

Stefano Capaldi

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Stefano Capaldi graduated from the University of Milan on 27/10/2000 in Pharmaceutical Chemistry and Technology. He was awarded the Philosophiae Doctor degree in Agroindustrial Biotechnology by the University of Verona on 30/03/2004 with the thesis entitled "The Three Dimensional Crystal Structure Of Carp Fish Egg Lectin" (supervisor Prof. Hugo L. Monaco). From January 2005 to February 2007 he held a Post Doc fellowship at the Biocrystallography Laboratory of the University of Verona with the research project: "Structural studies on hydrophobic molecule - binding proteins". Since March 2008 he has been a research fellow and since April 2022 an associate professor in Molecular Biology at the Department of Biotechnology, University of Verona.

Employment history

Apr 2022 – present: Associate Professor in Molecular Biology, Department of Biotechnology, University of Verona, Italy.

Mar 2008 – Mar 2022: Assistant Professor in Molecular Biology, Department of Biotechnology, University of Verona, Italy.

Jan 2005 – Feb 2008: post doc at the Biocrystallography laboratory, University of Verona, Italy.

Education & Qualifications:

Jan 2001 – Jan 2004: PhD in Agro-industrial Biotechnology, University of Verona, Italy.
(Supervisor Prof. Hugo L. Monaco).

Oct 1994 – Oct 2000: Master Degree in Pharmaceutical Chemistry and Technology. University of Milan, Italy.

10 Apr 2017: National Scientific Qualification for Associate Professor in Molecular Biology, (05/E2, BIO/11).

Main Research activities and results

Structural studies of proteins involved in the transport of hydrophobic molecules

Stefano Capaldi began his research activity during the master thesis with the characterization of a protein belonging to the Fatty-acid Binding Proteins (FABPs) family involved in the transport of hydrophobic molecules and bile acids. During his PhD, and subsequently as post-doc in Verona, he continued the study of this class of proteins, solving different structures of protein-ligand complexes and contributing to the definition of the binding specificity and the physiological function of some of them.

Structural studies of fungal lectins with anticancer properties

During his research activity in the group of Prof. Monaco, he contributed to the structural characterization of lectins obtained from various natural sources (one of which was the subject of his doctoral thesis). His activity in this field has led to the resolution of the structure and the

characterization of the binding properties of various lectins with interesting antiproliferative and anticancer properties extracted from various species of edible fungi.

Structural studies of proteins involved in the processes of apoptosis or cell proliferation

Over the years he has also dealt with the structural characterization of some proteins involved in cell proliferation processes, in particular a protein that binds the insulin-like growth factor 1 (IGFBP1) and a protein (SOUL) involved in the regulation of the apoptotic cascade through the interaction with the well-known antiapoptotic factor Bcl-XL.

Structural studies of membrane proteins

While he was visiting scientist at the MPC (Membrane protein crystallization) group at Imperial College London, he worked on some projects about the structural characterization of membrane proteins. In particular, he contributed to the determination of the structure of the eukaryotic transporter UapA. At the same time, as part of a project in collaboration with Prof. PS. Chae, he contributed to the characterization of innovative detergents developed for the study of membrane proteins.

Structural and functional characterization of GPCR receptors and other proteins involved in neurological and neurodegenerative diseases

In recent years he focused on proteins involved in pathological processes affecting the nervous system and neurodegenerative diseases. He undertook the characterization of a G-protein-coupled receptor involved in the onset of Alzheimer's disease (GPR3) and the study of another GPCR crucial for myelin degeneration in multiple sclerosis (the latter the subject of two research funded by FISM - Italian Multiple Sclerosis Foundation, in which the former participates as a member and in the latter as unit coordinator. In addition, he has participated and continues to work on several projects aimed at characterizing the processes of formation of amyloid aggregates by intrinsically disordered proteins (IDPs) including α -synuclein and Tau protein.

