AllerGen

Clinical Investigator Collaborative

BACKGROUNDER

CLINICAL INVESTIGATOR COLLABORATIVE (CIC)

LEGACY PROJECT

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OBJECTIVE

The Clinical Investigator Collaborative (CIC) was established to unite and leverage the strengths of Canadian clinical investigations studying the mechanisms of allergic asthma (AA) in Canada. The CIC-AA project is a multi-centered clinical trials group that evaluates potential new drugs for allergies and asthma. It has established major industrial partnerships with biopharmaceutical and biotechnological companies across Canada. This consortium is globally unique in its ability to undertake early-stage clinical trials to evaluate the efficacy of new molecules and compounds that treat lung inflammation, using well validated methods, with proprietary Standard Operating Procedures (SOPs).

Between 2005 and 2015, the CIC leveraged $21.5 million dollars in industry contributions, and created 40 new jobs in the health and private sector.

The CIC-AA has placed Canada at the forefront of related diagnostics and therapeutics, leading the discovery, development and commercialization of new tests and treatments. As a national, multi-centred clinical trials consortium with international reach, the CIC, in partnership with global pharmaceutical firms and small Canadian biotechnology companies, is diversifying and expanding its capacity by adding allergic rhinitis (AR) and severe asthma (SA) to its current expertise.

NEED FOR RESEARCH

Asthma presently affects 8.1% of the Canadian population, or 2.8 million people, and one in three Canadians will be diagnosed with asthma during their lifetime. The risk of developing asthma is comparable to that of diabetes or cancer, but while these chronic diseases tend to develop in older people, asthma is more likely to develop in the young and last a lifetime.

In Ontario alone, the healthcare costs associated with asthma have reached $1.8 billion annually and without innovative disease management strategies, the cost could reach more than $96 billion in 30 years. The incidence of allergic rhinitis (AR), or hayfever, is even higher than asthma, with lifetime prevalence between 30-50%.

ACCOMPLISHMENTS

The AllerGen CIC utilizes methods originally described by Canadian investigators for the allergen inhalation challenge—a reproducible method of inducing reversible bronchoconstriction, airway hyper-responsiveness and airway inflammation in mildly allergic asthmatic subjects. The airway effects of the allergen challenge fully resolve within two weeks, which allows the subjects to be used as their own controls in some studies. This clinical challenge model has been predictive for drugs that are likely to be effective in treating asthma.

Knowledge about the reproducibility of each of the allergen-induced airway responses using these methods has allowed precise estimation of the sample sizes needed for the studies to be adequately powered. Even with a parallel group study design, the studies require, at most,

between 24 and 30 subjects. The details of allergen inhalation challenge methodology and measurement of methacholine airway hyper-responsiveness and airway inflammation are included in copyrighted SOPs.

Adding the capacity to study new compounds to treat AR and SA will better enable industry partners to develop and promote new products for Canadians suffering from allergic airways diseases. Effective treatments for AR and SA are potentially deliverable within one to two years of commencement of clinical trials.

The expanded CIC will also continue to create new research alliances and industry partnerships among those currently involved in AR and asthma research and drug development.

EXPANSION

In 2010, the CIC established an international collaborating site, the Karolinska Institute, in Stockholm, Sweden, to extend the CIC's reach and capacity. There remain, however, more opportunities to study novel molecules than the CIC has the ability to undertake. For this reason, the CIC is exploring further expansion to sites in the United Kingdom and the Netherlands. A number of international investigative sites have also indicated interest in participating in the CIC. In addition to facilitating collaborative links with Network investigators in relation to the study of the pharmaco-genomics and metabolomics of allergen-induced responses in biomarker discovery, the CIC is creating synergies with other AllerGen researchers across disciplines.

Clinical Investigators Collaborative Enabling Platform Projects

12CIC-AR: *Clinical Investigator Collaborative (CIC) - Allergic Rhinitis (AR)*

(PI: Ellis)

Allergic rhinitis ('hay fever') is a very common condition, even more prevalent than asthma, affecting up to 50% of the Canadian population over their lifetime. Many, if not all, of the new compounds evaluated by the CIC for AA have a biologic rationale for efficacy in AR as well.

CIC-AR is a new network of allergic rhinitis researchers across Canada with expertise in the conduct of hay fever studies. This group has collaborated to develop a consensus protocol of nasal allergen challenge (*i.e.,* delivering allergens such as ragweed, cat allergen, *etc*. directly into a participant's nasal passage) to induce symptoms of allergic rhinitis.

This network follows recently piloted and refined SOPs in the conduct of future clinical trials studying new treatments for allergic rhinitis. By having multiple sites across Canada following identical protocols, new treatments for this disease can be studied more efficiently than by using typical single-centre studies. In each study, biological samples are collected prior to the treatment phase, allowing for the study of allergic responses at the cellular level, thereby enhancing our understanding of this common, yet complex condition.

Partnered funding from industry has been secured to help validate the revised pilot protocol, and the CIC-AR is well poised to conduct clinical investigations of allergic rhinitis across the country.

12CIC-SA: *Clinical Investigator Collaborative (CIC) - Severe Asthma (SA)*

(PI: Nair)

Although SA accounts for only 5-10% of asthmatics, it accounts for over 50% of costs related to asthma care in part due to a lack of understanding of the mechanisms of the disease. This knowledge gap results in severity, inappropriate management strategies, and a paucity of new treatment strategies. Therapies currently available do not effectively address the needs of this patient group.

There is an urgent need to identify new targets and to develop and evaluate new therapies for SA. A logical extension of the CIC is to develop a platform for SA studies and for evaluating new therapies for SA. No other well characterized cohort of patients with severe asthma is available through a collaborative network for the evaluation of new treatments.

The overall objective for CIC-SA over the next five years is to deepen understanding of the mechanisms of specific types of bronchitis and to develop and apply biomarkers in sputum to treat patients with severe obstructive airway diseases. The specific objectives of the CIC-SA are:

1) to develop novel biomarkers for severe asthma and to automate current methods (*diagnosis*);

2) to understand the mechanisms of specific types of bronchitis in severe asthma (*mechanisms*); and

3) to evaluate new therapies directed against specific types of bronchitis (*treatment*).

The expanded CIC will place Canada at the forefront of allergic disease therapeutics and help national biopharmaceutical and biotechnology industries gain prominence internationally in the arenas of allergic and respiratory disease.