Name employer

University of Pavia, Department of Molecular Medicine

Type of sector Position Academic, Faculty of Medicine, Head of laboratory and lecturer

Main responsibilities

Laboratory and research management, teaching and student supervision

#### PERSONAL INFORMATION

Name and surname Nationality

Hugo de Jonge

Dutch

## WORK EXPERIENCE

Dates (from - to)

## Currently:

Function: Group leader and lecturer, Department of Molecular Medicine, Unit of Immunology and General Pathology, University of Pavia, Italy.

#### August 2021 – 2024

Function: Lecturer and Researcher (RTDB), Department of Molecular Medicine, Unit of Immunology and General Pathology, University of Pavia, Italy.

## February 2016 - 2021

Function: Lecturer and Researcher (RTDA), Department of Molecular Medicine, Unit of Immunology and General Pathology, University of Pavia, Italy.

## *March* 2012 – *January* 2016

Function: Lecturer and post-doctoral researcher, Department of Molecular Medicine, University of Pavia, Italy.

## April 2009 - December 2011

Function: Post-doctoral researcher at the Department of Oncology, Cambridge University, UK.

## November 2005 - January 2009

Function: Post-doctoral researcher at the Department of Endocrinology & Metabolism, Faculty of Biology, Utrecht University, The Netherlands.

## February 2005 - April 2005

Function: Scientific consultant at Purely Proteins Ltd., Cambridge, UK.

## October 2000 - January 2005

Function: PhD student at the Growth Factors Group, Medical Research Council, Cambridge UK, funding provided by Pavia University, Italy.

#### February 2000 - October 2000

Function: Clinical Data Associate at Kendle International Inc., Utrecht, The Netherlands.

## December 1998 - January 2000

Function: Junior scientist at the Integrin Group, Department of Cell Biology, Netherlands Cancer Institute, Amsterdam, The Netherlands.

## **EDUCACTION**

Dates (from - to) Name and type of organisation Principal subjects Specialisation September 1993 – November 1998

Utrecht University

Biology

Molecular Biology and Biochemistry

### LANGUAGE SKILLS

Mother tongue Other languages

Dutch

Fluent in English, intermediate level German and Italian

## RESEARCH INTERESTS

My core research interest is to obtain detailed structural and mechanistic understanding of the ligand-induced and ligand-independent activation of the c-Met tyrosine kinase receptor, a common oncogenic driver in solid tumours. By combining protein engineering, antibody technology, cell biology, and structural biology, I aim at developing inhibitors of tumour growth and metastasis and extended this work through collaboration to target tumour cells with CAR-T and nanoparticles. We also developed potent agonistic molecules for application in regenerative medicine and have an ongoing research collaboration with Boehringer Ingelheim.

My post-doctoral research in The Netherlands focused on two human GPCRs: FSHR and the LHR. I recombinantly expressed and crystallised the extracellular domains and the glycoprotein hormones in yeast and overexpressed the full-length receptor in mammalian HEK293 and BHK cells. Using mutagenesis, cell-based assays and molecular modelling I studied receptor specificity and activation.

- My PhD research in Cambridge focused on the determination of the structure of angiostatin, a strong anti-angiogenic tumour inhibitor. I expressed and purified various recombinant forms consisting of multiple kringle domains and used them for biochemical and biological analysis, protein crystallography and investigation of the interactions with two potential receptors, c-Met and Fo·F1 ATPase, the latter in collaboration with Dr John Walker at the MRC Mitochondrial Biology Unit in Cambridge (UK).
- Before my PhD, I worked for one year at the Integrin research group at the department of Cell Biology of the Netherlands Cancer Institute (NKI) in Amsterdam and studied the interactions between α3β1 integrin and the tetraspanin CD151 and their involvement in renal pathologies and cancer.

#### COLLABORATIONS

I have several ongoing collaborations in Italy, both inside and outside Pavia, and international collaborations with laboratories in France (Lille and Paris), Hong Kong, Germany (Biberach and Braunschweig), and The Netherlands (LUMC Leiden).

