Matteo de Rosa

Research experience

2016-ongoing - Researcher
Institute of Biophysics (IBF) – National Research Council, Milano, Italy.
http://users.unimi.it/biolstru/ibf-cnr-lab.html

Actual position. Thanks to the support of two consecutive grants (as PI) I am still working on the project started during my previous postdoc. It aims at dissecting the molecular mechanism underlying gelsolin amyloidosis, a hereditary disease, and at finding novel drugs to inhibit the pathological aggregation of the protein through *in-silico* docking screening.
Moreover, I have been involved in two other projects whose first aim is the development of novel antiviral strategies. Briefly, the first project focuses on the RNA dependent RNA polymerase of Dengue virus, a previously validated pharmacological target. A structure-based approach has been exploited to rationally modify promising compounds and characterize their mechanism of action. The second project aims at identifying molecules interfering with the viral replication machinery of rotavirus or with specific cellular proteins essential for viral replication, but dispensable for cell survival.

2013-2015 - postdoctoral fellow
Structural Biology Unit, Department of Biosciences, University of Milano, Italy
http://users.unimi.it/biolstru/ricagno-lab.html

I was involved in two research projects, both involving the characterization of proteins prone to amyloid aggregation: i) *S. solfataricus* acylphosphatase (Sso AcP). This protein has been largely exploited as model for native-like aggregation. I focused on the structural determinants of Sso AcP aggregation to understand the basic principles of this mechanism. ii) human beta-2-microglobulin (b2m): b2m is responsible for two different amyloidosis: a sporadic and a genetic form of the disease: extensive structural and biophysical studies on this protein have been performed to dissect the determinants of b2m intrinsic amyloidogenicity and understand the role of D76N mutation in the familial form.

In addition, I started to develop an independent line of research focused on the characterization of the human protein gelsolin. Mutations in this protein are responsible for a rare disease, structural analysis of the pathological variants will pave the way for novel therapeutics strategies.

2009-2013 - post-doctoral fellow
Protein–Nucleic Acids Interactions group, Instituto Gulbenkian da Ciença (IGC), Oeiras, Portugal
http://www.igc.gulbenkian.pt/aathanasiadis

2008-2009 - post-doctoral fellow
Macromolecular Crystallography Unit, ITQB, Universidade Nova de Lisboa, Oeiras, Portugal (headed by Prof. Maria A. Carrondo)
http://mx.itqb.unl.pt

During these two postdocs, I was mainly involved in the characterization of proteins able to bind and stabilize the left-handed helical conformation of nucleic acids (Z-DNA). These proteins share high biomedical interest, being either i) defense mechanisms of the host (innate immunity) against viruses or ii) virulence factors to avoid the aforementioned mechanisms. X-ray crystallography and complementary biochemical techniques were mainly used to characterize three proteins belonging to this family: human ADAR1, viral ORF112 and fish PKZ.

Education

Dec 2007 - PhD in Molecular and Cell Biology
Enzymology Lab, Department of Biomolecular Sciences and Biotechnology
Majors: Biochemistry, Enzymology, Structural Biology
Supervisors: Prof. Giuliana Zanetti and Prof. Alessandro Aliverti
Thesis title: Characterization of ferredoxin-NADP+ reductases from pathogenic microorganisms

Several mammalian pathogens (Mycobacteria, Apicomplexa among others) possess plant-like enzymes, absent in the host. Structural and functional characterization of these proteins was the main focus of my thesis as they represent good targets for novel drugs. In addition, screening, validation and characterization of novel inhibitors were performed by different means (structure-based, rational design, screening of peptide libraries, etc).

