

Nitric oxide-Releasing Liposomes for Treatment of Nontuberculous Mycobacteria Respiratory Infections

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The use of antibiotics has greatly improved the length and quality of life for individuals prone to respiratory infections. Unfortunately, bacteria develop resistance to antibiotic interventions, particularly upon chronic use such as in the treatments of nontuberculous mycobacteria (NTM) infections.¹ The need for alternative therapeutics that do not engender resistance and are characterized with minimal adverse effects is significant.² Nitric oxide (NO) is an endogenous free radical involved in human physiology including our response to pathogens. In contrast to conventional antibiotics, nitric oxide has broad-spectrum activity and does not engender resistance due to its multiple mechanisms of antibacterial action.³ Furthermore, NO's short lifetime reduces many of the adverse effects common to antibiotics.

In this presentation, the development and characterization of NO-releasing liposomes capable of releasing therapeutic levels of NO will be described. The NO released is bactericidal against numerous species of bacteria including mycobacteria and thus represents an alternative treatment for chronic respiratory infections that currently fall short in resolving infections. The therapeutic utility of the NO-releasing liposomes will be demonstrated through in vitro and in vivo assays. Our results indicate that NO release is an effective strategy for eradicating NTM bacteria, including intracellularly, within granulomas, and in the lungs of mice, with a promising safety profile.

¹ Griffith DE, Aksamit T, Brown-Elliott BA, Catanzaro A, Daley C, Gordin F, Holland SM, Horsburgh R, Huitt G, Iademarco MF, Iseman M, Olivier K, Ruoss S, von Reyn CF, Wallace RJ, Winthrop K. *Am J Respir Crit Care Med* **2007**, *175*, 367–416.

² Stout JE, Koh WJ, Yew WW. *Int J Infect Dis* **2016**, *45*, 123-134.

³ Fang FC. *J Clin Invest* **1997**, *99*, 2818-2825.