ROMA TRE
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USING SINGLE-MOLECULE OPTICAL TWEEZERS TO UNRAVEL FUNCTIONAL DETAILS OF A MOLECULAR CHAPERONE

GUEST SPEAKER:
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HOST: ANTONIO BENEDETTO

Martedì 7 Febbraio 2023 ore 15:00
Piattaforma TEAMS (https://bit.ly/3HxGDsN)

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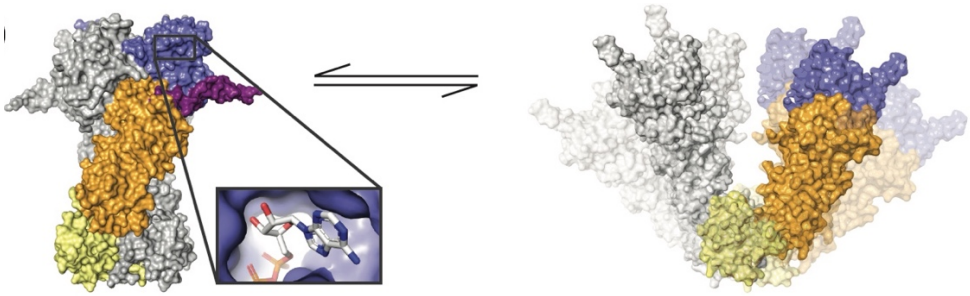
The Hsp90 molecular machine is known to undergo large conformational changes during its functional cycle. However, we do not currently have a full and detailed understanding how these conformational changes are affected by association with co-chaperones, clients and nucleotides. In addition to being of fundamental interest, knowledge of the molecular-level details of these processes will be critical in the development of the next generation of targeted drugs and therapeutic approaches.

Using single-molecule biophysics approaches, including the optical tweezers, mass photometry and fluorescence microscopy, we are able to directly observe the dynamics of Hsp90 and its clients and cochaperones in real-time. Our approach, in combination with the huge body of structural and biochemical characterization work performed by the Hsp90 community to date, enables us to start to fill in the existing gaps in our knowledge about how this essential chaperone functions.



Schematic illustration of the closed state of the Hsp90 homo-dimer (one monomer coloured by structural domain, one in grey), showing nucleotide binding pocket and the ensemble of open states of the dimer. Illustration based on PDB structures 2CG9 and 2IOP.

[1] Using Single-Molecule Optical Tweezers to Study the Conformational Cycle of the Hsp90 Molecular Chaperone, K. Tych, M. Rief - Optical Tweezers, 2022
[2] The Hsp90 isoforms from S. cerevisiae differ in structure, function and client range, H. Girstmair, F. Tippel, A. Lopez, K. Tych, F. Stein, P. Haberkant, P. Werner, N. Schmid, D. Helm, M. Rief, M. Sattler & J. Buchner, Nature Communications 10(1), 3626, 2019
[3] Nucleotide-Dependent Dimer Association and Dissociation of the Chaperone Hsp90, K. Tych, M. Jahn, F. Gegenfurtner, V.K. Hechtl, J. Buchner, T. Hugel, M. Rief, The Journal of Physical Chemistry B 122 (49), 11373-11380, 2018

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