Development of innovative diagnostic methods for the identification of amyloid aggregates in biological samples

He actively collaborates with the group of Prof. Zanusso of the Department of Neuroscience of Verona in the development of diagnostic methods for the detection of the presence of amyloid aggregates in biological samples, and in particular in the nasal mucosa, by means of RT-QuIC (real-time quaking-induced conversion) assays. In particular, he is responsible for the optimization of protocols for the expression and purification of engineered recombinant proteins used as substrates for aggregation assays.

Bibliometric indexes

- Total number of publications: 51
- H index: 21 (source Scopus)
- Total number of citations: 1521 (source Scopus)
- Orcid iD: 0000-0003-4632-8100
- Structures deposited in the Protein Data Bank (PDB): 59

Grants

1) Research Project call 2018 Grant (grant 2018/R/21, PI prof. L. Trincavelli)
Fondazione Italiana Sclerosi Multipla (FISM)
235K Euro

01/02/2019-31/04/2022

Title: Crystal structure and functional characterization of the GPR17 receptor, a novel pharmacological target for remyelination therapy in multiple sclerosis

Role on Project: Coordinator of Research Unit

2)Joint Projects 2019 (JPVR19S9PT)

University of Verona

20K Euro

01/12/2020-30/11/2021

Title: investigation of cyanobacteria in Lessinia caves: capturing the light in near-dark environments

Role on Project: PI

Individual research grants:

- Dec 2017: Individual Funding of Basic Research Activities from MIUR (amount € 3000).
- Cooperint 2008 – Junior Research Program, Mobility grant from the University of Verona (3600 Euro).
- Cooperint 2014 – Staff Mobility Program, Mobility grant from the University of Verona (4500 Euro).

Participation in Research Projects

- 2003-2006: Co-worker in the FIRB project n. RBNE03B8KK “Metodologie e tecnologie innovative per la farmaceutica”, coordinator Prof. Monaco.
- 2008-2010: Co-worker in the project: Structural and functional characterization of humanprostaglandin D synthase, grant Fondazione Cariverona 2008 to H-L. Monaco.
- 2011-2014: participant in the project: Verona Nanomedicine Initiative, Fondazione Carioverona.
- 2016-2020: participant in the ERC Starting Grant 2015 SOLENALGAE- 679814 to M. Ballottari.
- 2019-2022: participant in the project: “Development and validation of a novel molecular assay for alpha-synuclein in patients with Parkinson disease and other alpha-synucleinopathies”. Fondazione Cariverona - Bando Ricerca Scientifica di Eccellenza 2018, coordinatore Prof. Zanusso.

Visiting scientist experiences

Nov 06 – Jan 07: Universidad Nacional de Cordoba (Argentina), Glycobiology laboratory (led by Dr. J.A. Curtino).

Grant: Scientific Cooperation Italy-Argentina 2006-2007, Italian Ministry of Foreign Affairs.

May 10 – Aug 10: MPC (Membrane Protein Crystallization) Group (led by Dr. B.Byrne), Imperial College, London (UK).

Grant: Cooperint 2008, University of Verona.

May 15 – Aug 15: MPC (Membrane Protein Crystallization) Group (led by Dr. B.Byrne), Imperial College, London (UK).

Grant: Cooperint 2014, University of Verona.

Teaching

- Molecular Biology (6 CFU), Degree in Bioinformatics, University of Verona.

- Laboratory of Molecular Biology (2 CFU lectures + 4 CFU practical), Degree in Bioinformatics, University of Verona.

