

UNIVERSITÀ DEGLI STUDI DI MILANO

Procedura di selezione per la chiamata a professore di II fascia da ricoprire ai sensi dell'art. 18, comma 1 e 4, della Legge n. 240/2010 per il settore concorsuale 05/E2 - *Biologia Molecolare*, (settore scientifico-disciplinare BIO/11 - *Biologia Molecolare*) presso il Dipartimento di *Dipartimento di Biotecnologie Mediche e Medicina Traslazionale* - Codice concorso 5432

Matteo De March

CURRICULUM VITAE

(N.B. IL CURRICULUM NON DEVE ECCEDERE LE 30 PAGINE E DEVE CONTENERE GLI ELEMENTI CHE IL CANDIDATO RITIENE UTILI AI FINI DELLA VALUTAZIONE.

LE VOCI INSERITE NEL FACSIMILE SONO A TITOLO PURAMENTE ESEMPLIFICATIVO E POSSONO ESSERE SOSTITUITE, MODIFICATE O INTEGRATE)

INFORMAZIONI PERSONALI (NON INSERIRE INDIRIZZO PRIVATO E TELEFONO FISSO O CELLULARE)

COGNOME	DE MARCH
NOME	MATTEO
DATA DI NASCITA	[14.07.1983]

TITOLI

TITOLO DI STUDIO

(indicare la Laurea conseguita inserendo titolo, Ateneo, data di conseguimento, ecc.)

MSc in Biology - Functional Genomics (LS 6 - September 2007).
University of Trieste (Supervisor: G. Manfioletti). Molecular Biology and Epigenetics.

TITOLO DI DOTTORE DI RICERCA O EQUIVALENTI, OVVERO, PER I SETTORI INTERESSATI, DEL DIPLOMA DI SPECIALIZZAZIONE MEDICA O EQUIVALENTE, CONSEGUITO IN ITALIA O ALL'ESTERO

(inserire titolo, ente, data di conseguimento, ecc.)

PhD in Chemical and Pharmaceutical Sciences (2008 - 2011).
University of Trieste, Department of Chemical Sciences (Supervisor: S. Geremia). Molecular and Structural Biology (obtained on 05.04.2011).

ALTRI TITOLI CONSEGUITI

(inserire titolo, ente, data di conseguimento, ecc.)

- **Associate Professor** (Nov 2023). Applied Physics, FIS/07 (ASN).
- **Associate Professor** (Feb 2023). Molecular Biology, BIO/11 (ASN).
- **Assistant Professor** (Feb 2023). Biochemistry and Molecular Biology (University of Nova Gorica).
- **Biologist** (2020). ONB - Ordine Nazionale dei Biologi.
- **Professional Counsellor** (2020). Master in Counselling (2017-2020) CNI School Udine.

POSIZIONI RICOPERTE

POSIZIONE ATTUALE

- **Assistant Professor at UNG University of Nova Gorica**
Molecular Biology, Biochemistry, Structural Biology.
- **Guest Scientist at Chemistry Institute KI Ljubljana**
Biochemistry, Biophysics.

POSIZIONI PRECEDENTI

- **Visiting Scientist at SciLife Laboratories Stockholm - CryoEM facility (Feb 2023).**
Structural Biology.
- **Senior Research Associate at UNG University of Nova Gorica (2021 - 2023).**
Molecular Biology, Molecular & Structural Immunology. Antibody technology for oncology.
- **Visiting Scientist at ICGB Trieste - Biotechnology Transfer Unit (March - August 2021).**
Molecular Biology of SARS-CoV2.
- **Researcher at ELETTRA, Structural Biology Laboratory (2012 - 2020).**
Molecular and Structural Biology of DNA replication and repair proteins.
- **Research associate at University of Trieste, Department of Chemical Sciences (2011 - 2012).**
Biochemistry, Structural Biology, Biophysics.
- **Visiting fellow at National Hellenic Research Foundation (June 2008).**
Structural Biology.

