

IRB BARCELONA 2010 ANNUAL REPORT

SCIENCE AT IRB BARCELONA

Research Programmes

Chemistry and Molecular Pharmacology

Xavier Salvatella: Laboratory of molecular biophysics



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Highlights

- Residual Dipolar Couplings measured using Nuclear Magnetic Resonance in solution can be used, in combination with molecular simulations, to characterize the structural properties of disordered proteins that are prone to aggregate.
- The aggregation of human lysozyme in lysozyme amyloidosis is caused by the accumulation of a molten globular partially folded state rather than by a well-defined aggregation-prone intermediate.
- The structural heterogeneity of the amyloidogenic partially folded intermediate state of lysozyme is reflected in the morphology of the aggregates that it forms. This has implications for disease because the cytotoxicity of the fibrils depends on the size of the cross-beta core.

Publications

- Dhulesia A, Cremades N, Kumita JR, Hsu ST, Mossuto MF, Dumoulin M, Nietlispach D, Akke M, Salvatella X and Dobson CM. Local cooperativity in an amyloidogenic state of human lysozyme observed at atomic resolution. *J Am Chem Soc*, 132 (44), 15580-8 (2010)
- Esteban-Martín S, Fenwick RB and Salvatella X. Refinement of ensembles describing unstructured proteins using NMR residual dipolar couplings. *J Am Chem Soc*, 132 (13), 4626-32 (2010)
- Fenwick R. B., Esteban-Martín S. and Salvatella X. Influence of experimental uncertainties on the properties of ensembles derived from NMR residual dipolar couplings *J Phys Chem Lett*, 1, 3438-3441 (2010)
- Mossuto MF, Dhulesia A, Devlin G, Frare E, Kumita JR, de Laureto PP, Dumoulin M, Fontana A, Dobson CM and Salvatella X. The non-core regions of human lysozyme amyloid fibrils influence cytotoxicity. *J Mol Biol*, 402 (5), 783-96 (2010)

Collaborations

- 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 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)

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



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