EAACI Clinical Fellowship Final Report 2019

Name: Francesca Losa

Project title: Adverse effect of Inhaled β2-agonists

Fellowship Period: 22nd April – 22th July 2019

Host Institution: National Heart and Lung Institute, Imperial College London, Norfolk Place, London W2 1PG

Host Mentor: Prof. Sebastian L. Johnston

Home Institution: Department of Medical Sciences and Public Health, University of Cagliari and Unit of Allergy and Clinical Immunology, University Hospital "Duilio Casula", Monserrato (Cagliari), Italy

Home Supervisor: Prof. Stefano R. Del Giacco

I have been awarded the EAACI Clinical Fellowship 2019 and I spent three months in Asthma UK Centre in Allergic Mechanisms of Asthma, National Heart and Lung Institute, Imperial College London.

The aim of my fellowship was to broaden my knowledge in the adverse effect of Inhaled β2-agonists. During the years, Professor Johnston and his group have led several studies regarding the *in vitro* pro-inflammatory properties of Inhaled β2-agonists in Human Airway Epithelial Cells. In particular, these pro-inflammatory effects are enhanced by Rhinovirus (RV) infection, which is one of the commonest causes of asthma exacerbations. The project I took part is the MAELABA Study, which aim is to examine which pro-inflammatory mediators are upregulated by beta agonists in the human lung *in vitro* and *in vivo*. During my stay, I joined the first part of the study, that consists of stimulating bronchial epithelial cell (BEC) lines with all the commercially available βagonists to re-confirm upregulation of cAMP/CRE-dependent mediators (IL-6, IL-11, BDNF), see which βagonists are most potent and to explore optimal time points for induction. Moreover, we tested not only Inhaled β2-agonists, but also others drugs usually used in the management of asthma. In particular, we evaluated the commercially available combination of β2-agonists and corticosteroids and ipratropium bromide, a short-acting inhaled anticholinergic agent.
I had the opportunity to work with clinical residents and scientists, in a laboratory setting. I joined meetings to plan the experiments and to discuss the results. I have learnt how to culture BEAS-2B BECs and to treat them with several drugs (salmeterol, alone or plus fluticasone, ipratropium bromide, fenoterol, salbutamol, formoterol, indacaterol, olodaterol and vilanterol, with or without infection with RV-16. Using Salmeterol alone or in combination with Fluticasone, we collected supernatants and cell lysates at 8, 24, 48 and 72 hours post-stimulation. For the other drugs, we evaluated different concentrations at 24 hours post-stimulation. I observed and/or partly performed ELISA to measure BDNF, IL-6 and IL-11 in cell supernatants. Moreover, I examined the gene expression through qPCR (Taqman Chemistry), after RNA extraction from cell lysates. I am going to show the results of the project in the final thesis at the end of my specialization.

During my stay, I took part in a double bind study, regarding a novel therapeutic agent to stimulate innate immunity in the lung that may protect against lower respiratory tract infections. I observed and performed screening visits to assess the eligibility of the patients. Each visit consisted of the collection of medical history, the assignment of COPD Assessment Test (CAT) and spirometry. I performed also FeNO, nasal lavage, sputum induction and spirometry with or without bronchoreversibility in enrolled patients.

Every Thursday I joined respiratory clinic with Professor Johnston. In this outpatient clinic there were about six patients affected by asthma and COPD. In this context, I could see the differences in presentation and management of respiratory disease in the United Kingdom, and I learnt about the healthcare infrastructure of UK.

Finally, I joined weekly departmental meeting, where I could expand my knowledge in different fields of respiratory diseases.

I would like to thank Professor Johnston and all the team members for warm welcome, valuable advices and help, and the EAACI for this productive opportunity. I have developed new skills, in particular in molecular biology. I would strongly recommend this experience to junior physicians who work in the field of allergy and respiratory diseases.

I will remember to acknowledge EAACI in any future publication, which could relate to the Fellowship.

Francesca Losa

EAACI Clinical Fellowship 2019 Awardee