ATTIVITÀ DIDATTICA

INSEGNAMENTI E MODULI

(inserire periodo [gg/mm/aa inizio e fine], anno accademico, corso laurea, numero di ore frontali, eventuale CFU)

- **2017-2020: Structural Biology** for the Master degree in Functional Genomics (University of Trieste).
Series
of Seminars (20h) insight the course of “Espressione Genica” (Prof. G. Manfioletti).
- **2021-2023: Laboratory of Biochemistry & Bioinformatics** for the Bachelor degree in Environmental Science (University of Nova Gorica). 30h - first semester - practical course. Role: lecturer.
- **2023-2024: Toxicology and Carcinogenesis** for the Bachelor degree in Environmental Science (University of Nova Gorica). 30h - second semester. Role: lecturer.
- **2023-2024: Structural and Computational Biology** for the PhD in Molecular Genetics and Biotechnology (Joined University of Nova Gorica & ICGB). 30h - second semester. Role: lecturer.

ATTIVITÀ DI DIDATTICA INTEGRATIVA E DI SERVIZIO AGLI STUDENTI

ATTIVITÀ DI RELATORE DI ELABORATI DI LAUREA, DI TESI DI LAUREA MAGISTRALE, DI TESI DI DOTTORATO E DI TESI DI SPECIALIZZAZIONE

(inserire numero, anno accademico, ateneo, corso laurea, ecc.)

- Alessandro D'Angelo (2008). Master thesis in Functional Genomics at University of Trieste - IT.
- Nikolas Capra (2015). Master thesis in Functional Genomics at University of Trieste - IT.
- Veronica Del Soglio (2016). Master thesis in Biotechnology, University of Turin - IT.
- Sebastiano Baldassar (2019). Master thesis in Industrial Biotechnologies, University of Bologna - IT.
- Aymane ElFellah (2023). MSc in Biotechnology, Join University of Padova and Nova Gorica - IT/SLO.
- Urša Strancar (2023-2026). PhD-MR in Molecular Biomedicine University of Nova Gorica - SLO.
- Alejandro Pikoulas (2023-2024). BSc in Biology, Join University of Udine and Nova Gorica - IT/SLO

ATTIVITÀ DI TUTORATO DEGLI STUDENTI DI CORSI DI LAUREA E DI LAUREA MAGISTRALE E DI TUTORATO DI DOTTORANDI DI RICERCA

(inserire anno accademico, corso laurea, ecc.)

- Juliano Morimoto Borges (2013-2014). CNPq exchange student at Elettra Synchrotrone Trieste - IT.
- Ilaria Peschiera (2013). Master thesis in Functional Genomics University of Trieste - IT.

- Raheem Ullah (2017-2018). ICTP-TRIL PhD Fellow at Elettra Synchrotrone Trieste - IT.
- Majid Ali Shah Akhun (2018). PhD at NIBGE Faisalabad - PK.
- Shafiq Anjas (2023). MSc Internship (Bioinformatics from Remote) University of Nova Gorica - SLO.
- Yossma Waheed (2023). MSc Internship (Bioinformatics from Remote) University of Nova Gorica - SLO.

SEMINARI/CONGRESSI/SCUOLE

(inserire titolo del seminario, luogo, data, ecc.)

