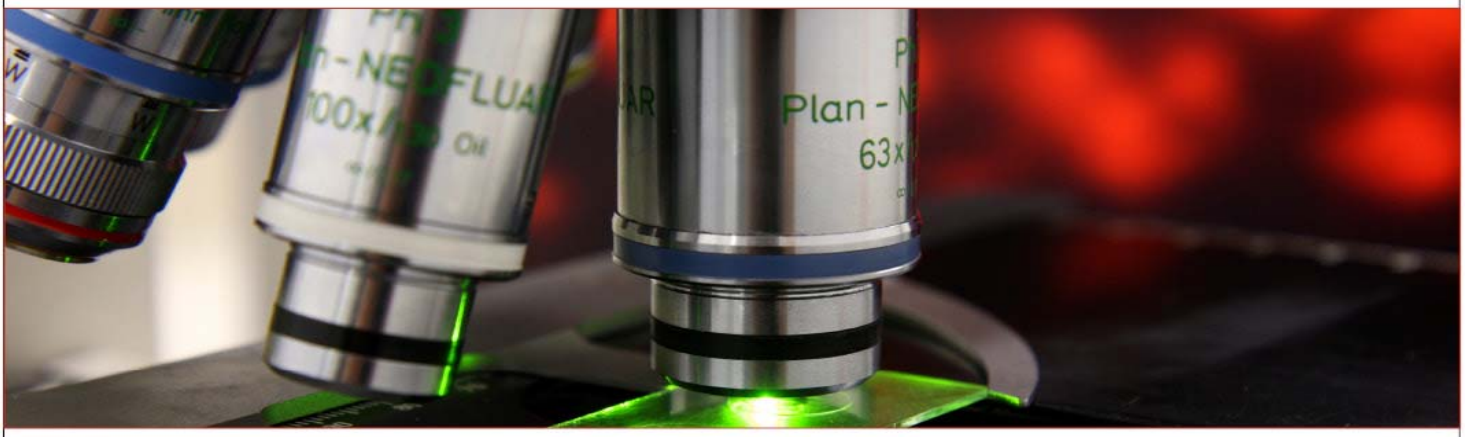
SÉMINAIRES ET CONFÉRENCES



Juan Alfonzo

Department of Microbiology
Ohio State University

« tRNA editing and modification in trypanosomes: Though this be madness, yet there is method in it »

Nucleic acids undergo naturally occurring chemical modifications. Over 100 different modifications have been described and every position in the purine and pyrimidine bases can be modified; often the sugar is also modified[1]. Despite recent progress, the mechanism for the biosynthesis of most modifications is not fully understood, owing, in part, to the difficulty associated with reconstituting enzyme activity *in vitro*. Whereas some modifications can be efficiently formed with purified components, others may require more intricate pathways[2]. A model for modification interdependence, in which one modification is a prerequisite for another, potentially explains a major hindrance in reconstituting enzymatic activity *in vitro*[3]. This model was prompted by the earlier discovery of tRNA cytosine-to-uridine editing in eukaryotes, a reaction that has not been recapitulated *in vitro* and the mechanism of which remains unknown. Here we show that cytosine 32 in the anticodon loop of *Trypanosoma brucei* $tRNA^{Thr}$ is methylated to 3-methylcytosine (m^3C) as a pre-requisite for C-to-U deamination. Formation of m^3C *in vitro* requires the presence of both the *T. brucei* m^3C methyltransferase TRM140 and the deaminase ADAT2/3. Once formed, m^3C is deaminated to 3-methyluridine (m^3U) by the same set of enzymes. ADAT2/3 is a highly mutagenic enzyme[4], but we also show that when co-expressed with the methyltransferase its mutagenicity is kept in check. This helps to explain how *T. brucei* escapes 'wholesale deamination'[5] of its genome while harbouring both enzymes in the nucleus. This observation has implications for the control of another mutagenic deaminase, human AID, and provides a rationale for its regulation.

Faculté de médecine
Département de biochimie et médecine moléculaire
Université de Montréal

Le lundi 24 avril 2017, 12h00

Pavillon Roger-Gaudry
Salle : D-225

Invité par Gertraud Burger

Tél : (514) 343-7936 courriel : gertraud.burger@umontreal.ca