Full List of Publications (* corresponding author)

- Bettin I, Brattini M, Kachoie EA, **Capaldi S**, Thalappil MA, Bernardi P, Ferrarini I, Fuhrmann G, Mariotto S, Butturini E. Extracellular Vesicles based STAT3 delivery as innovative therapeutic approach to restore STAT3 signaling deficiency. *N Biotechnol*. 2024 Sep 25;82:43-53.
- Leo G, Leone P, Ataie Kachoie E, Tolomeo M, Galluccio M, Indiveri C, Barile M, **Capaldi S***. Structural insights into the bifunctional enzyme human FAD synthase. *Structure*. 2024 Jul 11;32(7):953-965.e5.
- Sardar S, Caferri R, Camargo FVA, **Capaldi S**, Ghezzi A, Dall'Osto L, D'Andrea C, Cerullo G, Bassi R. Site-Directed Mutagenesis of the Chlorophyll-Binding Sites Modulates Excited-State Lifetime and Chlorophyll-Xanthophyll Energy Transfer in the Monomeric Light-Harvesting Complex CP29. *J Phys Chem Lett*. 2024 Mar 21;15(11):3149-3158.
- Parolini F, Ataie Kachoie E, Leo G, Civiero L, Bubacco L, Arrigoni G, Munari F, Assfalg M, D'Onofrio M, **Capaldi S***. Site-Specific Ubiquitination of Tau Amyloids Promoted by the E3 Ligase CHIP. *Angew Chem Int Ed Engl*. 2023 Dec 11;62(50):e202310230.
- Tira R, Viola G, Barracchia CG, Parolini F, Munari F, **Capaldi S**, Assfalg M, D'Onofrio M. Espresso Coffee Mitigates the Aggregation and Condensation of Alzheimer's Associated Tau Protein. *J Agric Food Chem*. 2023 Aug 2;71(30):11429-11441.
- Daniele S, Saporiti S, **Capaldi S**, Pietrobono D, Russo L, Guerrini U, Laurenzi T, Ataie Kachoie E, Palazzolo L, Russo V, Abbracchio MP, Eberini I, Trincavelli ML. Functional Heterodimerization between the G Protein-Coupled Receptor GPR17 and the Chemokine Receptors 2 and 4: New Evidence. *Int J Mol Sci*. 2022 Dec 23;24(1):261.
- Viola G, Barracchia CG, Tira R, Parolini F, Leo G, Bellanda M, Munari F, **Capaldi S**, D'Onofrio M, Assfalg M. New Paradigm for Nano-Bio Interactions: Multimolecular Assembly of a Prototypical Disordered Protein with Ultrasmall Nanoparticles. *Nano Lett*. 2022 Nov 23;22(22):8875-8882.
- Bongianni M, Catalan M, Perra D, Fontana E, Janes F, Bertolotti C, Sacchetto L, **Capaldi S**, Tagliapietra M, Polverino P, Tommasini V, Bellavita G, Kachoie EA, Baruca R, Bernardini A, Valente M, Fiorini M, Bronzato E, Tamburin S, Bertolasi L, Brozzetti L, Cecchini MP, Gigli G, Monaco S, Manganotti P, Zanusso G. Olfactory swab sampling optimization for α -synuclein aggregate detection in patients with Parkinson's disease. *Transl Neurodegener*. 2022 Jul 28;11(1):37.
- Barracchia CG, Parolini F, Volpe A, Gori D, Munari F, **Capaldi S**, D'Onofrio M, Assfalg M. Camouflaged Fluorescent Silica Nanoparticles Target Aggregates and Condensates of the Amyloidogenic Protein Tau. *Bioconj Chem*. 2022 Jul 20;33(7):1261-1268. doi: 10.1021/acs.bioconjchem.2c00168.
- Sardar S, Caferri R, Camargo FVA, Pamos Serrano J, Ghezzi A, **Capaldi S**, Dall'Osto L, Bassi R, D'Andrea C, Cerullo G.J. Molecular mechanisms of light harvesting in the minor antenna CP29 in near-native membrane lipidic environment. *Chem Phys*. 2022 May 28;156(20):205101.

