

Vitamin B12 and mycobacterial persistence

Tuberculosis, caused by *Mycobacterium tuberculosis*, is now one of the most feared infectious diseases in the world. It affects millions of people. Each year, more than a million people die because of it. Tuberculosis is very difficult to treat. The therapy requires taking a series of antibiotics for at least six months. The long duration of treatment is thought to be related with the transition of the part of the infecting bacteria into so-called persistent state. These bacteria are able to persist thru adverse conditions, for example thru antibiotic treatment. Persistent bacteria were observed in bacterial cultures with limited availability of oxygen and nutrients. It has been observed that the molecular mechanism associated with the induction of the state of persistence is the stringent response.

Our hypothesis is that vitamin B12 availability is one of the factors associated with the transition of bacteria to the state of persistence. In our preliminary studies, we generated a mutant of environmental bacterium *Mycobacterium smegmatis* with disturbed pathway of synthesis of vitamin B12. The changes that we have observed within mutant cells, when compared to the parental strain, suggest that mutant triggered stringent response followed by entering the state of persistence. Within this project we would like to thoroughly analyze the changes that have occurred in the mutant of *M. smegmatis*. We also want to test whether similar mechanisms are present in tubercle bacillus with impaired acquisition of vitamin B12. The results may be important from the point of view of current pharmacotherapy of tuberculosis. What's more, confirmation of our research hypothesis in environmental and pathogenic mycobacteria may point out one of the elements of *M. tuberculosis* adaptation to life niche within the host organism.