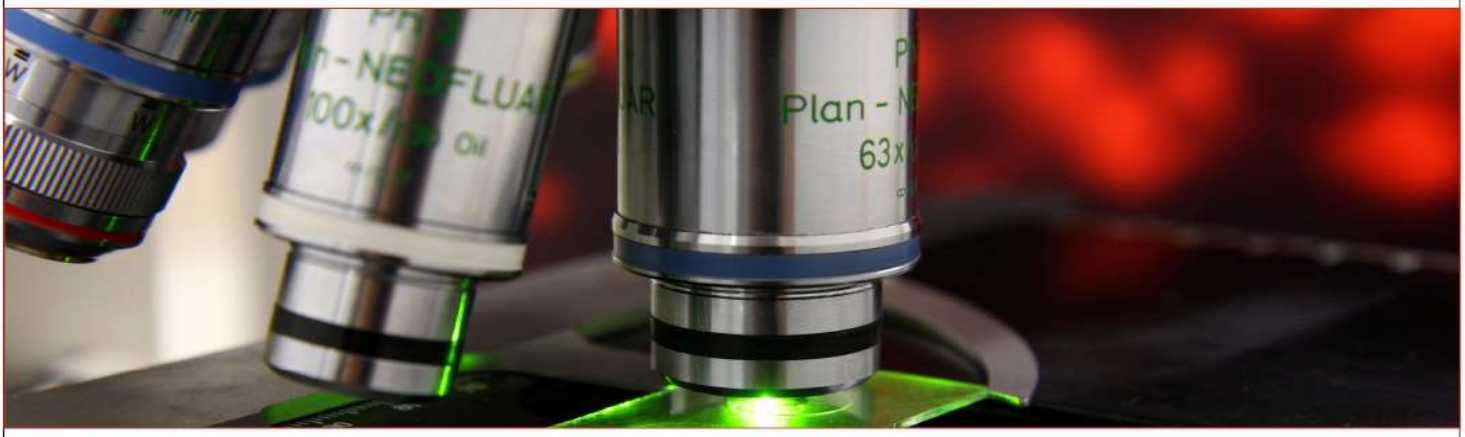
# SÉMINAIRES ET CONFÉRENCES




## Guy Poirier

## CHU de Québec, Faculté de médecine, Université Laval


## « Cross-talk between covalent and non-covalent poly(ADP-ribose) interactions during DNA damage response»

There has always been a lot of confusion about the intricate and complicated relationships between covalent and non-covalent poly(ADP-ribosylation) (PARylation). The exceptionally strong non-covalent interactions of poly(ADP-ribose) (PAR)-binding proteins with this homopolymer has mostly been responsible for the confusion between the two concepts. Most biochemical assays used in the past were not be able to provide a conclusive distinction between covalent and non-covalent protein PARylation. The development of mass spectrometry-based detection of ADP-ribosylation events can now help us to simplify and clarify the ADP-ribosylation status of a PAR-associated protein.

Early proteomics studies targeting cellular PARylation were primarily identifying proteins with high affinity for PAR. We and other reported the identification of more than 1000 PAR-associated proteins that were generally viewed as PAR-interacting proteins in a non-covalent fashion. Although this represents a large number of putative interactors, only a small fraction of the expressed proteome has been screened assuming that tissue culture cells can express several thousand proteins out of the detection range of most mass spectrometry instruments. The relatively limited linear dynamic range for the identification of proteins isolated by affinity-purification coupled to tandem mass spectrometry (AP-MS/MS) led us to use a *in silico* bioinformatics approach to identify non-covalent PAR-binding proteins based on the presence of a growing family of PAR-binding modules. Owing to the analytical versatility of mass spectrometry, several methods were developed recently for the identification of covalently ADP-ribosylated substrates of a variety of ADP-ribosyl transferases. Cross datasets comparison provided and in-depth analysis of protein PARylation. Collectively, covalent and non-covalent PARylation appear to be a fundamentally important regulatory mechanism with a widespread occurrence in human cells. We are currently designing a targeted approach to analyze factors involved in DNA damage signaling in response to double-strand breaks via either homologous recombination (HR) or nonhomologous end joining (NHEJ). We are also developing alternative methods to identify all covalently modified residues on ADP-ribosyl transferases susbtrates by mass spectrometry.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Faculté de médecine
Département de biochimie et médecine moléculaire
Université de Montréal

**Pavillon Roger-Gaudry**
**Salle : G-415**


**John Pascal**
Tél : (514) 343-4890 courriel john.pascal@umontreal.ca