UFR de Chimie et de Biologie
UNIVERSITÉ Grenoble Alpes

Master's degree in Biology – Chemistry-Biology Department

Master 2 internship project
Year 2020-2021

Laboratory/Institute: Institut de Biologie Structurale (IBS) **Director:** Winfried Weissenhorn
Team: Kadlec Team – Epigenetic regulators, Viral infection and cancer group (VIC)

Head of the team: Jan Kadlec

Name and status of the scientist in charge of the project: Jan KADLEC **HDR: yes** ☑ **no** ☐
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Program of the Master's degree in Biology:

☐ Immunology, Microbiology, Infectious Diseases ☑ Integrative Structural Biology
☑ Physiology, Epigenetics, Differentiation, Cancer ☐ Neurosciences and Neurobiology
☐ Planta International

Title of the project:

Structural studies on targeted RNA degradation.

Objectives (up to 3 lines):

To biochemically, biophysically and structurally characterize the interactions of the ARS2 protein within the MTREC complex.

Abstract (up to 10 lines):

The availability of RNA in the cell depends on the rate of both transcription and RNA degradation. In the nucleus, specific and tightly regulated RNA degradation is mediated by the nuclear RNA exosome, which is loaded onto the RNA transcripts to be eliminated with the help of various exosome adapters. In humans, these adapters are known as the NEXT or PAXT complexes, corresponding to the MTREC complex in yeast. All these complexes contain a protein called ARS2 that links them to the nuclear cap-binding complex (CBC). Our preliminary work identified novel interactions including ARS2 within the MTREC complex. The aim of this project is to characterize how ARS2 is incorporated into these assemblies and determine structures of the complexes with its binding partners. Structural information will then guide functional experiments in vivo aimed to better understand the role of ARS2 in targeted RNA degradation.

Methods (up to 3 lines):

Molecular cloning, biophysics, protein expression and purification, X-ray crystallography, electron microscopy

Up to 3 relevant publications of the team:

Kumar, R., Oliver, C., Brun, C., Juarez-Martinez, A.B., Tarabay, Y., Kadlec, J. and de Massy B. Mouse REC114 is essential for meiotic DNA double-strand break formation and forms a complex with MEI4. Life Sci. Alliance, 1:e201800259. (2018)

Touat-Todeschini, L., Shichino, Y., Dangin, M., Thierry-Mieg, N., Gilquin, B., Hiriart, E., Sachidanandam, R., Lambert, E., Brettschneider, J., Reuter, M., Kadlec, J., Pillai, R., Yamashita, A., Yamamoto, M., and Verdel. A. Selective termination of lncRNA transcription promotes heterochromatin silencing and cell differentiation. EMBO J. 36:2626-2641. (2017)

Dias, J., Nguyen, N., Georgiev, P., Gaub, A., Brettschneider, J., Cusack, S., Kadlec, J.* and Akhtar, A.* Structural analysis of the KANSL1/WDR5/KANSL2 complex reveals that WDR5 is required for efficient assembly and chromatin targeting of the NSL complex. Genes Dev. 28: 929-942 (2014)

Requested domains of expertise (up to 5 keywords):

Gene expression , RNA regulation, RNA complexes, X-ray crystallography