- "Recent Advances in Macromolecular Crystallography Workshop" and "Meeting of the Italian and Spanish Crystallographic Associations". Copanello di Staletti, 23-28 September 2007. **Selected Talk**
- "8° Workshop on Pharmaco Bio-metallics". Ravenna, 24-26 October 2008. **Selected Talk**
- "X-Ray Synchrotron Light Source (SILS)". Trieste, 7-18 September 2009. **Poster**
- "XXVIII National Congress of Inorganic Chemistry". Trieste, 13-16 September 2010. **Poster**
- "EMBL-CCP4 European School for Macromolecular Crystallography". EMBL Hamburg, 19-26 November 2012. **Poster**
- "The 6th European Conference of Chemistry towards Biology". Trieste, 10-13 September 2013. **Poster**
- "Synchrotron radiation techniques and nanotechnologies: a synergic approach to life sciences and medicine". ICTP Advanced School, iThembaLab - CapeTown, South Africa. 11-21 November 2013. **Tutor in protein crystallography**
- "4th NEUROBIOLOGY SUMMER SCHOOL". SISSA Trieste, 14-25 July 2014. **Tutor in protein crystallography**
- "Advance school of synchrotron radiation to visualize macromolecules". ICTP Trieste, 15-20 December 2014. **Lecturer in protein crystallography**
- "5th NEURON TECHNOLOGY SUMMER SCHOOL". SISSA Trieste, 8-19 June 2015. **Lecturer in protein crystallography**
- "School on synchrotron radiation". Graz University of Technology & Montan University Leoben. Elettra Trieste. 8-10 June 2015. **Lecturer in protein crystallography**
- "XLIV Annual Meeting of the AIC". Vercelli, September 14-18, 2015. **Selected Talk**
- "Synchrotron radiation in chemistry and life sciences" University of Padua, DSV. June 17 2016. **Invited Speaker**
- "Molecular biophysics" University of Florence. March 15 2018. **Invited Speaker**
- "School on synchrotron radiation". Graz University of Technology. Elettra Trieste. 18-21 June 2018. **Lecturer and tutor in protein crystallography**
- "LELS seminar". UNG University of Nova Gorica. Nova Gorica, Slovenia. 05 May 2021. **Invited Speaker**
- "19th P4EU meeting: Protein preparation and characterization". Trieste, Italy. 22-23 May 2023.
- "2th MOSBRI Conference: Molecular-scale Biophysics". Zaragoza, Spain. 05-07 June 2023. **Poster**
- "Supercomputing Day". Ljubljana, Slovenia. 16 Oct 2023. **Invited Speaker**

ATTIVITÀ DI RICERCA SCIENTIFICA

PUBBLICAZIONI SCIENTIFICHE

(per ciascuna pubblicazione indicare: nomi degli autori, titolo completo, casa editrice, data e luogo di pubblicazione, codice ISBN, ISSN, DOI o altro equivalente)

Scopus: 55340029900. ORCID: 0000-0002-3447-957X

1. De March M, D'Ercole C, Veggiani G, Oloketuyi S, Svirgelj R, de Marco A. Biological applications of synthetic binders isolated from a conceptually new Adhiron library. *Accepted in Biomolecules (IF 5)*.
2. De March M*, Hikey N, Geremia S. Analysis of the crystal structure of a parallel three-stranded coiled coil. *Proteins*, 2023, 91(9), 10254-1260.
3. Spinello A, Lapenta F, De March M*. The avidin-theophylline complex: a structural and computational study. *Proteins*, 2023, June 15, HPUB.
4. Neumair J, D'Ercole C, De March M, Elsner M, Seidel M, de Marco A. Macroporous Epoxy-Based Monoliths Functionalized with Anti-CD63 Nanobodies for Effective Isolation of Extracellular Vesicles in Urine. *Int J Mol Sci*, 2023, 24(7), 6131.
5. De March M*, Terdoslavich M, Polez S, Guarnaccia C, Poggianella M, Marcello A, Skoko N, de Marco A. Expression of SARS CoV-2 in ExpiCHO cells. *Prot and Purif. J.* 2022, 194, 106071.
6. De March M, Onesti S, De Biasio A. Reply to: "Does PCNA diffusion on DNA follow a rotation-coupled translation mechanism?". *Nat. Commun.*, 2020, 11, 4999.

