COMPILED AND EDITED BY THE **CONNECT TEAM** BASED ON INPUT FROM THE FEATURED **RESEARCHERS**

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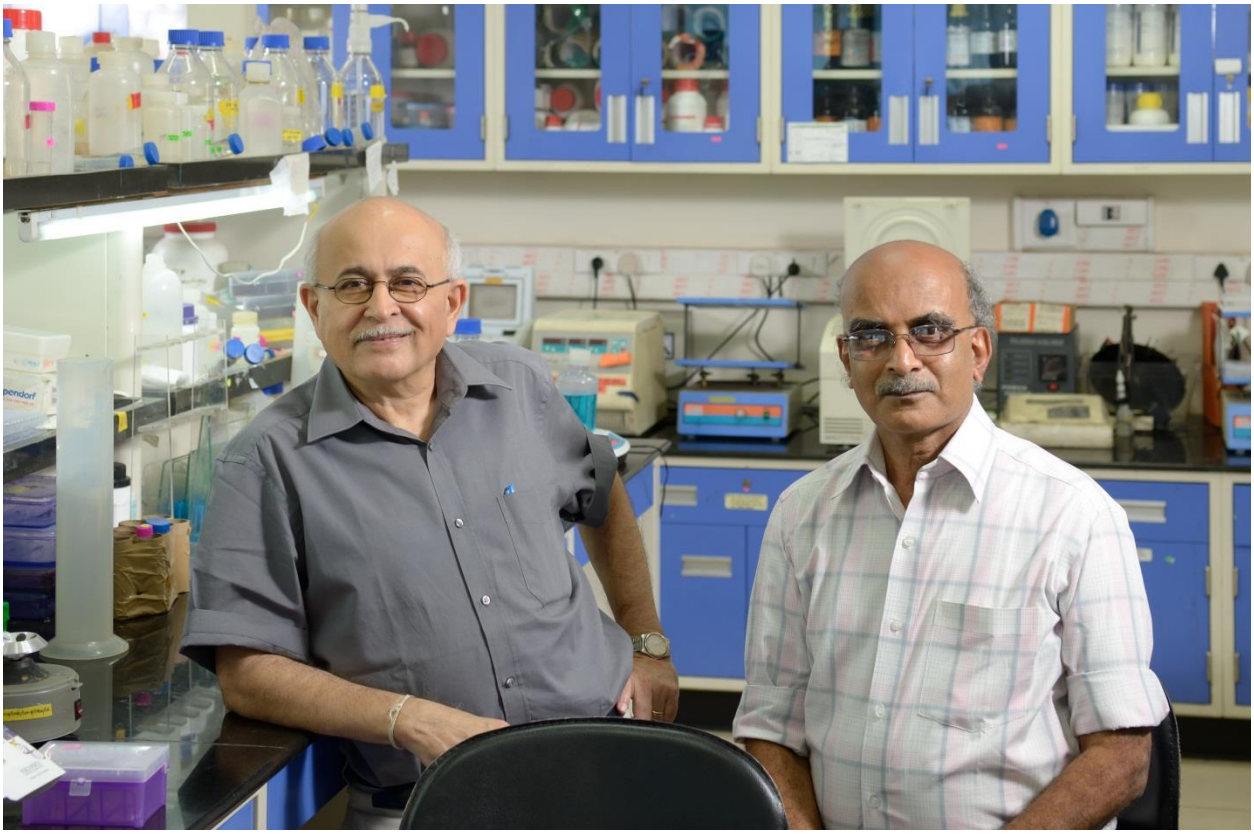

(MANOJ SUDHAKARAN)

Combating tuberculosis

Mycobacterium tuberculosis is an ancient pathogen that causes the disease tuberculosis (TB), infecting millions of people every year; the disease has a very high rate of mortality and morbidity. The TB challenge has only grown with the emergence of drug-resistant strains of this bacterium. To combat the disease caused by these drug-resistant strains, researchers across the world are employing diverse strategies, including finding new drug molecules.

Nagaraja, a molecular biologist has been trying to understand the organism's key biological processes which are essential for its growth and survival. Now in collaboration with Ramakumar, a physicist, he is using an interdisciplinary approach to investigate how a TB causing bacterium's DNA in the chromosome is compacted, coiled or unwound by enzymes and DNA binding proteins.

Nagaraja's and Ramakumar's labs have carried out structural and functional studies of one such DNA organizing protein *HU*, essential for the survival of the pathogen. They believe that knocking out this protein's function would kill the TB causing bacterium. So far the progress achieved by using this approach has been impressive—they have successfully cloned, expressed and purified the *HU* protein. This collaboration has also led to the deciphering of the three dimensional structure of this protein and the identification of small molecules that bind to the key pocket in the protein. In addition, they have shown that these molecules inhibit the protein, decompact the chromosome and affect the bacterial growth. Thus, with the combined know-how and effort from both the labs, they have identified small molecules that target the *HU* protein to inhibit TB causing bacteria. This is the first time the proteins of this class have been targeted for inhibition from any organism.

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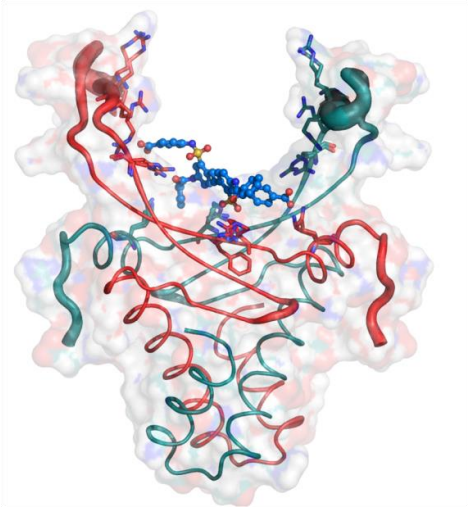

***HU* from *Mycobacterium tuberculosis* bound to Stilbene derivative inhibitor (COURTESY: V NAGARAJA)**

Nagaraja and Ramakumar with their teams (MANOJ SUDHAKARAN)