May 2004 Master (five-year degree) in Biological Sciences
Final grade: 110/110 *cum Laude*
Majors: Biochemistry, Molecular Biology, Biophysics
Thesis title: The catalytic mechanism of M. tuberculosis FprA studied by protein engineering

Grants and Fellowships

2018 Research Grant
Amyloidosis Foundation research grant as main proponent of the project "From protein structure to novel drugs against Agel amyloidosis: a fast and cost-effective route to the development of new therapeutics"
2016-2017 Research Grant
Telethon exploratory grant (GEP15070) awarded by Fondazione Telethon as Principal Investigator of the project "Characterization of recently identified gelsolin mutants responsible for a novel renal amyloidosis".
2011-2013 Individual Fellowship
Postdoctoral fellowship (SFRH/BPD/71629/2010) awarded by FCT (Portuguese Federation for Science and Technology) to work at the Gulbenkian Institute for Science, Portugal
2010 Individual Fellowship
Research grant in memory of Professor Bruno Curti awarded by SIB (Italian society of Biochemistry)
2009 Individual Fellowship
FEBS short-term fellowship (by Federation of European Biochemical Societies) to visit ITQB, New University of Lisbon, Oeiras, Portugal.

Conference communication

M. de Rosa "Structural bases of gelsolin amyloidosis" Invited speaker at XVth International Symposium on Amyloidosis, Kumamoto, Japan. March 2018

M. de Rosa "From protein structure to novel drugs against gelsolin amyloidosis" Invited speaker at Convention Scientifica Telethon, Riva del Garda, Italy. March 2017

F. Boni, , A. Barbiroli, M. Bolognesi, S. Ricagno.and M. de Rosa (poster) "Characterization of a recently identified gelsolin variant responsible for a novel renal amyloidosis" Proteine2016, Bologna, Italy

F. Boni, M. de Rosa*, A. Barbiroli, M. Bolognesi and S. Ricagno. Characterization of recently identified Gelsolin variants leading to novel renal amyloidosis. 6th european conference "Chemistry in the life sciences". Lisbon, Portugal, 2015 (poster,)

M de Rosa, F. Bemporad, S. Pellegrino, F. Chiti, M. Bolognesi, S. Ricagno. Edge strand engineering prevents native-like aggregation in Sulfolobus solfataricus acylphosphatase. Proteine 2014, Padova, Italy, March 2014 (poster)

M. de Rosa (oral communication) Structural basis for Z-DNA binding and stabilization by the zebrafish Z-DNA dependent protein kinase (PKZ). Protein physics: structure, dynamics and function. Bressanone, Italy, february 2014

M. de Rosa, D. de Sanctis, A.L. Rosario, M. Archer, A. Rich, A. Athanasiadis and M.A. Carrondo. (poster, best poster award) The Crystal Structure of a Junction Between Two Z-DNA Helices. SIB 2011, Catania, Italy

M. de Rosa, A. Athanasiadis, D. de Sanctis, A. L. Rosario, M. Archer, A. Rich, and M. A. Carrondo The structure of conformational junctions in DNA and genomic instability ECM-26 2010, Darmstad, Germany (poster).

M. de Rosa, A. Athanasiadis, D. de Sanctis, A. L. Rosario, M. Archer, A. Rich, and M. A. Carrondo. The Crystal Structure of a Junction Between Two Z-DNA Helices. "Getting the most from the ESRF MX beamlines" 2010. Grenoble, France (oral and poster)

M de Rosa, C D'Angiò, A Pennati, A Aliverti and G Zanetti. (selected for oral communication) The unusual NADP+ oxidase activity of flavoenzymes belonging to the adrenodoxin reductase family. Trends in Enzymology 2006 Como, Italy

M de Rosa, C D'Angiò, A Pennati, A Aliverti and G Zanetti. The unusual NADP+ oxidase activity of flavoenzymes belonging to the adrenodoxin reductase family. Proteine 2006 Novara, Italy (poster)

M de Rosa, C D'Angiò, A Pennati, A Aliverti and G Zanetti. A new catalytic activity of the NADPH-ferredoxin reductuse of M. tuberculosis. SIB 2005, Riccione, Italy (poster)

Publications on peer-reviewed journals:

Le Marchand T, **de Rosa M**, Salvi N, Sala BM, Andreas LB, Barbet-Massin E, Sormanni P, Barbiroli A, Porcari R, Sousa Mota C, de Sanctis D, Bolognesi M, Emsley L, Bellotti V, Blackledge M, Camilloni C, Pintacuda G, Ricagno S. Conformational dynamics in crystals reveal the molecular bases for D76N beta-2 microglobulin aggregation propensity. Nat Commun. 2018 Apr 25;9(1):1658. doi: 10.1038/s41467-018-04078-y.

