

2nd International Conference on **Influenza**

September 12-13, 2016 Berlin, Germany

Kallikrein-related peptidase 5 contributes to H3N2 influenza virus infection in human lungs

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The cleavage of the influenza A virus hemagglutinin (HA) by host serine-proteases is essential for viral infectivity. Several serine proteases of the kallikrein-related peptidase (KLK) family are produced and secreted by the airways and we investigated whether KLK1, 5 and 14 were involved in seasonal IAV infection. Expression of KLK1, 5 and 14 was assessed at the protein levels, in human tracheal aspirates from flu patients in intensive care unit, using ELISA. Primary human bronchial epithelial cells (hBEC) cultured at the Air-liquid interface were infected with IAV and the expression of KLKs was analyzed by RT-qPCR and flow cytometry. We also investigated in vitro if KLK1, 5 and 14 were able to cleave HA precursors. Finally, inactivated virions (mouse adapted A/Scotland20/74, H3N2) were treated with KLKs and the infectiveness was determined in MDCK cells and in mice. Flu infection selectively increased expression of KLK5 in hBEC and its secretion in the human airways. KLK1, 5 and 14 were able to cleave in vitro HA precursor from several subtypes of influenza viruses. Furthermore, only the KLK5 treatment of H3N2 virions promoted IAV infection in MDCK cells. In mice, the treated virus led to severe infection with KLK5 treatment and to moderate one with KLK14 treatment. KLK1 virus treatment did not result in infection. Expression and secretion of KLK5 is specifically induced in airways upon flu. This induction likely contributes to the propagation of the virus in favoring its multi-cycle replication through activation of the HA precursor.

Biography

Melia Magnen is currently pursuing her PhD at the CEPR, Tours, France, working under Dr. Yves Courty, Centre d'Étude des Pathologies Respiratoires (INSERM U1100). Her research interest mainly focuses on influenza and other respiratory viruses.

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