UNIVERSITÀ DEGLI STUDI DI BRESCIA

I SEMINARI DEL DIPARTIMENTO DI MEDICINA MOLECOLARE E TRASLAZIONALE

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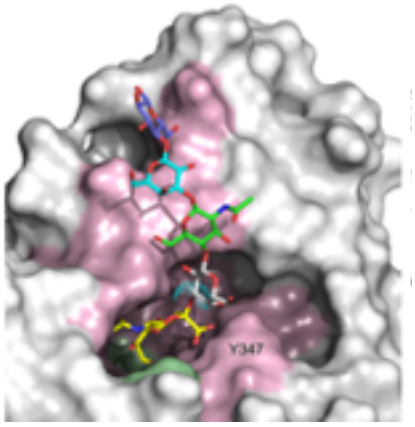
Structural characterization and molecular recognition of bio-macromolecules by NMR and MD simulation



Bio-macromolecules drive biological processes, in tissue in living systems, their activities strongly depend on structural, chemical, and physical events that take place in local, complex environments, whose length scales span from angstrom to nanometres. At these levels all the processes that sustain life are subject to atomic and intermolecular forces, therefore an exhaustive description cannot exclude a microscopic view. Several viruses such as human herpes simplex, Zika and human coronaviruses employ the heparan sulfate (HS) of the extracellular matrix as co-receptor. ^{1}H Saturation Transfer Difference (STD) NMR and MD simulation underline how the receptor binding domain (S1-RBD), the distal subunit of the protein S (Spike) of SARS-CoV-2, binds HS oligosaccharides with low specificity. This suggests new molecular mechanisms in which HS behave (initially) as first anchor point of SARS-CoV-2 virions. Later, HS promotes the interaction between S1-RBD and Angiontensin Converting Enzyme2 receptor. This supports why, heparin and mimetics of HS inhibit SARS-CoV-2 infections in cells in-vitro.

Influenza A virus (IV) is diffused in bird farms, only rarely it infects and transmits between humans by aerosol becoming potentially pandemic. IV presents two recognition proteins: hemagglutinin (HA) and neuraminidase (NA), the former binds specifically α2-3 (avian) or a2-6 (human) Neu5Ac-Gal terminated glycoconjugates of cell host surface. NA removes the Neu5Ac cap, allowing the releases of the newly formed virus. STD NMR and MD simulation suggests why only few amino acid mutations in the active site of HA or NA are required to switch their specificity toward α2-3 or α2-6 Neu5Ac-Gal, resulting in alteration of the virus preference toward a host specie. This predicts critical mutations in HA or NA that allows IV to gain human adapted features, and to design new antiviral strategies.

Mercoledì 20 marzo 2024, Ore 13:00, aula A2

Ospite: Prof. Maura Poli, Prof. Paolo Bergese