

# MICROBIOLOGIE, INFECTIOLOGIE ET IMMUNOLOGIE

Université   
de Montréal

## CONFÉRENCE

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#### **The regulation of annealing of tRNA<sup>Lys3</sup> to HIV-1 genomic RNA by viral and host factors**

During HIV-1 infection, the conversion of the HIV-1 RNA genome into a double-stranded DNA that can be integrated into the host cell's genome is accomplished by reverse transcription. The initiation of this reverse transcription requires a specific cellular tRNA<sup>Lys3</sup> to act as a primer. This tRNA is annealed during assembly of new HIV-1, i.e., the infecting virus already contains tRNA<sup>Lys3</sup> that is annealed to viral RNA. The 3' 18 nts of tRNA<sup>Lys3</sup> anneal to a complementary 18nt sequences in the viral RNA termed the primer binding site (PBS), and in this presentation, we will discuss the cellular and viral factors that promote the ability of the tRNA<sup>Lys3</sup> to locate the 18 nt sequence within the 9.7 kilobases comprising the HIV-1 viral RNA genome. We will discuss three such factors: 1) A 10 fold increase in the concentration of tRNA<sup>Lys3</sup> at the cytoplasmic site of viral assembly, relative to other tRNAs, which is due to a specific binding of the major viral structural protein Gag to the major tRNA<sup>Lys3</sup> binding protein, lysyl tRNA synthetase (LysRS). 2) The binding of the Gag/LysRS/ tRNA<sup>Lys3</sup> complex to a viral RNA sequence 25 nt upstream of the PBS, due to this sequence's strong affinity for LysRS. 3) The organization of an early viral assembly intermediate in the cytoplasm composed of Gag, GagPol, LysRS, and viral RNA, whose proposed architecture is predicted to promote the annealing of tRNA<sup>Lys3</sup> to viral RNA. We will also discuss microarray evidence indicating that the early formation of this complex, and the concentration and annealing of tRNA<sup>Lys3</sup> to viral RNA within the complex, occurs at the site of translation of Gag and GagPol. Finally, we show that in addition to facilitating the initiation of reverse transcription, annealing of tRNA<sup>Lys3</sup> to viral RNA promotes a conformation in the viral RNA that promotes viral RNA dimerization required for its packaging into the virus.

**Jeudi 19 février 2015 à 11h30**  
**Pavillon Claire-McNicoll, salle Z-255**

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