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Efflux Inhibition During Tuberculosis Treatment

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Drug resistance during tuberculosis treatment is a major health concern today in the developing countries. One of the mechanisms contributing to the resistance is the efflux of the tuberculosis drugs out of the cell through a variety of pumps. Efflux pump inhibitors such as verapamil may help overcome this tolerance and resistance mechanism and enhance the activity of tuberculosis drugs. Verapamil is an FDA approved drug used to treat heart disease and hypertension. We have recently found that adding verapamil to standard chemotherapy reduced the time required to successful treatment from standard six months to four months, but also significantly decreased the risk of relapse. Another drug that has been recently approved by FDA for tuberculosis treatment is bedaquiline, also known as TMC-207. We found that co-administration of verapamil with sub-inhibitory doses of bedaquiline gave the same bactericidal effect in mice as full bedaquiline dose. In addition to, we also found that adding verapamil to bedaquiline monotherapy protected from development of resistant mutants in vivo. Thus, use of verapamil with bedaquiline may enable use of lower doses of bedaquiline, thereby reducing its dose-related toxicities in tuberculosis patients.

Biography

Shashank Gupta has completed his graduate studies from ICGEB, New Delhi, India in 2009 and moved to Johns Hopkins University as a postdoctoral fellow in early 2010. Currently, he is a research associate with HHMI and working on tuberculosis field at Johns Hopkins University. His studies with *Mycobacterium* tuberculosis will help understand the underlying mechanisms of host-pathogen interaction with special focus on mycobacterial pathogenesis and the other pathways involved in tuberculosis. His recent studies with efflux pump inhibitors have shown that verapamil can be used to accelerate both the bactericidal and the sterilizing activity of standard tuberculosis treatment.

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