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IISc designs novel 3D hydrogel culture to study tuberculosis infection and treatment

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Current culture models used to study Mtb infection have several limitations

Researchers from the Department of Bioengineering (BE), Indian Institute of Science (IISc), Bengaluru have designed a novel 3D hydrogel culture system that mimics the mammalian lung environment. It provides a powerful platform to track and study how tuberculosis (TB) bacteria (*Mycobacterium tuberculosis or Mtb*) infect lung cells and test the efficacy of therapeutics used to treat TB.

Current culture models used to study *Mtb* infection have several limitations. They are typically culture plates that are monolayered and do not accurately mimic the 3D microenvironment inside the lungs. The microenvironment experienced by the cells in such 2D culture is vastly different from the actual extracellular matrix (ECM) surrounding lung tissue.

The researchers have now designed a novel 3D hydrogel culture made of collagen, a key molecule present in the ECM of lung cells. Collagen is soluble in water at a slightly acidic pH. As the pH is increased, the collagen forms fibrils which cross-link to form a gel-like 3D structure. At the time of gelling, the researchers added human macrophages – immune cells involved in fighting infection – along with *Mtb.* This entrapped both the macrophages and the bacteria in the collagen and allowed the researchers to track how the bacteria infect the macrophages.

The team tested the effect of pyrazinamide, one of the four most common drugs given to TB patients. They found that even a small amount (10 µg/ml) of the drug was quite effective in clearing out *Mtb* in the hydrogel culture.

Moving forward, the researchers plan to mimic granulomas – clusters of infected white blood cells – in their 3D hydrogel culture to explore why some people have latent TB, while others show aggressive symptoms. The team is also interested in understanding the mechanism of action of pyrazinamide, which may help discover new drugs that are more or just as efficient.