

Giovedì 4 Luglio, ore 14:00

Aula Magna

Viale Regina Elena 295

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***The Dual Role of Integrase in HIV-1
Replication***

The HIV-1 integrase is a critical enzyme that catalyzes irreversible insertion of a viral DNA copy of its RNA genome into human chromosome, an essential requirement for viral replication. Therefore, integrase is an important therapeutic target. Productive integration into the host chromatin results in the formation of the strand transfer complex (STC) containing catalytically joined HIV-1 integrase tetramers, viral and target DNA strands. We have used cryo-EM, coupled with biochemistry and virology experiments, to obtain high-resolution structures for STCs and to characterize the integrase multi-subunit assemblies into large, nucleoprotein complexes. We are currently extending these studies to elucidate the structural basis for the mode of action of clinically used integrase strand transfer inhibitors (INSTIs) that bind to the enzyme active in the context of the integrase-viral DNA complex and block the strand transfer reaction. Parallel efforts are focused on studying allosteric HIV-1 integrase inhibitors (ALLINIs) that are currently undergoing clinical trials.



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