7. Ullah R, Shehzad A, Shah MA, **De March M**, Ismat F, Iqbal M, Onesti S, Rahman M, McPherson MJ. C-Terminal Domain of the Human Zinc Transporter hZnT8 Is Structurally Indistinguishable from Its Disease Risk Variant (R325W). *Int J Mol Sci.*, 2020, 21(3).
8. Lazzari E, El-Halawany M, **De March M**, Valentino F, Cantatore F, Migliore C, Onesti S, Meroni G. Analysis of the Zn-binding domains of TRIM32, the E3 ubiquitin ligase mutated in Limb Girdle Muscular Dystrophy 2H. *Cells*, 2019.
9. **De March M**, Barrera-Vilarmau S, Crespan E, Mentegari E, Merino N., Gonzalez-Magana A., Romano-Moreno M, Maga G, Crehuet R, Onesti S, Blanco FJ, De Biasio A. p15PAF binding to PCNA modulates the DNA sliding surface. *Nucleic Acids Res.* 2018, 46, 9816-9828.
10. Napolitano LMR, Marchesi A, Rodriguez A, **De March M**, Onesti S, Laio A, Torre V. The permeation mechanism of organic cations through a CNG mimic channel. *PLoS Comput. Biol.* 2018, 14, e1006295.
11. Ali Shah M, Ullah R, **De March M**, Salahuddin Shaha M, Ismata F, Habib M, Iqbala M, Onesti S, Rahman M. Overexpression and characterization of the 100K protein of Fowl adenovirus-4 as an antiviral target. *Virus Research*, 2017. [Epub ahead of print]
12. **De March M**, De Biasio A. The dark side of the ring: role of the DNA sliding surface of PCNA. *Crit Rev Biochem Mol Biol.* 2017, 663-673.
13. **De March M**, Carroni M, Medagli B, Krastanova I, Taylor IA, Amenitsch H, Araki H, Pisani FM, Patwardhan A, Onesti S. New insights into the GINS complex explain the controversy between existing structural models. *Sci Rep.* 2017, 7, 40188.
14. **De March M**, Merino N, Barrera-Vilarmau S, Crehuet R, Onesti S, Blanco FJ, De Biasio A. Structural basis of human PCNA sliding on DNA. *Nat Commun.* 2017, 8, 13935.
15. Mojumdar A, **De March M**, Marino F, Onesti S. The Human RecQ4 Helicase Contains a Functional RecQ C-terminal Region (RQC) That Is Essential for Activity. *J Biol Chem.* 2017, 292, 4176-4184.
16. **De March M**, Brancatelli G, Demitri N, De Zorzi R, Hickey N, Geremia S. A general exit strategy of monoheme cytochromes c and c2 in electron transfer complexes? *IUBMB Life.* 2015, 67, 694-700.
17. Napolitano LM, Bisha I, **De March M**, Marchesi A, Arcangeletti M, Demitri N, Mazzolini M, Rodriguez A, Magistrato A, Onesti S, Laio A, Torre V. A structural, functional, and computational analysis suggests pore flexibility as the base for the poor selectivity of CNG channels. *Proc Natl Acad Sci U S A.* 2015, 112, E3619-28.
18. Benedetti F, Berti F, Campaner P, Fanfoni L, Demitri N, Olajuyigbe FM, **De March M**, Geremia S. Impact of Stereochemistry on Ligand Binding: X-ray Crystallographic Analysis of an Epoxide-Based HIV Protease Inhibitor. *ACS Med Chem Lett.* 2014, 5, 968-72.
19. **De March M**, Demitri N, De Zorzi R, Casini A, Gabbiani C, Guerri A, Messori L, Geremia S. Nitrate as a probe of cytochrome c surface: crystallographic identification of crucial "hot spots" for protein-protein recognition. Impact of Stereochemistry on Ligand Binding: X-ray Crystallographic Analysis of an Epoxide-Based HIV Protease Inhibitor. *J Inorg Biochem.* 2014, 135, 58-67.
20. **De March M**, Di Rocco G, Hickey N, Geremia S. High-resolution crystal structure of the recombinant diheme cytochrome c from *Shewanella baltica* (OS155). *J Biomol Struct Dyn.* 2015, 33, 395-403.
21. **De March M**, Demitri N, Geremia S, Hickey N, Randaccio L. Trans and cis influences and effects in cobalamins and in their simple models. *J Inorg Biochem.* 2012, 116, 215-27.

