UFR de Chimie

Master Molécules, Matériaux, Surfaces

université PARIS DIDEROT PARIS 7

Séminaire de Chimie Autour des Nanosciences

ERIC ENNIFAR

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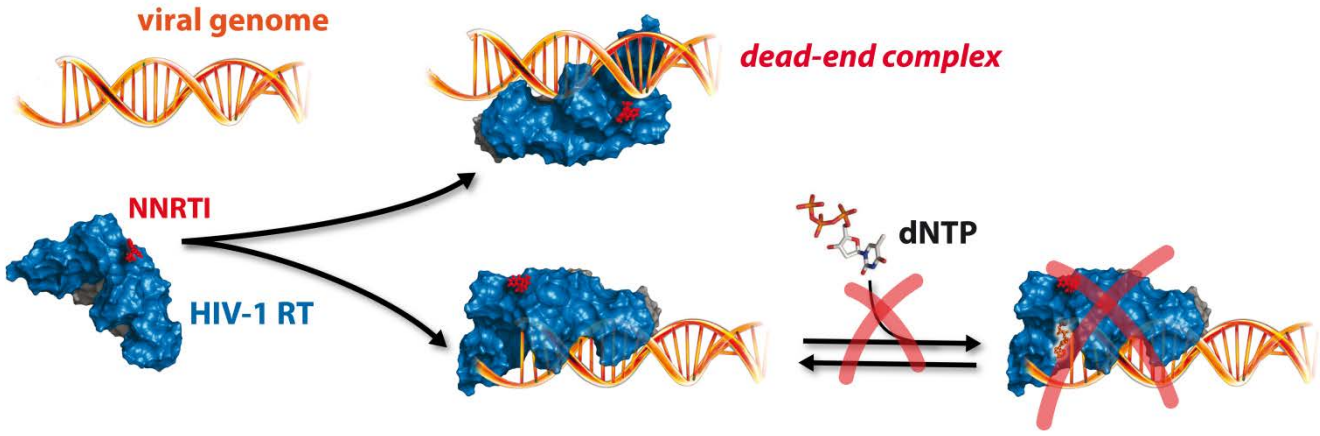
Donnera une conférence sur le thème :

THERMODYNAMICS OF HIV-1 REVERSE TRANSCRIPTASE IN ACTION REVEALS THE MECHANISM OF ACTION OF NON-NUCLEOSIDE INHIBITORS

HIV-1 reverse transcriptase (RT) is a heterodimeric enzyme that converts the genomic viral RNA into proviral DNA. Despite intensive biochemical and structural studies, direct thermodynamic data regarding RT interactions with its substrates are still lacking. Here we addressed the mechanism of action of RT and of non-nucleoside RT inhibitors (NNRTIs) by isothermal titration calorimetry (ITC). Using a new incremental-ITC approach, a step-by-step thermodynamic dissection of the RT polymerization activity showed that most of the driving force for DNA synthesis is provided by initial dNTP binding. Surprisingly, thermodynamic and kinetic data led to a re-interpretation of the mechanism of inhibition of NNRTIs. Binding of NNRTIs to preformed RT/DNA complexes is hindered by a kinetic barrier and NNRTIs mostly interact with free RT. Once formed, RT/NNRTI complexes bind DNA either in a seemingly polymerase-competent orientation, or form high-affinity dead-end complexes, both RT/NNRTI/DNA complexes being unable to bind the incoming nucleotide substrate.



LE VENDREDI 21 FEVRIER À 11H00

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