BIOLOGIA ESTRUCTURAL. MODIFICACIÓ DE PROTEINES
DAVID REVERTER

PROFILE

Our lab uses protein crystallography with synchrotron radiation as a major procedure to decipher the molecular mechanisms that lay behind the atomic structure of proteins and protein complexes. In our lab we combine this powerful structural technique with a functional and biochemical characterization using either in vitro or in vivo methods. In the last decades protein-function characterization of proteins and protein complexes have shed light into the most relevant discoveries in biochemistry and molecular biology.

RESEARCH

RESEARCH INTERESTS

Our lab uses protein crystallography with synchrotron radiation as a major procedure to decipher the molecular mechanisms that lay behind the atomic structure of proteins and protein complexes. In our lab we combine this powerful structural technique with a functional and biochemical characterization using either in vitro or in vivo methods. In the last decades protein-function characterization of proteins and protein complexes have shed light into the most relevant discoveries in biochemistry and molecular biology.

STRATEGIC OBJECTIVES

SUMO and ubiquitin are small protein modifiers that can be attached via an iso-peptidic bond to lysine residues of target proteins. This type of post-translational modification is very common and regulate almost all processes of cell life, including cell division, DNA repair or gene expression. For example, ubiquitin modification through Lys48 regulates the half-life of many proteins by degradation with the proteasome system and is essential for the protein homeostasis in the cell.

The conjugation of ***ubiquitin*** and ***SUMO*** (***Ubl***) to target proteins is conducted via a conserved multistep enzymatic cascade through ***E1*** (activating enzyme), ***E2*** (conjugating enzyme), and ***E3*** (ligase enzyme). Reversely, deubiquitinating enzymes (***DUBs***) can remove ubiquitin by catalyzing the hydrolysis of the isopeptide bond. Therefore, ubiquitin and ***SUMO*** conjugation and deconjugation are balanced and tightly regulated by ***E3*** ligases conjugation and ***DUBs*** deconjugation.

MAIN RESEARCH LINES

Our research lines in the medium-long term period include the functional and structural characterization of protein complexes of the ubiquitin/SUMO pathway, such as the SUMO E3 ligase activity of the Nse2 subunit of the Smc5/6 complex, which is involved in the DNA micro-compaction and acts as a giant E3 ligase involved in DNA damage repair pathways.

Currently we are also working in the deconjugation mechanisms of SUMO and ubiquitin proteases. We have recently described the mechanism of regulation of the USP25 deubiquitinase, which moves from dimer (active) to tetramer (inactive) quaternary conformation. We have just published the complex structure of USPL1, which is an unusual de-ubiquitinase that instead of ubiquitin cleaves off SUMO from protein targets.

LAB FEATURED PUBLICATIONS

- Li, Y., De Bolòs, A., Amador, V. & Reverter, D*. (2022) Structural basis for the SUMO2 isoform specificity of SENP7. **J. Mol. Biol.** doi.org/10.1016/j.jmb.2022.167875.
- Li, Y., Varejão, N. & Reverter, D.* (2022) Structural basis for the SUMO protease activity of the atypical ubiquitin-specific protease USPL1. **Nature Communications 13,** 1819 (2022). doi.org/10.1038/s41467-022-29485-0.
- Varejão, N., Lascorz, J., Codina-Fabra, J., Bellí, G, Borràs-Gas, H., Torres-Rosell, J. & Reverter, D.* (2021) Structural basis for the E3 ligase activity enhancement of yeast Nse2 by SUMO-Interacting Motifs. **Nature Communications 12,** 7013 (2021). doi.org/10.1038/s41467-021-27301-9.
- Lascorz, J., Codina-Fabra, J., Reverter, D.* & Torres-Rosell, J.* (2021) SUMO-SIM interactions: from structure to biological functions. **Sem. Cell and Dev. Biol.** Nov 25;S1084-9521(21)00283-4.
- Zhang, J., Liu, B., Gu, D., Hao, Y., Chen, M., Ma, Y., Zhou, X., Zhang, Y., Reverter, D.*, & Wang, Q.* (2021). Binding site profiles and N-terminal minor groove interactions of the master quorum-sensing regulator LuxR enable flexible control of gene activation and repression. ***Nucleic Acids Research***. 49(6):3274-3293. doi: 10.1093/nar/gkab150.
- Li, Y. & **Reverter, D.*** (2021). Molecular Mechanisms of DUBs regulation in signaling and disease. **Int. J. Mol. Sci.** 22:986. doi:10.3390/ijms22030986.
- Liu, B., Sureda-Gómez, M., Zhen, Y., Amador, V. & Reverter, D.* (2018). A quaternary tetramer assembly inhibits the deubiquitinating activity of USP25. **Nature Communications**, 9: 4973.
- Varejão, N., Ibars, E., Lascorz, J., Colomina, N., Torres-Rosell, J.*, Reverter, D.* (2018). DNA activates the Nse2/Mms21 SUMO E3 ligase in the Smc5/6 complex. **EMBO J**. pii: e98306.