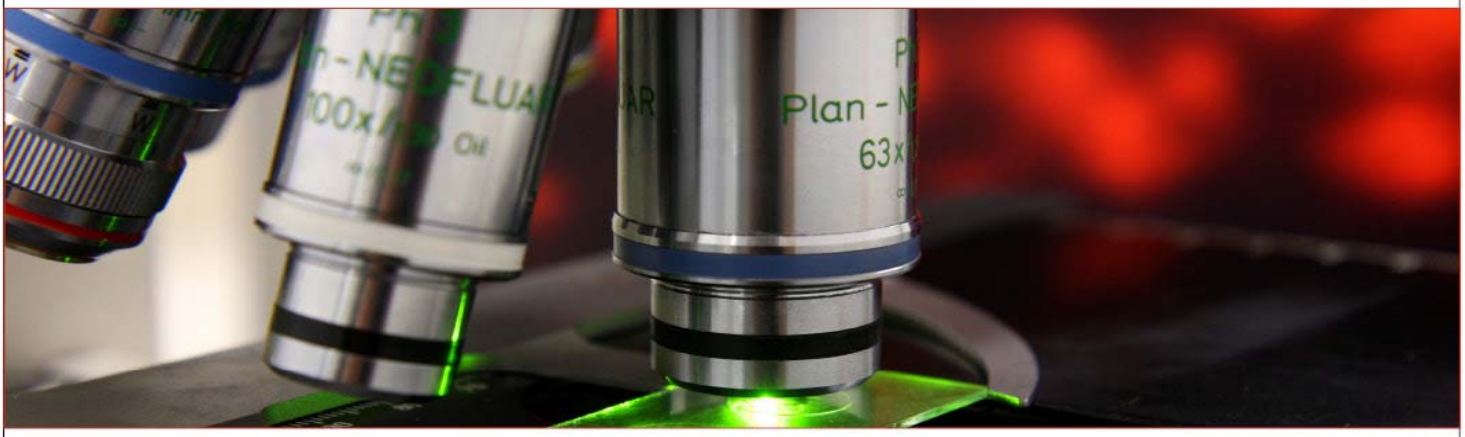
SÉMINAIRES ET CONFÉRENCES



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« Exploring the loss of function hypothesis for TDP-43 in ALS pathogenesis»

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease characterized by the selective loss of motor neurons. Efforts to design effective therapies are crippled by our lack of understanding the molecular lesions and aberrant processes that lead to disease pathogenesis. While several new players in ALS pathogenesis have recently emerged, RNA binding proteins, such as TDP-43 and hnRNP A1, have become a primary focus. However, little is understood about how these proteins interact and/or coordinate RNA processing and metabolism. RBPs such as TDP-43 and hnRNP A1 are both mutated in familial ALS cases and mislocalized into cytoplasmic aggregates in the motor neurons of affected patients. In the case of TDP-43, cytoplasmic inclusions are accompanied by a depletion of nuclear TDP-43. It is our hypothesis that mislocalisation of TDP-43 disrupts physiological functions within the nucleus. We have examined the downstream consequences of nuclear TDP-43 depletion on various aspects of RNA metabolism. One particular focus is on the stress granule mechanism as it serves as an interface between genetics and potential environmental contributions to disease. Our data support that a compromised stress granule p[illegible]P-43 nucl[illegible]n, [illegible]ute to neuronal vulnerability in ALS.

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Le lundi 4 février 2019, 11h30

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