#### **SUPERVISION**

Throughout my career in the UK, The Netherlands, and Italy, I have supervised with great dedication and enjoyment more than twenty undergraduate students, one Medical specialisation-school student, three PhD students, and one post-doctoral fellow. I am proud to say that most of my students have continued to pursue a career in science and several are currently in post-doc positions, in Italy and abroad.

**Bachelor students**: Anselmo Canciani (2012/2013, Biologia e Biotecnologie, "Biotech"), Michele Lodato (2013/2014 Biotech), Alessia Rovelli 2016/2017 (Biotech), and Noemi Bellani (2020/2021, Biotech)

Master students: Marta Zanchi (2011/2012, Biotech), Laura Parma (2013/2014, Biotech), Anselmo Canciani (2014/2015, Biotech), Michele Lodato (2015/2016, Biotech), Francesco Brunelli (2017/2018, Medicine and Surgery), Greta Severino (2017/2018, Biotech), Lorenzo Vallino (2018/2019, Biotech), Alessia Rovelli (2018/2019, Biotech), Federico Di Tullio (2019/2020, Medicine and Surgery), Dhruvkumar Soni (2020/2021, Biotech), Silvia Calandra (202/2021, Biotech), Chiara Artale (2021/2022, Biotech), Alessia Scaravonati (2022/2023, Biotech), and four current master students: Bogachan Maden, Gianluca Bandera, Benedetta Cordera, and Melika Alizadehghannad from the Biotechnology course.

**Medical Specialisation-school**: Carlo Ganini (2016/2017, Immunology and General Pathology).

**PhD students**: Giovanni De Nola (2012/2015, Biologia Molecolare e Cellulare), Enrica Bovio (2020/2021, Translational Medicine), and currently Patrick Peleu. External PhD supervisor for Michele Lodato (2020/2024, University of Lille, France). **Erasmus student supervision (external & internal**): Laura Parma (2014, LUMC), Bogachan Maden (2016), Amineh Dadkhah (2017, LUMC), Gamze Aydin (2017, Pavia), Kateryna Len (2017), and Michele Lodato (2017).

## **TEACHING**

Since 2012 I have been organising and teaching laboratory tutorials ("practicals") for the Immunology and General Pathology courses of the 2<sup>nd</sup> year of Harvey Medicine.

- In 2014 I coordinated the medical language and communication course "English language 2" of the 2<sup>nd</sup> year Harvey Medicine course.
- Since 2014 I teach the 1<sup>st</sup> year Medicine pre-term course "Essay writing techniques" to prepare students for their new academic life and possibly new exam formats.
- Since 2015 I teach in the Italian-French Erasmus Intensive course in Oncology in Florence.
- Since 2016 I teach the Precision Medicine course in the 3<sup>rd</sup> year of Harvey Medicine.
- In 2016 and 2017 I taught in the Molecular Pharmacology master course at the Department of Biology and Biotechnology.
  - Since 2023 I am organising and teaching laboratory tutorials for the fifth year Biotechnology students (course Degenerative & Cancer, Roots of Disease III).
  - In 2024 I started teaching part of the 2<sup>nd</sup> year Harvey Medicine General Pathology course.

## **ORGANISATIONAL ROLES**

I am managing a laboratory, all research projects, and are collaborating on different funded research projects with Italian, French, Dutch and German colleagues.

- Since 2012 I am responsible for the organisation of the scientific seminars within the Unit of Immunology and General Pathology.
- In April 2003, I was part of organising the large international congress and celebration of "DNA: 50 years of double helix" that took place in Cambridge. An unforgettable experience.
- I am organising a yearly Stem Cell Medicine course for Medicine and Biotechnology students, taught by Prof. Rio Sugimura from Hong Kong University at Collegio Volta.
- With Dr Marta Bordoni, I have been involved in the "Harvey White Coat ceremony" from its conception in 2017.