SUBMITTED/ONGOING

(per ciascuna pubblicazione indicare: nomi degli autori, titolo completo, casa editrice, data e luogo di pubblicazione, codice ISBN, ISSN, DOI o altro equivalente)

1. De March M*, Medagli B, Krastanova I, De Biasio A, Onesti S. Structure of Cdc45 from *M. jannashii*. Submitted to *Int. J. of Biol. Macromol (IF 8)*.
2. De March M*, Borisek J, Medagli B, Krastanova I, Capra N, Magistrato A, Onesti S. Structural bases of the Archaeal 3'-5' DNA resection. In preparation for *ACS Catalysis (IF 11)*.
3. Yossma W, Mojumdar A, Shafiq A, de Marco A, De March M*. Can the yet unknown fork remodeler HLTF be consider a double agent? Submitted to *BBA - Gene Regulation Mechanisms (IF 5)*.
4. Borisek J, Mojumdar A, Yossma W, D'Ercole C, Lapenta F, de Marco A, De March M*. MD simulations the RecA1/A2 ATP-ase domain suggest HLTF as a new chromatin remodeler. In preparation for *Structure (IF 6)*.
5. Yossma W, Shafiq A, Gerdol M, Borisek J, De March M*. Regulation of ZRANB3 in Cancer. *Work in progress*.
- 6-10. Others as middle name collaborator

ORGANIZZAZIONE, DIREZIONE E COORDINAMENTO DI CENTRI O GRUPPI DI RICERCA NAZIONALI E INTERNAZIONALI O PARTECIPAZIONE AGLI STESSI

(per ciascuna voce inserire anno, ruolo, gruppo di ricerca, ecc.)

- 2022-2026: ARRS Slovenian Program n. P3-0428 - Comparative Oncology (Member - Investigator - PI A. de Marco)
- 2018-2022: Grant AIRC n. IG20778 - Role of RecQ helicases (Investigator - PI S. Onesti).
- 2010-2013: Grant AIRC n. IG10646 - Role of CMG helicase (Investigator - PI S. Onesti).
- 2016 - 2019: Grant AFM Telethon n. 177446 - Role of TRIM32 in ubiquitination (Investigator - PI S. Onesti).
- 2008-2009: Fellowship from C.I.R.C.M.S.B. of Bari (PI).
- 2009-2010: Grant from Regione Autonoma FVG (Investigator).
- 2010-2012: Fellowship from University Federico II and CNR-IBB of Naples (PI).

COLLABORAZIONI

- A. De Biasio, Group leader in Structural Biology, KAUST University.
- M. Carroni, Head of the Cryo-EM facility, SciLIFE Lab Stockholm.
- M. Podobnik, Head of Biological Department, Chemistry Institute Ljubljana
- H. Amenitsch, Head of the AustroSAXS beamline, Elettra Synchrotron.
- A. Magistrato, Group Leader in Computational Biology, SISSA Trieste.
- J. Borisek, Researcher in Computational Chemistry, Chemistry Institute Ljubljana.
- A. Spinello, Assistant Professor in Computational Chemistry, University of Palermo.
- M. Gerdol, Associate Professor in Genetics, University of Trieste.
- A. Mojumdar, Assistant Professor in Biochemistry, University of Victoria.
- M. Marinozzi, Full Professor in Medicinal Chemistry, University of Perugia

ATTIVITÀ QUALI LA DIREZIONE O LA PARTECIPAZIONE A COMITATI EDITORIALI DI RIVISTE SCIENTIFICHE

(per ciascuna voce inserire anno, ruolo, rivista scientifica, ecc.)

- **Academic Editor** for PLOS ONE (ISSN: 1932-6203)
- **Member of Topical Advisory Board** for Int. J. of Molecular Sciences MDPI (ISSN: 1422-0067)

ATTIVITÀ GESTIONALI, ORGANIZZATIVE E DI SERVIZIO

INCARICHI DI GESTIONE E AD IMPEGNI ASSUNTI IN ORGANI COLLEGIALI E COMMISSIONI, PRESSO RILEVANTI ENTI PUBBLICI E PRIVATI E ORGANIZZAZIONI SCIENTIFICHE E CULTURALI, OVVERO PRESSO L'ATENEIO O ALTRI ATENEI

(inserire incarico/impegno, ente, data, ecc.)

- **Member of Board of Directors INSTRUCT-Ceric for Slovenia.** Consortium for Structural Biology and Biophysics (2023-ongoing). Organizational activity, conferences, schools, seminars, grants.
- **Coorganizer of Elettra Trieste NEXT.** Structural and Computational Biology section - AlphaFold, FoldIT (2015-2019). Street Science/Public Speaking.

