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A Tale of Two Cities and Two Drug Discovery Research Projects, PGD$_2$ and NcRTI

This presentation will review two drug discovery projects; prostaglandin D$_2$ (PGD$_2$) receptor antagonist project for the treatment of allergic rhinitis and hyperlipidemia, and nucleotide competing reverse transcriptase (NcRTI) for the treatment of HIV infection. In particular, this seminar will focus on approaches employed during the optimization of several chemical series to identify clinical candidates. In the PGD$_2$ antagonist project, strategies to reduce biliary excretion and mitigate the formation of reactive intermediates will be presented. This research led to discovery of Laropiprant, for use in the treatment of hypercholesterolemia.

In the second part of the presentation, our research to discovery novel NcRTI inhibitors will be presented. Currently, approximately 34 million individuals are living with the human immunodeficiency virus (HIV). In addition, it is estimated that 2.5 million people contracted HIV annually and the number of Acquired Immune Deficiency Syndrome (AIDS) related deaths worldwide was estimated to be 1.7 million in 2010. While 30 years of HIV research has resulted in more than 25 approved antiretroviral agents, there still however remains a need for novel medicines for use in combination therapy to treat the resistant mutants of the HIV virus. Recently, a novel approach to inhibit the HIV reverse transcriptase enzyme has been reported. Our research in optimizing a tricyclic series of NcRTI inhibitors will be highlighting with a focus on improving antiviral activity and oral bioavailability. Taken together, these two case studies illustrate some of the challenges encountered in drug discovery and the power of chemistry to address important biological and human health issues.