

IRB BARCELONA 2011 ANNUAL REPORT

Research Programmes

CHEMICAL AND MOLECULAR PHARMACOLOGY

Xavier Salvatella: Laboratory of Molecular Biophysics



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Highlights

- We have identified in a model protein weak long-range correlated motions such as those responsible for allostery using NMR in combination with molecular simulations.
- In a model protein, we have discovered that disulfide bonds can decrease the entropic cost of forming well-ordered and relatively innocuous amyloid fibrils.
- We have found that disulfide bonds are likely to have evolved in secreted proteins to minimize toxic aggregation by promoting the formation of inert fibrils.

Publications

- Fenwick RB, Esteban-Martín S, Richter B, Lee D, Walter KF, Milovanovic D, Becker S, Lakomek NA, Griesinger C and Salvatella X.
Weak long-range correlated motions in a surface patch of ubiquitin involved in molecular recognition
J Am Chem Soc, **133**, 10336-9 (2011)
- Mossuto MF, Bolognesi B, Guixer B, Dhulesia A, Agostini F, Kumita JR, Tartaglia GG, Dumoulin M, Dobson CM and Salvatella X.
Disulfide bonds reduce the toxicity of the amyloid fibrils formed by an extracellular protein
Angew Chem Int Edit, **50**, 7048-51 (2011)
- Fenwick RB, Esteban-Martín S and Salvatella X.
Understanding biomolecular motion, recognition, and allostery by use of conformational ensembles
Eur Biophys J Biophys, **40**, 1339-55 (2011)
- Ban D, Funk M, Gulich R, Egger D, Sabo TM, Walter KF, Fenwick RB, Giller K, Pichierri F, de Groot BL, Lange OF, Grubmüller H, Salvatella X, Wolf M, Loidl A, Kree R, Becker S, Lakomek NA, Lee D, Lunkenheimer P and Griesinger C.
Kinetics of conformational sampling in ubiquitin
Angew Chem Int Edit, **50**, 11437-40 (2011)
- Lamberto GR, Torres-Monserrat V, Bertoncini CW, Salvatella X, Zweckstetter M, Griesinger C and Fernández CO.
Toward the discovery of effective polycyclic inhibitors of alpha-synuclein amyloid assembly
J Biol Chem, **286**, 32036-44 (2011)

- Buell AK, Dhulesia A, Mossuto MF, Cremades N, Kumita JR, Dumoulin M, Welland ME, Knowles TP, Salvatella X and Dobson CM.

Population of nonnative states of lysozyme variants drives amyloid fibril formation

J Am Chem Soc, **133**, 7737-43 (2011)

Research projects

- Laboratori de biofísica molecular, Grups de Recerca reconeguts per la Generalitat de Catalunya 2009-2013 (2009 SGR 1514). Agency for Administration of University and Research Grants (AGAUR). Principal investigator: Xavier Salvatella
- Structural characterization of key conformational transitions in protein deposition diseases. Proyectos de investigación fundamental (CTQ2009-08850-BQU). Spanish Ministry of Science and Innovation (MICINN). 2010-2012. Principal investigator: Xavier Salvatella
- Identification of the aggregates of Androgen Receptor that cause Spinal Bulbar Muscular Atrophy (102030) Fundació Marató de TV3 (2011-2013) Principal Investigator and coordinator: Xavier Salvatella

Collaborations

- *Correlated motions in globular proteins*, Donghan Lee , Max Planck Institute for Biophysical Chemistry (Göttingen, Germany); Christian Griesinger , Max Planck Institute for Biophysical Chemistry (Göttingen, Germany); Modesto Orozco, IRB Barcelona (Barcelona, Spain)
- *Correlated motions in multi-domain proteins*, Victor Guallar , Barcelona Supercomputing Centre (Barcelona, Spain); Magnus Wolf-Watz , Umeå University (Umeå, Sweden)
- *Methods for the simultaneous determination of the structure and dynamics of native proteins using residual dipolar couplings*, Christian Griesinger, Max Planck Institute for Biophysical Chemistry (Göttingen, Germany)
- *Structure-activity relationships in androgen receptor aggregates involved in spinal bulbar muscular atrophy*, Eva Estébanez-Perpiñá , University of Barcelona (Barcelona, Spain); Leila Luheshi , University of Cambridge (Cambridge, United Kingdom)
- *Structure-activity relationships in protein aggregates*, Christopher Dobson, University of Cambridge (Cambridge, United Kingdom)
- *Use of protein native ensembles in protein-protein docking*, Juan Fernández-Recio, Barcelona Supercomputing Centre (Barcelona, Spain)



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