Seminar Speaker Series

in the framework of Interreg V-A project CAPSID

presents

Dr. Claudio Alfieri

The Institute for Cancer Research, London, UK

Molecular snapshots of cell cycle control by cryo-EM

10. 06. 2021 at **14:00**

Online virtual talk via Zoom

Join this talk here

Organized by:

Dr Claudio Alfieri

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AREAS OF EXPERTISE

Dr Claudio Alfieri is Team Leader of the **Molecular Mechanisms of Cell Cycle Regulation** Team at the Institute for Cancer Research (ICR). His research focuses on how the cell cycle is regulated by large macromolecular complexes during cell division, cell cycle exit and re-entry.

SEMINAR ANNOTATION

The maintenance of genome stability in mitosis is coordinated by the spindle assembly checkpoint (SAC) through its effector the mitotic checkpoint complex (MCC), an APC/C inhibitor. Unattached kinetochores control MCC assembly by catalysing a change in topology of the β-sheet of Mad2, an MCC subunit. Disassembly of free MCC, required for SAC inactivation and chromosome segregation, is an ATP-dependent process driven by the AAA+ ATPase TRIP13. In combination with the SAC antagonist p31comet, TRIP13 remodels C-Mad2 into inactive open Mad2 (O-Mad2). Here, we present a mechanism to explain how TRIP13-p31 disassembles the MCC. Our study provides insights into how specific substrates are recruited to AAA+ ATPases through adaptor proteins and suggests a model of how translocation through the axial pore of AAA+ ATPases is coupled to protein remodelling.

SHORT BIO

Dr Claudio Alfieri studied Molecular Biology at the Universities of Palermo (BSc) and Milano (MSc). During his PhD at the EMBL (Heidelberg) he studied the establishment of heritable chromatin domains, which during development, are transcriptionally silenced by Polycomb-group proteins by employing biochemical, biophysical and structural analysis (x-ray crystallography). For his postdoctoral research, supported by a EMBO Advanced Fellowship he solved the cryo-electron microscopy structure of the anaphase-promoting complex (APC/C) with the Mitotic checkpoint complex (MCC), and determined the structural basis for the MCC complex disassembly by the AAA+ ATPase TRIP13 and its adaptor p31comet. For this work, in 2018, he has been **awarded the Brenner Postdoc Prize**. In October 2019 he joined the ICR as a Sir Henry Dale Fellow working on the structure and molecular function of the Muv-B complexes in regulating cell cycle-dependent transcription.

REFERENCES

[1] **Alfieri C**, Chang L, Barford D. Mechanism for remodelling of the cell cycle checkpoint protein MAD2 by the ATPase TRIP13. **NATURE**. *2018* Jul;559(7713):274-278.

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