

**Mohapatra, Shyam S.**

College of Medicine  
University of South Florida

2003 Program

Small Business Technology Transfer  
(1-year project)

**Project Title:** Development of a Novel Mucosal Therapy for Chronic Pulmonary Disease

**Project Summary:** Atrial natriuretic peptide (ANP) produced by the heart and lungs is a potent bronchodilator. This research tested the hypothesis that mucosally delivered nanoparticles carrying plasmids encoding NP73102 can provide a significant breakthrough in treatment of chronic asthma. The results of this work enabled not only safety and dose ranging studies, but also the pharmacokinetic and toxicological analyses which are essential to move pNP73102 into phase I trial as a therapeutic candidate for asthma.

**Project Successes:** Intranasally administered nanoparticles carrying pNP73102 were found to induce protection against asthma in mice. Furthermore, prophylaxis with these nanoparticles induced a significant decrease in airway reactivity and pulmonary inflammation in two strains of mice. These findings are important since they establish the potential of such nanoparticle therapeutics for humans. In collaboration with TransGenex Nanobiotech, Inc., these researchers found that these nanoparticles can be produced in milligram quantities. The particles were found to be safe and more effective in gene transfection over a three week period. Further scaling up is currently underway for testing the efficacy of these particles in large animal models of asthma. These studies have set the foundation for the clinical potential of nanoparticles carrying pNP73102 for asthma and related airway diseases.

**Selected publications from BRP funded research in Peer Reviewed Journals:**

Kumar RMNV, Hellermann G, Lockey RF, **Mohapatra SS**, Nanoparticle-mediated gene therapy: state of the art. *Expert Opin Biol Ther.* 2004;4(8):1213-1224.

Kumar RMNV, Sameti M, **Mohapatra SS**, Kong X, Lockey RF, Bakowsky U, Lindenblatt G, Schmidt H, Lehr CM. Cationic silica nanoparticles as gene carriers: synthesis, characterization and transfection efficiency in vitro & in vivo. *J Nanosci & Nanotechnol* 2004;4:876-881.

RaviKumar MNV, **Mohapatra SS**, Kong X, Jena PK, Bakowsky U, Lehr CM. Cationic Poly(lactide-co-glycolide) nanoparticles as new gene transfection agents in vitro and in vivo. *J Nanosci & Nanotechnol.* 2004;4:1-5.

Kumar M, Kong X, Behera A, Hellerman G, Lockey RF, **Mohapatra SS**. Chitosan IFN- $\gamma$ -pDNA nanoparticle (CIN) therapy for allergic asthma. *Genet Vaccines Ther.* 2003;1:3.

Kumar M, Behera AK, Lockey RF, Zhang J, Perez de la Cruz C, Chen I, Leong KW, Huang S-K, **Mohapatra SS**. Intranasal gene transfer by chitosan-DNA nanospheres protects BALB/C mice against acute respiratory syncytial virus infection. *Hum Gene Ther.* 2002;13:1415-1425.

**Selected presentations from BRP funded research:**

**Mohapatra, SS**, Singam R, Kong X, Behera S, Hellerman G., Mohapatra S., San Juan H., Jena P., Yang H., Zhang W., Lockey R. Chitosan Lipid nanoparticles (CLNs) Augment Gene Delivery and Expression in Mice. Controlled Release Society 31<sup>st</sup> Annual Meeting Transactions. 2004

Zhang W, Kong X, Behera S, Lockey R, **Mohapatra SS.**, Prophylaxis of Respiratory Syncytial Virus Infection with Intranasal siRNA-Nanoparticles of the NS1 Gene *in vivo*. AAAAI submitted for 2005.

**New grants based in part on BRP-funded work:**

NIH-NHLBI

Title: Chlipoplex nanoparticles prophylactics for RSV infection

Project period: Sept.2004 – April 2005

Award amount: \$157,000

NIH-NHLBI

Title: Chliposome nanoparticles prophylactics for allergic asthma

Project period: Sept.2004 – April 2005

Award amount: \$110,000