Eichwald C, De Lorenzo G, Schraner EM, Papa G, Bollati M, Swuec P, **de Rosa M**, Milani M, Mastrangelo E, Ackermann M, Burrone OR, Arnoldi F. Identification of a small molecule that compromises the structural integrity of viroplasms and rotavirus double-layered particles. J Virol. 2017 Nov 15. pii: JVI.01943-17. doi: 10.1128/JVI.01943-17.

Bonì F, Milani M, Barbiroli A, Diomede L, Mastrangelo E, **de Rosa M**. Gelsolin pathogenic Gly167Arg mutation promotes domain-swap dimerization of the protein. Hum Mol Genet. 2018 Jan 1;27(1):53-65. doi: 10.1093/hmg/ddx383. PubMed PMID:29069428.

Brambilla V, Martignago D, Goretti D, Cerise M, Somssich M, **de Rosa M**, Galbiati F, Shrestha R, Lazzaro F, Simon R, Fornara F. Antagonistic Transcription Factor Complexes Modulate the Floral Transition in Rice. Plant Cell. 2017 Nov;29(11):2801-2816. doi: 10.1105/tpc.17.00645. Epub 2017 Oct 17. PubMed PMID: 29042404; PubMed Central PMCID: PMC5728136.

de Rosa M, Halabelian L, Barbiroli A, Bolognesi M, Bellotti V, Ricagno S. An Asp to Asn mutation is a toxic trigger in beta-2 microglobulin: structure and biophysics. Amyloid. 2017 Mar;24(sup1):15-16. doi: 10.1080/13506129.2016.1272450. PubMed PMID: 28434301.

Bonì F, Milani M, Porcari R, Barbiroli A, Ricagno S, **de Rosa M**. Molecular basis of a novel renal amyloidosis due to N184K gelsolin variant. Sci Rep. 2016 Sep 16;6:33463. doi: 10.1038/srep33463. PubMed PMID: 27633054; PubMed Central PMCID: PMC5025852.

Camilloni C, Sala BM, Sormanni P, Porcari R, Corazza A, **De Rosa M**, Zanini S, Barbiroli A, Esposito G, Bolognesi M, Bellotti V, Vendruscolo M, Ricagno S. Rational design of mutations that change the aggregation rate of a protein while

maintaining its native structure and stability. Sci Rep. 2016 May 6;6:25559. doi:10.1038/srep25559. PubMed PMID: 27150430; PubMed Central PMCID: PMC4858664.

de Rosa M, Barbiroli A, Giorgetti S, Mangione PP, Bolognesi M, Ricagno S. Decoding the Structural Bases of D76N ß2-Microglobulin High Amyloidogenicity through Crystallography and Asn-Scan Mutagenesis. PLoS One. 2015 Dec 1;10(12):e0144061. doi: 10.1371/journal.pone.0144061. eCollection 2015. PubMed PMID: 26625273; PubMed Central PMCID: PMC4666650.

de Rosa M, Bemporad F, Pellegrino S, Chiti F, Bolognesi M, Ricagno S. Edge strand engineering prevents native-like aggregation in Sulfolobus solfataricus acylphosphatase. FEBS J. 2014 Sep;281(18):4072-84. doi: 10.1111/febs.12861. Epub 2014 Jun 13. PubMed PMID: 24893801.