#### **FUNDING**

I currently receive funding from national grants PRIN (Progetti di Ricerca di Interesse Nazionale), Immuno-HUB (Immunoterapia: cura e prevenzione di malattie infettive e tumorali), and industry, through collaboration with Boehringer Ingelheim Germany.

## COURSES AND CERTIFICATIONS

EMBO Practical Integrative Structural Biology course, EMBL Hamburg 2019
The macroscopic, microscopic and pathologic anatomy of the mouse, Amsterdam Medical Centre, The Netherlands.

- Teaching Undergraduates in the Biological, Medical and Veterinary Sciences course, Cambridge University, UK.
- Project management and Risk assessment course, Cambridge University, UK.
- Certified for Safe Microbiological Techniques (VMT), Utrecht University.
- Certified for working with open radioactive sources; Health Physics expert level 5B, University of Delft, The Netherlands.
- Health and Safety, first aid, and firefighting courses in the UK and currently in Italy, as a member of the emergency response unit in Golgi-Spallanzani.

# PRESENTATIONS AND POSTERS

Research presentations for the Immuno-HUB in Pisa in 2023 and Milan in 2024. Poster presentation at Diamond Light Source in Oxford in November 2023.

- Poster presentation at DESY in Hamburg in 2019.
- Poster presentation at the 6<sup>th</sup> Annual AriSLA Conference in Milan, October 2016.
- Poster presentation at the National ALS symposium in Naples in November 2015.
- Poster presentation at the 51<sup>st</sup> Annual meeting Studiegroep Eiwitonderzoek in Lunteren in December 2007, The Netherlands.
- Oral presentation at the NIH Glycoprotein Hormone work meeting in Venice in November 2007.
- Oral presentation Science retreat in Kerkrade in October 1999, The Netherlands.
- Oral and poster presentation at the 4<sup>th</sup> Benelux Congress of Zoology on 14-15 November 1997, Utrecht, The Netherlands.

## EDITORIAL & REVIEWING ACTIVITES

Associate editor of Frontiers in Oncology and Frontiers in Molecular Diagnostics and Therapeutics.

*Reviewer* for Frontiers Journal, Oncotarget, Scientific Reports, Antibodies, eLife, Angewandte Chemie, FEBS Letters, Int. J of Hepatology, and several other journals.

## COMMERCIAL ACTIVITIES

Co-founder of Ardis S.r.l., a small biotech company generating antibody-based therapeutics for cancer therapy and providing an paid-for SPR-service. Ardis won first prize in the Life Science category at the "Start Cup Milano-Lombardia 2012" and a prize from the Camera di Commercio in 2013 in support of our R&D activities.

#### **PATENTS**

WO2016116577A1: Met receptor agonist proteins (2016)

WO2016116578A1: multimeric compounds of a kringle domain from HGF (2016)

## LEISURE ACTIVITIES

I am an avid cyclist and enjoy sailing and kayaking. I like drawing, painting, and enjoy designing and printing objects in 3D also to support my teaching activities.

## **PUBLICATIONS**

Peptides inhibiting the assembly of monomeric human 1-lactate dehydrogenase into catalytically active homotetramer decrease the synthesis of lactate in cultured cells. **Protein Science**, 2024; 33.

