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## Structural communication in transcription factors

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L ittle is known about the molecular mechanisms related to the conformational changes induced at distal sites in many Ltranscription factors which are often related to cancer disease, such as p53, MZF1 and the family of ARID domains. Thus, my group is focusing on the characterization of their structural dynamics to enrich the knowledge on this important group of regulatory proteins. In particular, we are employing a combined approach that integrates atomistic microsecond molecular dynamics simulations, enhanced sampling techniques, methods inspired by graph theory and cross-validation of the simulated ensembles with NMR data. To relate these properties to protein function, we studied both the free and DNA-bound forms of wild type, mutated and phosphorylated variants of p53, ARID proteins and MZF1. The interaction with DNA not only stabilizes the conformations of the DNA-binding loops, but also strengthens pre-existing paths in the free protein for longrange communication to potential interface for cofactor recruitment. Conformational states of these distal regions that are only a minor population of the free ensemble are promoted by DNA interactions, altering the preferences for certain classes of biological partners and thus influencing the signaling pathways mediated by these proteins. Moreover, mutations or posttranslational modifications can also contribute to reshape the population of these interfaces even in domains that are not necessarily involved in DNA-binding.

## **Biography**

Elena Papaleo completed her PhD in 2006 and Post-doctoral from 2007-2009 at the Department of Biotechnology and Bioscience at the University of Milano-Bicocca (Italy) in the group of Prof. Luca De Gioia and Prof. Piercarlo Fantucci. She was then appointed as Adjunct Professor in Computational Biology at the University of Milano-Bicocca from 2010-2012. Afterwards, she was Senior Post-Doctoral Researcher in the group of Prof. Lindorff-Larsen at the Department of Biology of the University of Copenhagen (Denmark) from 2011-2015. She has been Visiting Researcher at many international institutes including the group of Prof. Salvador Ventura at the Institute of Biotechnology and Biomedicine (IBB, Barcelona, Spain) and the group of Prof. Francesco Luigi Gervasio at the Spanish National Cancer Research Center (CNIO, Madrid, Spain). In August 2015, she joined as Group Leader of the Computational Biology (CBL) Laboratory at the Danish Cancer Society Research Center (Copenhagen, Denmark). She has authored more than 50 scientific papers as main or senior author and she is Academic Editor of *PLoS One, Frontiers in Molecular Biosciences* (Nature publishing group), *PeerJ* and *Journal of Molecular Graphics and Modelling*. The main research of CBL focuses on "Molecular modelling and simulations integrated with experimental data and network theory to the study structure-function relationship in key cancer proteins as well as on the analyses of high-throughput sequencing and omics data from profiling of cancer patients".

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