- Munari F, Mollica L, Valente C, Parolini F, Kachoe EA, Arrigoni G, D'Onofrio M, **Capaldi S***, Assfalg M. Structural Basis for Chaperone-Independent Ubiquitination of Tau Protein by Its E3 Ligase CHIP. *Angew Chem Int Ed Engl*. 2022 Apr 4;61(15):e202112374.
- Parolini F, Tira R, Barracchia CG, Munari F, **Capaldi S**, D'Onofrio M, Assfalg M. Ubiquitination of Alzheimer's-related tau protein affects liquid-liquid phase separation in a site- and cofactor-dependent manner. *Int J Biol Macromol*. 2022 Mar 15;201:173-181.
- Perra D, Bongianni M, Novi G, Janes F, Bessi V, **Capaldi S**, Sacchetto L, Tagliapietra M, Schenone G, Morbelli S, Fiorini M, Cattaruzza T, Mazzon G, Orrù CD, Catalan M, Polverino P, Bernardini A, Pellitteri G, Valente M, Bertolotti C, Nacmias B, Maggiore G, Cavallaro T, Manganotti P, Gigli G, Monaco S, Nobili F, Zanusso G. Alpha-synuclein seeds in olfactory mucosa and cerebrospinal fluid of patients with dementia with Lewy bodies. *Brain Commun*. 2021 Mar 22;3(2):fcab045.
- Stefani A, Iranzo A, Holzknecht E, Perra D, Bongianni M, Gaig C, Heim B, Serradell M, Sacchetto L, Garrido A, **Capaldi S**, Sánchez-Gómez A, Cecchini MP, Mariotto S, Ferrari S, Fiorini M, Schmutzhard J, Cocchiara P, Vilaseca I, Brozzetti L, Monaco S, Jose Marti M, Seppi K, Tolosa E, Santamaria J, Högl B, Poewe W, Zanusso G; SINBAR (Sleep Innsbruck Barcelona) group. Alpha-synuclein seeds in olfactory mucosa of patients with isolated REM sleep behaviour disorder. *Brain*. 2021 May 7;144(4):1118-1126.
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- Fiorini M, Iselle G, Perra D, Bongianni M, **Capaldi S**, Sacchetto L, Ferrari S, Mombello A, Vascellari S, Testi S, Monaco S, Zanusso G. High Diagnostic Accuracy of RT-QuIC Assay in a Prospective Study of Patients with Suspected sCJD. *Int J Mol Sci*. 2020 Jan 30;21(3):880.
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- Perduca M, Destefanis L, Bovi M, Galliano M, Munari F, Assfalg M, Ferrari F, Monaco HL, **Capaldi S***. Structure and properties of the oyster mushroom (*Pleurotus ostreatus*) lectin. *Glycobiology*. 2020 Jul 16;30(8):550-562.
- Bongianni M, Ladogana A, **Capaldi S**, Klotz S, Baiardi S, Cagnin A, Perra D, Fiorini M, Poggi A, Legname G, Cattaruzza T, Janes F, Tabaton M, Ghetti B, Monaco S, Kovacs GG, Parchi P, Pocchiari M, Zanusso G. α -Synuclein RT-QuIC assay in cerebrospinal fluid of patients with dementia with Lewy bodies. *Ann Clin Transl Neurol*. 2019 Oct;6(10):2120-2126.
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- Sadaf A, Mortensen JS, **Capaldi S**, Tikhonova E, Hariharan P, de Castro Ribeiro O, Loland CJ, Guan L, Byrne B, Chae PS. A Class of Rigid Linker-bearing Glucosides for Membrane Protein Structural Study. *Chem Sci*. 2016 Mar 1;7(3):1933-1939.
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- **Capaldi S**, Faggion B, Carrizo M.E., Destefanis L, Gonzalez M.C., Perduca M, Bovi M, Galliano M, Monaco H.L. Three-dimensional structure and ligand-binding site of carp fishellectin (FEL). *Acta Crystallogr D Biol Crystallogr*. 2015 May;71(Pt 5):1123-35.
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- **Capaldi S**, Guariento M, Perduca M, Di Pietro SM, Santomé JA, Monaco HL. Crystal structure of axolotl (*Ambystoma mexicanum*) liver bile acid-binding protein bound to cholic

and oleic acid. *Proteins*. 2006 Jul 1;64(1):79-88.

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