

Investigation of the structure/function relationships in the HIV-1 packaging signal by high-resolution mass spectrometry

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Invité par Frank WIEN

**Vendredi 14 septembre à 15h00
Amphi du Bât. Accueil Soleil**

High-resolution mass spectrometry (MS) is poised to assume a major role in structural and functional genomics, which extends beyond the identification and quantification of proteins and post-translational modifications typical of proteomics applications. On one hand, the development of new strategies combining chemical footprinting and bifunctional crosslinking with high-resolution MS, collectively known as MS3D, is opening the way for the elucidation of the 3D structure of large biomolecular complexes that exceed the size accessible to NMR and are too flexible for crystallization. On the other, the ability of electrospray ionization (ESI) to transfer intact non-covalent complexes to the gas phase is expected to expand the contributions of mass spectrometry to the functional study of these assemblies, as well, by enabling the direct investigation of the binding determinants, the subunits dynamics, and the factors affecting the complex stability.

We have taken advantage of these recent developments to investigate the specific interactions between the nucleocapsid (NC) protein and the packaging signal (Ψ -RNA) of HIV-1, and their roles in the mechanism of genome recognition, dimerization, and packaging in the life cycle of the etiologic agent of AIDS. In this talk, we will discuss MS-based strategies employed to measure the binding affinity of NC toward the different stemloop domains present in Ψ -RNA and to evaluate the inhibitory properties of archetypical nucleic acids ligands on the NC-stemloop complexes. The ability of NC to mediate the dimerization and isomerization of stemloop 1 (SL1) was studied by ESI on a Fourier transform ion cyclotron resonance (FTICR) mass analyzer to obtain new insights into the chaperone activity of this viral protein. Finally, we will also show how the spatial constraints provided by crosslinking methods and ESI-FTICR detection were utilized to complete the 3D structure of full-length Ψ -RNA according to a novel MS3D strategy.

Formalités d'entrée : accès libre dans l'amphi du Pavillon d'Accueil. Si la manifestation a lieu dans le Grand Amphi Soleil du Bâtiment Central, merci de vous munir d'une pièce d'identité (à échanger à l'accueil contre un badge d'accès).

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