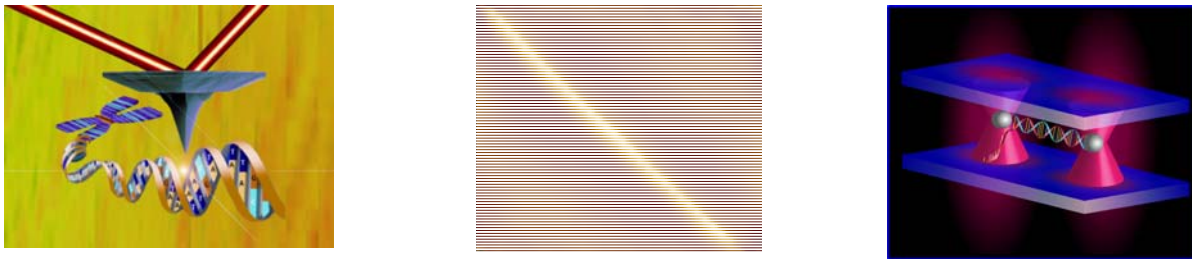


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# Key role of tau proteins in DNA protection

DIRECTEUR DE THESE : Mounir MAALOUM  
INSTITUT CHARLES SADRON, 23, RUE DU LOESS 67034 STRASBOURG  
TEL : 03 88 41 40 02 ; E-MAIL : [MOUNIR.MAALOUM@ICS-UNISTRA.FR](mailto:MOUNIR.MAALOUM@ICS-UNISTRA.FR)

Alzheimer disease is the result of the accumulation of anomalous tau protein in nerve cells, causing their degeneration. This dysfunction comes from an excess of phosphorylation of tau protein, leading to their aggregation. In 2010, a French team observed, in neurons of mice deficient in protein tau, DNA damage under conditions of cellular stress, which is not the case in healthy neurons. This result shows that tau protein, in its dephosphorylated form, is able under conditions of stress, to enter in the nucleus in order to protect it. However, the mechanism by which this protein protects DNA is unknown. This project aims to study the interaction between tau protein and DNA using atomic force microscopy in liquid and optical tweezers. This project will provide more fundamental knowledge of the importance of tau in DNA protection.



*Figure 1: left : schema of AFM tip probing DNA. Middle : AFM image (60 nm x 60 nm) of DNA at high resolution showing the double helix. Right : principle measurement of mechanical stretching of DNA using optical tweezers.*

The complexes formed by DNA and tau are particularly intriguing examples whose molecular origins are not understood in terms of structural biophysics. We hope to increase our expertise in single molecule manipulation and to develop our physics instrumentation for research in the field of Alzheimer's disease.

The work proposed in this PhD project should open new perspectives regarding the interactions between tau proteins and DNA in cell nucleus and provide an unprecedented insight into structural changes associated with pathogenic tau forms.

[1] Sultan, A et al, *Nuclear Tau, a Key Player in Neuronal DNA Protection*, Journal of Biological Chemistry **286**, 4566-4575 (2011).