Nogly P, Matias PM, **de Rosa M**, Castro R, Santos H, Neves AR, Archer M. High-resolution structure of an atypical α-phosphoglucomutase related to eukaryotic phosphomannomutases. Acta Crystallogr D Biol Crystallogr. 2013 Oct;69(Pt 10):2008-16. doi: 10.1107/S0907444913017046. Epub 2013 Sep 20. PubMed PMID: 24100319.

de Rosa M, Zacarias S, Athanasiadis A. Structural basis for Z-DNA binding andstabilization by the zebrafish Z-DNA dependent protein kinase PKZ. Nucleic Acids Res. 2013 Nov;41(21):9924-33. doi: 10.1093/nar/gkt743. Epub 2013 Aug 23. PubMedPMID: 23975196; PubMed Central PMCID: PMC3834819.

Tomé AR, Kuś K, Correia S, Paulo LM, Zacarias S, **de Rosa M**, Figueiredo D,Parkhouse RM, Athanasiadis A. Crystal structure of a poxvirus-like zalpha domain from cyprinid herpesvirus 3. J Virol. 2013 Apr;87(7):3998-4004. doi: 10.1128/JVI.03116-12. Epub 2013 Jan 30. PubMed PMID: 23365431; PubMed Central PMCID: PMC3624203.

Nogly P, Castro R, **de Rosa M**, Neves AR, Santos H, Archer M. Production and crystallization of α-phosphoglucomutase from Lactococcus lactis. Acta Crystallogr Sect F Struct Biol Cryst Commun. 2012 Sep 1;68(Pt 9):1113-5. doi:10.1107/S1744309112032629. Epub 2012 Aug 31. Erratum in: Acta Crystallogr Sect F Struct Biol Cryst Commun. 2013 Nov;69(Pt 11):1313. PubMed PMID: 22949208; PubMed Central PMCID: PMC3433211.

Colombo M, **de Rosa M**, Bellotti V, Ricagno S, Bolognesi M. A recurrent D-strand association interface is observed in β-2 microglobulin oligomers. FEBS J. 2012 Mar;279(6):1131-43. doi: 10.1111/j.1742-4658.2012.08510.x. Epub 2012 Feb 23. PubMed PMID: 22289140.

de Rosa M, de Sanctis D, Rosario AL, Archer M, Rich A, Athanasiadis A, Carrondo MA. Crystal structure of a junction between two Z-DNA helices. Proc Natl Acad Sci U S A. 2010 May 18;107(20):9088-92. doi: 10.1073/pnas.1003182107. Epub 2010 May 3. PubMed PMID: 20439751; PubMed Central PMCID: PMC2889044.

Ricagno S, Colombo M, **de Rosa M**, Sangiovanni E, Giorgetti S, Raimondi S, Bellotti V, Bolognesi M. DE loop mutations affect beta2-microglobulin stabilityand amyloid aggregation. Biochem Biophys Res Commun. 2008 Dec 5;377(1):146-50.doi: 10.1016/j.bbrc.2008.09.108. Epub 2008 Oct 1. PubMed PMID: 18835253.

Aliverti A, Pandini V, Pennati A, **de Rosa M**, Zanetti G. Structural and functional diversity of ferredoxin-NADP(+) reductases. Arch Biochem Biophys. 2008 Jun 15;474(2):283-91. doi: 10.1016/j.abb.2008.02.014. Epub 2008 Feb 16. Review. PubMed PMID: 18307973.

de Rosa M, Pennati A, Pandini V, Monzani E, Zanetti G, Aliverti A. Enzymatic oxidation of NADP+ to its 4-oxo derivative is a side-reaction displayed only by the adrenodoxin reductase type of ferredoxin-NADP+ reductases. FEBS J. 2007 Aug;274(15):3998-4007. Epub 2007 Jul 16. PubMed PMID: 17635583.

Ricagno S, **de Rosa M**, Aliverti A, Zanetti G, Bolognesi M. The crystal structure of FdxA, a 7Fe ferredoxin from Mycobacterium smegmatis. Biochem Biophys Res Commun. 2007 Aug 17;360(1):97-102. Epub 2007 Jun 12. Erratum in: Biochem Biophys Res Commun. 2008 Jan 25;365(4):890. PubMed PMID: 17577575.