Overview of Scholarly Research Activities:

A. **Pathophysiological Mechanisms of Allergy and Asthma and Development of Better Therapeutic Approaches**: A widespread inflammation in the lung of patients with bronchial asthma is a common finding. An allergic patient, upon exposure to an allergen such as cockroach and house dust mite, feels difficulty in breathing due to increased mucus secretion and increased susceptibility of the airways to constrict, which restrict the airflow and develops the clinical symptoms of asthma. The research efforts in my laboratory are focused to delineate the underlying pathophysiological basis of allergic asthma at the cellular and molecular level. We are also engaged in examining the underlying mechanisms of the effect of novel mediators to control clinically-relevant allergen-induced immune response. The information obtained from these studies should provide an opportunity to formulate superior therapeutic approaches in bronchial asthma.

The currently active research projects in the field of allergy and asthma are given below.

1. Dendritic cell subtypes in the lung and their migration to lymph nodes
2. Th17 and T-regulatory cells in the pathogenesis of allergic asthma
3. Suppressors of cytokine signaling (SOCS) proteins in allergic airway inflammation
4. Chloride ion channels in airway epithelial cells and human blood eosinophils in chronic asthma
5. Mechanisms underlying recruitment and migration of human blood eosinophils to the lung in allergy and asthma
6. Vitamin D and the pathogenesis of bronchial asthma
7. Cathelicidin and other antimicrobials agents in regulating the function of immune cells in the airways
8. Immunomodulators in the treatment of allergic airway inflammation and chronic asthma
B. Pathogenesis of Occlusive Vascular Diseases: Occlusive vascular diseases, such as atherosclerosis, intimal hyperplasia and in-stent restenosis, are major health problems all over the world. My research interests in this area are focused on the following three major questions:

- **Stenosis in Carotid Artery:** Many patients with blockade of their neck artery develop neurological symptoms including transient ischemic attack or stroke. This is primarily due to breaking off the atherosclerotic plaque in the neck artery. Why some patients are symptomatic and others not, even though the degree of blockade due to atherosclerotic plaque is similar in both populations of patients?

- **Coronary Artery Bypass Graft:** Long term outcome of coronary artery bypass surgeries is compromised by re-closure of the vessels, which predominantly occurs in saphenous vein grafts while the internal mammary artery remains almost resistant to re-closure. Why is the internal mammary artery graft almost immune to restenosis? Why does saphenous vein graft get re-stenosed in almost 20% subjects within the first-year and in about 50% patients in 5-years?

- **Intravascular Stents in Coronary Artery:** Re-narrowing of coronary arteries in the heart after balloon angioplasty or placement of stents is a serious problem. This is primarily due to uncontrolled growth of smooth muscle cells at the site of injury due to balloon angioplasty or the placement of stent in coronary artery. Coronary arteries following deployment of bare metal stents become re-stenosed in about 30% subjects within the first year. The restenosis rate after deployment of drug-eluting stent is also about 10% within the first year. Thus, drug-eluting stents cause less intimal hyperplasia and less late luminal loss, but inhibit re-endothelialization of the stented segment making it more susceptible to thrombosis requiring longer periods of anti-platelet therapy. What are the underlying cellular and molecular mechanisms? Could we develop a better therapeutic approach, such as gene therapy?

The active research projects in the field of occlusive vascular diseases are given below.

1. Neuropeptide Y regulating the function of dendritic cells and T-regulatory cells in atherosclerotic plaques of patients with carotid Stenosis
2. Regulatory mechanisms underlying apoptosis of plaque smooth muscle cells in symptomatic and asymptomatic patients with carotid Stenosis
3. Mechanisms underlying vein-graft disease: Why is internal mammary artery almost immune to restenosis?
4. Gene therapy in in-stent restenosis in a swine model
5. Vitamin D and intimal hyperplasia following balloon angioplasty and intravascular stenting
6. Mesenchymal stem cells and endothelial progenitor cells in gene delivery to the site of injury in coronary arteries

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