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Auditorium COPL (salle 1168)

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Probing the Catalytic Mechanism of Neuraminidases: The "N" in H5N1

In mammalian systems, the sugar *N*-acetylneuraminic acid (sialic acid) is an important component of many carbohydrate-containing biomolecules whose function is to modulate cellular responses in a range of physiological processes, including differentiation, proliferation and apoptosis. Enzymes known as neuraminidases (sialidases) are a specific type of glycosyl hydrolase that hydrolyzes sialic acid, removing the sugar unit from its end-cap position on a glycoconjugate. Given the critical importance of sialic acid to mammalian function, it is unsurprising that certain viruses, bacteria and trypanosomes have developed, as part of their weaponry, enzymes that catalyze removal (neuraminidases) or transfer (*trans*-sialidases) of these host cell components.

Neuraminidases have been classified into three glycosyl hydrolase families (GH) based on bioinformatic analyses of amino acid sequences and predicted structural similarities. The influenza viral enzymes are in family GH 34. All of these enzymes contain a six-fold b-propeller as the prominent structural motif. In the case of influenza viruses, the presence of the neuraminidase (the 'N' in H5N1) is essential for the release of progeny virus particles from infected cells. We have been investigating the mechanism of action for neuraminidases, using many techniques, including: site-directed mutagenesis, inhibitor design and kinetic isotope effects. Results from our recent studies will be presented.

Cordiale bienvenue à toutes et à tous!