Brief Bio-Sketch and Scientific Project @ Università degli Studi di Milano

My previous research was primarily conducted at Elettra Synchrotron and focused on **molecular and structural biology of DNA helicases and replication factors involved in genome stability and cancer**. Few accomplishments that I would like to highlight are:

- in De March et al., Nat. Commun., 2017, 8, 13935 we showed that the human sliding clamp PCNA recognizes DNA through a double patch of basic residues within the ring channel, arranged in a right-hand spiral that matches the pitch of B-DNA. We proposed that PCNA slides by tracking the DNA backbone via a cogwheel mechanism explaining its implication for the assembly of the replication-competent PCNA-pol δ holoenzyme during Translesion Synthesis. This was the first structure of Human PCNA with DNA and the first crystallographic structure of a dynamic protein-DNA complex (De March et al., Nat. Commun., 2020, 11, 1-3). Moreover, we showed that p15PAF, an oncogenic intrinsically disordered protein that regulates DNA replication and lesion bypass by interacting with the human sliding clamp PCNA, reduces the available sliding surfaces of PCNA fastening the DNA to the clamp during synthesis by the replicative pol δ (De March et al., Nucleic Acid. Res., 2018, 46, 9816-9828);

- in Mojumdar et al., J. Biol. Chem., 2017, 292, 4176-4184 our bioinformatic and experimental analyses showed that human RecQ4 helicase, a paralogue of RecQ1, Bloom, Werner and RecQ5 involved in three distinct genetic disorders, contains the RecQ C-terminal region critical for the enzyme activity.

In 2021, I moved to University of Nova Gorica and had research periods as visiting/guest scientist at ICGEB in Trieste, Chemistry Institute in Ljubljana and SciLife Laboratories in Stockholm. The group at UNG has strong **expertise with recombinant antibody technology applied to biomedicine, immunology and cancer**. Although I'm here collaborating with Prof. A. de Marco developing new strategies for the improvement of the selection, characterization and application of new biomedical highly-selective scaffolds against important known biomarkers, **I successfully started in parallel a new research line aimed at unravelling the role of two not yet characterized SNF2 ATPases and chromatin remodellers involved in cancer**.

Stress conditions such as, DNA lesions, un-replicated or harmful-replicated sequences and nucleotide depletion, can destabilize the correct cell replication and can consequently favor tumorigenesis (Kitao et al. 2018). To escape such consequences our body has evolved multiple DNA damage repair pathways, such as the DNA damage tolerance (DDT) (Branzei et al. 2016) and, in particular, the replication fork reversal (RFR) (Berti et al. 2020). In order to maintain fork structure and prevent excessive degradation by nucleases at stalled forks, the activity of the Helicase-Like Transcription Factor (HLTF) and Zn finger RAN Binding protein 3 (ZRANB3) is critical (Poole et al. 2017). However, not much is known yet about these two proteins. Mainly, HLTF-deficient cells are vulnerable to replication stress and instability (Dhont et al. 2016). Similarly, defects in ZRANB3 function cause genome instability and hyper-sensitivity to DNA damaging agents (Cortez et al. 2019) and that specific mutations lead to cancer (Lawrence et al. 2014). HLTF-deficient cells also exhibit reduced double-strand break (DSB) formation and increased replication-stressed survivals (Takaoka et al. 2018). ZRANB3 and HLTF seems to be linked to the activity of p53 and the associated translesion polymerase (Hampp et al. 2016).

The aim of my research is to uncover the structural and functional basis of both HLTF and ZRANB3 in the cell through the use a combination of bioinformatic tools (i.e. MD simulations, PPI network, in-silico gene expression profile), structural biology techniques (X-ray crystallography and SAXS, NMR, Cryo-EM), biochemical and cellular assays. Further, in collaboration with A. de Marco and using the newly phage-display library of adhirons recently developed, it will be possible to select new highly-selective immunomolecules recognizing HLTF and/or ZRANB3 mutants as novel biosensors and/or effective target therapies.

Data

03.01.24

Luogo

Belluno