Research Programmes

STRUCTURAL AND COMPUTATIONAL BIOLOGY

Patrick Aloy: Structural Bionformatics and Network Biology

Highlights

- We have identified 200 high-confidence interactors directly related to Alzheimer´s disease (AD). Our results point to a putative role of PDCD4 as a neuronal death regulator and ECSIT as a molecular link between oxidative stress, inflammation, and mitochondrial dysfunction in AD.
- Through the analyses of 2090 unique unbound - bound transitions, we have shown that two-thirds of these proteins do not undergo significant structural changes upon binding. Among the remaining proteins, one-third explores the bound conformation in the unbound state (conformational selection model) and, while most transitions are possible from an energetic perspective, a few do require external help to break the thermodynamic barrier (induced fit model).
- We have also found that domains interacting with many partners undergo smaller changes upon association, and are less likely to freely explore larger conformational changes.

Publications

- Soler-López M, Zanzoni A, Lluís R, Stelzl U and Aloy P.
  Interactome mapping suggests new mechanistic details underlying Alzheimer's disease
  Genome Res, **21**, 364-76 (2011)
- Aranda B, Blankenburg H, Kerrien S, Brinkman FS, Ceol A, Chautard E, Dana JM, De Las Rivas J, Dumousseau M, Galeota E, Gaulton A, Goll J, Hancock RE, Isserlin R, Jimenez RC, Kerssemakers J, Khadake J, Lynn DJ, Michaut M, O'Kelly G, Ono K, Orchard S, Prieto C, Razick S, Rigina O, Salwinski L, Simonovic M, Velankar S, Winter A, Wu G, Bader GD, Cesareni G, Donaldson IM, Eisenberg D, Kleywegt GJ, Overington J, Ricard-Blum S, Tyers M, Albrecht M and Hermjakob H.
  PSICQUIC and PSISCORE: accessing and scoring molecular interactions
  Nat Methods, **8**, 528-9 (2011)
- Stein A, Rueda M, Panjkovich A, Orozco M and Aloy P.
  A systematic study of the energetics involved in structural changes upon association and connectivity in protein interaction networks
  Structure, **19**, 881-9 (2011)
- Stein A, Mosca R and Aloy P.
  Three-dimensional modeling of protein interactions and complexes is going 'omics
  Curr Opin Struc Biol, **21**, 200-8 (2011)
- Feliu E, Aloy P and Oliva B.
  On the analysis of protein-protein interactions via knowledge-based potentials for the prediction of protein-protein docking
  Protein Sci, **20**, 529-41 (2011)

Group Members

Group Leader

Patrick Aloy (ICREA)

Research Associates

Roberto Mosca
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PhD Students

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Victor Alcalde

- Zanzoni A, Carbajo D, Diella F, Gherardini PF, Tramontano A, Helmer-Citterich M and Via A.
  Phospho3D 2.0: an enhanced database of three-dimensional structures of phosphorylation sites
  Nucleic Acids Res, **39**, D268-71 (2011)
- Stein A, Céol A and Aloy P.
  3did: identification and classification of domain-based interactions of known three-dimensional structure
  Nucleic Acids Res, **39**, D718-23 (2011)

PhD Theses

- A novel framework for the computational analyses of biological networks. Roland A Pache, University of Barcelona (2011). Thesis director: Patrick Aloy. Honors: Cum Laude

Patents

- *Methods and Systems for identifying molecules or processes of biological interest by using knowledge discovery in biological data*
  Mas JM, Pujol A, Farrés J and Aloy P
  Applicant: Anaxomics Biotech SL
  Publication number/date: WO2011051805 (05/05/2011)

Research projects

- A network medicine approach to colorectal and breast cancer. Proyectos Investigación Fundamental Spanish (BIO2010-22073). Ministry of Science and Innovation (MICINN). 2010-2013. Principal investigator: Patrick Aloy
- Identification and validation of novel drug targets in Gram-negative bacteria by global search: a trans-system approach (ANTIPATHOGN), European Commission (223101). 2009-2013. Principal investigator: Patrick Aloy
- Identification of secondary targets and drug design through the structural and functional analyses of biological networks. Proyectos Singulares Estratégicos (PSE-010000-2009-008 2009). Spanish Ministry of Science and Innovation (MICINN) (MICINN). 2009-2011. Principal investigator: Patrick Aloy
- Structural bioinformatics and network biology, Grups de Recerca reconeguts per la Generalitat de Catalunya 2009-2013 (2009 SGR 1519). Agency for Administration of University and Research Grants (AGAUR). 2009-2013. Principal investigator: Patrick Aloy

Collaborations

- *Identification of novel genes involved in DNA repair processes*, Travis Stracker, IRB Barcelona (Barcelona, Spain)
- *Identification of novel substrates for p53.* , Angel R. Nebreda, IRB Barcelona (Barcelona, Spain)
- *Network medicine approaches to Alzheimer´s disease*, Ulrich Stelzl, MPI for Molecular Genetics (Berlin, Germany)
- *Novel strategy for network-based therapeutics*, Modesto Orozco, IRB Barcelona (Barcelona, Spain); José Manuel Mas, Infociencia & Anaxomics Biotech (Barcelona, Spain)
- *Novel ways of assessing protein-DNA interactions*, Anastassis Perrakis, Nederlands Kanker Instituut (Amsterdam, Netherlands)
- *Structural systems biology*. B Oliva, Pompeu Fabra University (Barcelona, Spain); M Madan Babu, LMB-MRC (Cambridge, United Kingdom); Miquel Pons, IRB Barcelona (Barcelona, Spain); J Fernández-Recio, Barcelona Supercomputing Center (BSC) (Barcelona, Spain)

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