LECTURE SERIES & WORKSHOPS 2020

INFECTION & IMMUNITY

LUXEMBOURG INSTITUTE OF HEALTH
RESEARCH DEDICATED TO LIFE

24 SEPT 2020
Thursday

LECTURE*
Lycée Guillaume Kroll
d'Esch/Alzette
Room: *Salle de Projection**
Registration mandatory
(max 30 persons)
11.00-12.00pm

MEET & EAT*
Light lunch provided
Annex of canteen
Registration mandatory
(max 15 persons)
12.30-2.00pm

9 10 11 12 1 2 3 4

*Please register by sending a mail to florence.henry@lih.lu

Spontaneous protein crystallization as a treatable trait in asthma

ABSTRACT

Mucus plugging or mucoid impaction of the airways is one of the ignored reasons for persistent airflow limitation in asthma, for which there are currently few therapeutic options. How exactly plug formation is initiated and maintained is an enigma. Spontaneous protein crystallization is a rare event in vivo, yet Charcot-Leyden crystals (CLC) consisting of the protein galectin-10 (Gal10) are frequently observed in asthma plugs. It is unclear if they exacerbate disease. Release of Gal10 and extracellular crystallization was associated with EEtosis of eosinophils in human primary eosinophils and patients with allergic mucin. We found that recombinant crystalline Gal10 was completely biosimilar to in vivo obtained CLCs and induced innate airway inflammation, whereas a soluble Gal10 engineered to resist crystallization was inert in the airways. When co-administered with harmless antigens, only crystalline Gal10 stimulated adaptive immunity, Th2 sensitization, goblet cell metaplasia and airway eosinophilia. Transgenic mice engineered to overexpress human Gal10 in eosinophils (Galileo mice) or ubiquitously (Galactic mice) had enhanced features of asthma including mucus plugging and bronchial hyperreactivity. CLCs recruited neutrophils, which subsequently underwent NETosis. To probe for the druggability of this pathway, we generated a panel of antibodies. Antibodies directed against key epitopes of the crystallization interface of Gal10 dissolved pre-existing CLC in patient-derived mucus within hours, and reversed crystal driven inflammation, goblet cell metaplasia, IgE synthesis and bronchial hyperreactivity in a humanized asthma model and Galileo mice. Thus, Gal10 and CLC promote mucus formation and inflammation in asthma and can be targeted by crystal dissolving antibodies.

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SPEAKER

Prof Bart N. LAMBRECHT

Professor of Medicine, Department Director Center for Infammation Research, VIB- UGent- Center for Inflammation Research, Belgium

HOST:
Department of Infection and Immunity (LIH)

RESPONSIBLE LIH SCIENTIST:
Prof Dr Markus Ollert / (markus.ollert@lih.lu)

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Social distancing rules and sanitary regulations will be in place

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