- A novel HGF/SF receptor (MET) agonist promotes human pluripotent stem cells differentiation into hepatocytes-like cells. **Development Growth and Differentiation**, 2022; 64: p527-536.
- Dimerization of kringle 1 domain from hepatocyte growth factor/scatter factor provides a potent MET receptor agonist. 2022; 5, e202201424: p1-18.
- Side-by-Side Comparison of uPAR-Targeting Optical Imaging Antibodies and Antibody Fragments for Fluorescence-Guided Surgery of Solid Tumors. **Molecular Imaging and Biology**, 2021; 25: p122-132.
- LANCL1 binds abscisic acid and stimulates glucose transport and mitochondrial respiration in muscle cells via the AMPK/PGC-1α/Sirt1 pathway. **Molecular Metabolism**, 2021; 53: p101263.
- Harnessing the hERG1/β1 Integrin Complex via a Novel Bispecific Single-chain Antibody: An Effective Strategy against Solid Cancers. **Molecular Cancer Therapy**, 2021; 20: p1338.
- Anti-Cancer Auto-Antibodies: Roles, Applications and Open Issues. **Cancers** (**Basel**). 2021, 13: p813.
- A multimodal molecular imaging approach targeting uPAR for the diagnosis, resection, and surveillance of urothelial cell carcinoma. **European Journal of Cancer**. 2021, 146: p11-20.
- A Novel HGF/SF Receptor (MET) Agonist Transiently Delays the Disease Progression in an Amyotrophic Lateral Sclerosis Mouse Model by Promoting Neuronal Survival and Dampening the Immune Dysregulation. **International Journal of Molecular Sciences**. 2020, 21 (22): p8542.
- High Resolution Structure of Human Apolipoprotein (a) Kringle IV Type 2: Beyond the Lysine Binding Site. **Journal of Lipid Research** 2020, 61 (12): p1687–96.
- Distinguishing Between Monomeric scFv and Diabody in Solution Using Light and Small Angle X-ray Scattering. **Antibodies** (Basel). 2019, 8: p1-20.
- Generation and characterization of novel recombinant anti-hERG1 scFv antibodies for cancer molecular imaging. **Oncotarget** 2018; 9(79): p34972-34989.
- Ingegnerizzazione di mAb per scopi teraupeutici. Chapter in **Farmacologia generale e molecolare.** 2018, 93-98. ISBN: 8821444368
- Identification of a high affinity binding site for abscisic acid on human lanthionine synthetase component C-like protein 2. **Int J Biochem Cell Biol.** 2018, 97: p52-61.
- SMARCA4 inactivating mutations cause concomitant Coffin-Siris syndrome, microphthalmia and small-cell carcinoma of the ovary hypercalcaemic type. **J Pathology**. 2017, 243(1): p9-15.
- Semi-synthesis of an HGF/SF kringle one (K1) domain scaffold generates a potent in vivo MET receptor agonist. **J. Chem. Sci.** 2015, 6: p2110-2121.

  Growth factors and tumour progression. **Edizioni Medico-Scientifiche**, Pavia. 2013: 42-47.
- Functional differences of invariant and highly conserved residues in the extracellular domain of the glycoprotein hormone receptors. **J Biol Chem.** 2010, 285: p34813-34827.
- Coupling growth-factor engineering with nanotechnology for therapeutic angiogenesis. **Proc Natl Acad Sci USA.** 2010, 107: p13608-13613.
- Studies in zebrafish reveal unusual cellular expression patterns of gonadotropin receptor messenger ribonucleic acids in the testis and unexpected functional differentiation of the gonadotropins. **Endocrinology.** 2010, 151: p2349-2360.
- Molecular cloning and functional characterization of a zebrafish nuclear progesterone receptor. **Biol Reprod.** 2010, 82: p171-181.
- Oestrogen-induced androgen insufficiency results in a reduction of proliferation and differentiation of spermatogonia in the zebrafish testis. **J Endocrinol.** 2009, 202: p287-297.
- Stimulation of cell surface F1-ATPase activity by apolipoprotein A-I inhibits endothelial cell apoptosis and promotes proliferation. **Arterioscler Thromb Vasc Biol.** 2009, 29: p1125-1130.
- Towards the Structure of Plasminogen and its Internal Fragment Angiostatin. de Jonge H. 2005, **Tesi di dottorato in Fisiopatologia Sperimentale XVI ciclo** (anno accademico 2003-2004).

- A new crystal form of the NK1 splice variant of HGF/SF demonstrates extensive hinge movement and suggests that the NK1 dimer originates by domain swapping. **J Mol Biol.** 2002, 319: p283-288.

  The phospholipase C signaling pathway in locust fat body is activated via G(q) and not affected by cAMP. **Insect Biochemistry and Molecular Biology** 1998, 28: p483-
- 490.