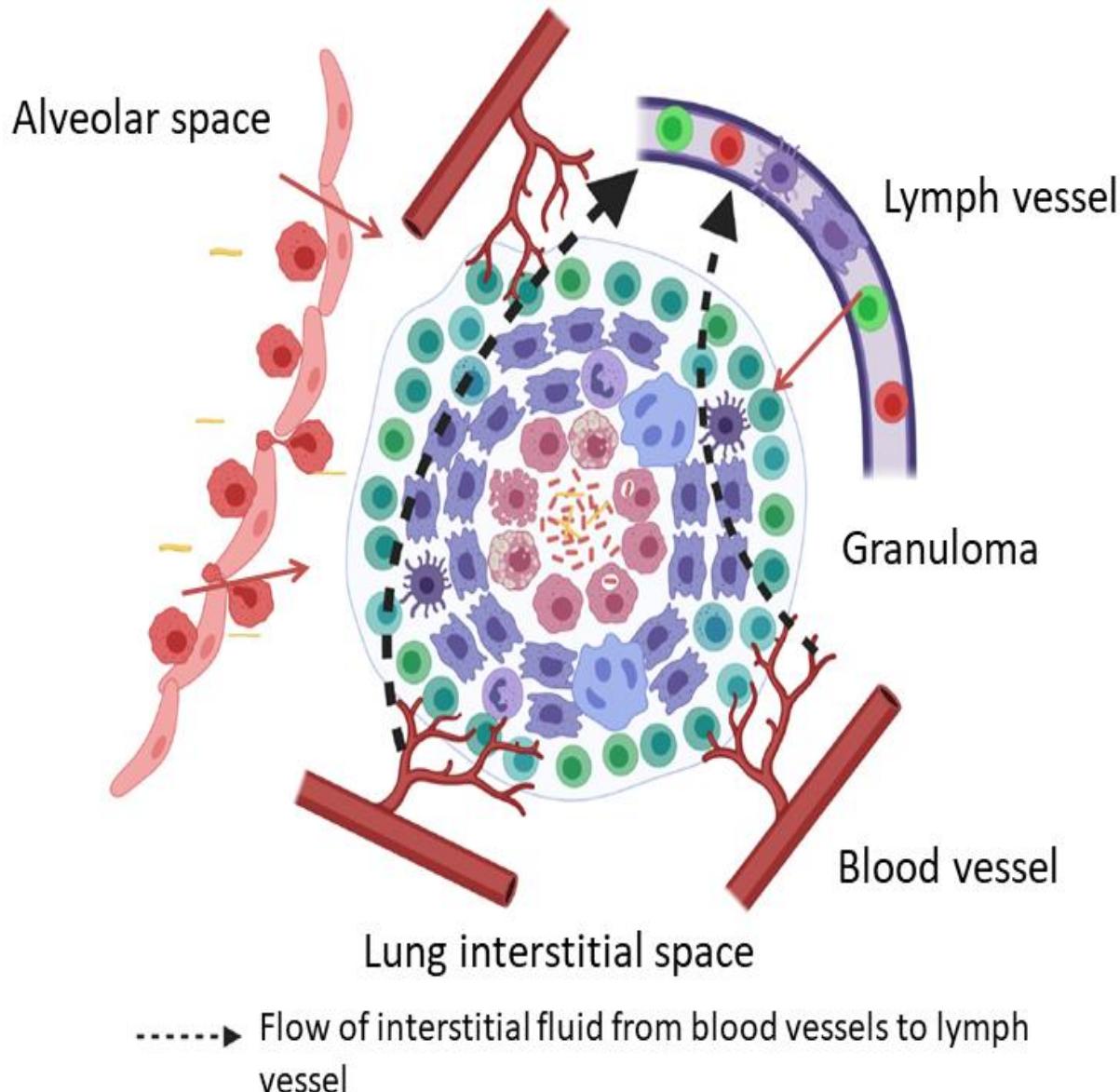
* μCT image of TB infected lung, Wells et. Al 2021



A granuloma model for understanding host-pathogen interaction in tuberculosis – Why?

- Tuberculosis granuloma – A host protective structure as well as beneficial to *Mtb*
- The pathogen spends most of its time in the granuloma when in host
- The granulomatous environment is complex – eg. limited supply of nutrients for pathogen, diffusion limitations
- No model of hypoxic necrotic granuloma with human components and *Mtb*

Project Representation



Learnings and major techniques

Students working on this project will develop following expertise:

- Problem solving ability and time management!
- Engineering materials for biological applications
- Designing and engineering organs, biomechanical aspects and microfabrication
- Microscopic techniques such as fluorescence imaging and scanning electron microscopy
- Histology and cryo-sectioning
- Mammalian and bacterial cell culture
- Working with clinical samples and in biosafety level 3 facilities

Further reading

- M. J. Marakalala et al., Inflammatory signaling in human tuberculosis granulomas is spatially organized. *Nature Medicine* 22, 531-538 (2016).
- L. B. Tezera et al., Dissection of the host-pathogen interaction in human tuberculosis using a bioengineered 3-dimensional model. *Elife* 6, (2017).