

Immunology & Inflammation (I&I)

**Strategic Areas of Interest for Third Party Research Proposals
(Investigator Initiated Studies and Research Collaborations)**

DERMATOLOGY

- **Current Indications: dupilumab in Atopic Dermatitis**
 - Evaluate the [optimal] utilization of dupilumab for the treatment of AD within the evolving therapeutic landscape
 - Real world AD patient / disease characteristics, burden of AD and comorbid conditions
 - Dupilumab use patterns, effectiveness, and other attributes in real-world setting
 - Special populations (e.g., skin of color, etc.)
 - Studies to measure the effect of dupilumab on AD symptoms and other important disease domains that are insufficiently characterized (e.g. sleep, pain, mental health, sensory processing, executive function, etc.)
 - New mechanistic insights into dupilumab MOA, including effect on important inflammation markers in lesional and non-lesional skin not studied previously
 - Effect of dupilumab in AD patients with comorbid type 2 inflammatory diseases (e.g. AD with comorbid asthma ± allergic rhinitis ± food allergy, etc.)
 - Effect of early AD treatment with dupilumab on the development of type 2 comorbidities, atopic march and disease modifying aspects in general
 - Dupilumab in the context of COVID-19 pandemic
 - Effectiveness of dupilumab across different phenotypes and endotypes
- **AD Disease State**
 - AD time course (natural history)
 - New mechanistic insights into AD pathophysiology, including the identification of distinct phenotypes and endotypes
- **AD Epidemiology**
 - Prevalence of AD by gender, age group, age of onset, associated comorbidities, special populations
 - Treatment patterns throughout the course of AD
- **Mechanistic**
 - Further understand the AD mechanism of disease, or dupilumab mechanism of action in relevant pathobiological contexts

DERMATOLOGY (cont'd)

- **New Disease Areas**
 - Other dermatologic diseases where existing data support that IL-4 and / or IL-13 might play a central role (beyond the ones already initiated such as PN, CSU, BP, CPUO, etc.)
 - NOTE: For areas where we already have ongoing programs or ISS, proposals will need to undergo a preliminary evaluation to confirm they are not overlapping with internal initiatives and assessed for regulatory / patent risk. (Including: prurigo nodularis, bullous pemphigoid, chronic spontaneous urticaria, hand and foot dermatitis, and dermatological indications in ongoing IIS's: e.g., alopecia areata, scleroderma, keloid formation, nummular eczema). To the extent possible, this should be done before submission to the IIS portal.

ASTHMA

- **Mechanism of Action (MOA)**
 - Biomarkers
 - Pathophysiology
 - Phenotyping/endotyping
 - Airway hyperresponsiveness
 - Skin prick testing sensitivity
 - Fungal sensitization
 - Eosinophilia
- **Special Populations**
 - Type 2 comorbidities
 - Asthmatics with smoking history
 - Obese
 - Exercise induced asthma
 - Acute exacerbations
- **Comparative Data**
 - Dupilumab comparative efficacy studies (indirect/switch)
- **Mechanistic**
 - Airway remodeling
 - Dupilumab bronchial concentration
- **Observational Studies**
 - Epidemiology
 - RWE

Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)

- **Mechanism of Action (MOA)**
 - Prevention of nasal polyp regrowth and relationship to surgery
 - Mechanism of polyp and symptom recurrence, relationship between type 2 inflammation and symptom
 - Factors (phenotypes/endotypes) predicting relapse after surgery in CRSwNP
 - Factors responsible for clinical effects of dupilumab treatment including onset of improvement
 - Imaging (e.g. CT, LMK)
 - Disease Modification
 - Type 2 inflammatory pathways & role of Type 2 cytokines on CRSwNP development & progression
 - Influence of IL-4Ra-mediated mechanisms on epithelial barrier function
 - IL-4Ra-mediated mechanisms on smell loss or improvement
- **Special Populations**
 - Type 2 comorbidities
 - CRS outcomes and biomarkers
 - Sleep disturbance due to CRSwNP symptoms or comorbid OSA
 - Impact on smell, taste and hearing
 - OCS use & surgery use
- **Comparative Data**
 - Dupilumab Comparative Efficacy Studies (indirect treatment comparison/switching data)
- **Pathophysiology**
 - Burden of Disease
 - Epithelial barrier defects, microbiome, Type 2 inflammatory cells and cytokines in CRS
 - Role of IL-4 and IL-13 in de novo polyp formation
 - Chronic Rhinosinusitis without Nasal Polyps (CRSsNP) phenotypes and the role of IL4/13
- **Observational Studies**
 - Epidemiology (disease or treatment)
 - RWE
 - Registries
 - Database