Investigation of Clinical Oral Drug Candidate MIDD0301 for Severe Asthma and COPD

Our research addresses the unmet need for a safe non-steroidal asthma and COPD treatment by targeting GABA$_A$ receptors (GABA$_A$R) in lung tissues. This first-in-class drug candidate is expected to be more effective than current COPD treatments and can be administered orally and inhaled overcoming corticosteroid side effects and resistance of current treatment options.

MIDD0301, a novel GABA$_A$R modulator, was well absorbed in the lung and exhibited very low brain localization. Using different routes of administration, we demonstrated that MIDD0301 reduced airway hyperresponsiveness in different asthma models. Furthermore, MIDD0301 increased lung function in a smoke-induced COPD model and reduced numbers of inflammatory cells and cytokine levels in the lung. Using ex vivo lung slices, we showed that MIDD0301 rapidly increased the diameter of constricted airway when treated with MIDD0301. Nebulized MIDD0301 rapidly relaxed methacholine-contracted mouse lungs. Metabolic studies demonstrated slow phase I metabolism but significant glucuronidation of secreted MIDD0301. Identification of reduced permeability of MIDD0301 under acid condition was overcome with a proprietary formulation that significantly decrease the therapeutics oral dose of MIDD0301.

MIDD0301 is an advanced clinical drug candidate shown to be orally active in alleviating cardinal signs of asthma in multiple asthma models: airway hyperresponsiveness mediated by ASM constriction, eosinophilia, and inflammation.

Monday, April 6th, 2020
4:00pm
Chemistry Building, Room 1220