Centre for BioSystems Science and Engineering

THESIS COLLOQUIUM

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Development of anti-infective therapy against intracellular pathogens using targeted particulate delivery systems.

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The study of material-biology interactions opens up possibilities for developing technologies to either augment or to repair/restore biological functions. Among the methods to restore functions affected by disease include, increasing the residence time of pharmacological agents at the desired site of drug action and directing the agent to the specific region and avoid non-specific delivery. To achieve such a desired biological outcome, the interacting scale of the biological tissue with the in-animate material needs to be considered. To improve the delivery of pharmacological agents such as small molecules/peptides/DNA/RNA etc., both microscale and nanoscale materials have been developed in the recent years. Directing the movement of such drug-loaded particles to the affected region can drastically improve therapy of cancer or bacterial infections. One such gauntlet is thrown by pathogens such as Salmonella, Mycobacterium tuberculosis, Listeria etc, which can not only survive but also replicate intracellularly by forming vacuoles. Treatment of such intracellular infections by conventional therapy is no longer effective as the pathogens have developed ingenious defenses to limit their exposure to anti-bacterial agents. The challenge is to home-in on intracellular niche formed by such pathogenic bacteria and eliminate them.In this presentation, we discuss various methods employed to improve the intracellular targeting of the particulate system to the vacuolar niche of the pathogen and direct it to the infection affected region. We synthesized mesoporous silica nanoparticles (MSN) and investigated the role of lipid and polyelectrolyte coating in the delivery of ciprofloxacin against Salmonella Typhimurium infection. The lipid coat was achieved through sonication with liposomes while polyelectrolyte coating was based on electrostatic attraction between the oppositely charged coating polymers using Layer-by-Layer chemistry. We observed interesting results with lipid coated mesoporous silica nanoparticles which exhibited co-localization with the intracellular Salmonella-containing vacuole (SCV). The polyelectrolyte coated particle with arginine was taken up specifically into cells infected with Salmonella. Its endocytosis was found to be dependent on the cationic arginine transporter system which also directed the particles to the SCV thus bringing the particles in close proximity with the intracellular pathogen. As a result the therapeutic outcomes in both in-vitro and in-vivo infections were significantly improved using lipid and arginine coated MSN particles. The results from pulmonary delivery of MSN-PLGA particulate system to treat Mycobacterium infections will also be discussed. The efficient targeting and delivery methods developed have the capacity to be translated for treating other obstinate intracellular infections.

For more information and artwork depicting the research (http://www.be.iisc.ernet.in/seminars.html)