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Peptide-Based Platform for Differentiation of Antigenic Variations within Influenza Virus Subtypes (Flutype)

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Abstract : The influenza viruses cause flu epidemics every year and serious pandemics in larger time intervals. The only cost-effective protection against influenza is vaccination. Due to rapid mutation continuously new subtypes appear, what requires annual reimmunization. For a correct vaccination recommendation, the circulating influenza strains had to be detected promptly and exactly and characterized due to their antigenic properties. During the flu season 2016/17, a wrong vaccination recommendation has been given because of the great time interval between identification of the relevant influenza vaccine strains and outbreak of the flu epidemic during the following winter. Due to such recurring incidents of vaccine mismatches, there is a great need to speed up the process chain from identifying the right vaccine strains to their administration. The monitoring of subtypes as part of this process chain is carried out by national reference laboratories within the WHO Global Influenza Surveillance and Response System (GISRS). To this end, thousands of viruses from patient samples (e.g., throat smears) are isolated and analyzed each year. Currently, this analysis involves complex and time-intensive (several weeks) animal experiments to produce specific hyperimmune sera in ferrets, which are necessary for the determination of the antigen profiles of circulating virus strains. These tests also bear difficulties in standardization and reproducibility, which restricts the significance of the results. To replace this test a peptide-based assay for influenza virus subtyping from corresponding virus samples was developed. The differentiation of the viruses takes place by a set of specifically designed peptidic recognition molecules which interact differently with the different influenza virus subtypes. The differentiation of influenza subtypes is performed by pattern recognition guided by machine learning algorithms, without any animal experiments. Synthetic peptides are immobilized in multiplex format on various platforms (e.g., 96-well microtiter plate, microarray). Afterwards, the viruses are incubated and analyzed comparing different signaling mechanisms and a variety of assay conditions. Differentiation of a range of influenza subtypes, including H1N1, H3N2, H5N1, as well as fine differentiation of single strains within these subtypes is possible using the peptide-based subtyping platform. Thereby, the platform could be capable of replacing the current antigenic characterization of influenza strains using ferret hyperimmune sera.

Keywords : antigenic characterization, influenza-binding peptides, influenza subtyping, influenza surveillance
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