IMS-P7 **Identification of Pharmacophore of the Natural Isoflavone Lead as Interleukin-5 Antagonist for Novel Anti-Allergic Drug**

Dong-Hyun KIM[1], PullaReddy BOGGU[1], Manoj MANICKAM[1], Eeda Venkateswara RAO[1], Youngsoo KIM[2], ○Sang-Hun JUNG[1]

[1]College of Pharmacy, Chungnam National University, [2]College of Pharmacy, Chungbuk National University

Interleukin (IL)-5 appears to be one of the main proinflammatory mediators among a growing number of cytokines and chemokines that induce eosinophilic inflammation. Interfering with the action of IL-5 represents one of the new immunomodulatory therapeutic strategies in the treatment of allergic diseases including bronchial asthma. Compared to established immunosuppressive agents like corticosteroids, a major advantage of this strategy is the specificity of reducing eosinophilic inflammation, thus possibly acting nearly without side effects. However small organic compounds to inhibit IL-5 activity have been rarely found. Our screening effort with natural products resulted in identification of sophoricoside and its analogs isolated from *Sophora japonica*, a plant of Leguminosae family, as novel and selective inhibitors of interleukin (IL)-5 bioactivity with differential inhibition of IL-3 and GM-CSF bioactivities. However sophoricoside is chemically and metabolically unstable glycoside and thus is required to formation of stable analogs as a candidate. Therefore, structural requirements of this isoflavonone for its inhibitory activity against IL-5 were investigated by design and preparation of novel isoflavonones and their glycosides. The necessary structural features of these isoflavonone analogs comprise a planar chromen-4-one ring, the existence of hydrogen bonding acceptor at 4-position of B ring, and introduction of hydrophobic groups at 5 position, which might adjust permeability of these isoflavones. However, the glycopyranosyl moiety of sophoricoside is not needed for the activity. Further exploration of the strucuture activity relationship of these isoflavones in the inhibition of IL-5 bioactivity will be discussed.