



## PERSONAL INFORMATION

**Manuela Viola**

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ORCID: 0000-0002-0634-6390

Date of birth 08/03/1974

Nationality Italian

## POSITION

Associate Professor in Biochemistry (SSD BIO/10) Department of Medicine and Surgery, University of Insubria (D.R. Rep. N. 167/2017 27/02/2017).

## ACADEMIC ROLES & RESPONSIBILITIES

2013-present: member of the scientific committee of SiBA (Library system of the university) (DR Rep. 839/2013 10/07/2013; DR Rep. 653/2016 30/08/2016; DR Rep. 236/2020)

2015-present: commission for distribution of University Research grants (FAR) (DR Rep. 618/2015 17/07/2015; DR Rep. 113/2018 15/02//2018)

2019-2022: Board member of PQA (Presidio per la qualità di Ateneo), quality assurance organism (DR rep. N. 130/2019 27/02/2019)

## WORK EXPERIENCE

31/12/2002-28/03/2017      Researcher in Biochemistry (SSD BIO/10) University of Insubria

1st October 2008 – 30th September 2009      "Visitor researcher" in Dr M. Götte laboratory at the Muenster University (Germany), in the Department of Obstetrics and Gynecology (Klinik und Poliklinik für Frauenheilkunde und Geburtshilfe, director Prof. Dr. L. Kiesel)

DAAD (Deutscher Akademischer Austauschdienst) fellowship for the period March - May 2009

2000-2002      Instructor of Biochemistry and Enzimology, Biological Sciences, University of Pavia

## EDUCATION AND TRAINING

2002      Doctoral Degree in Biochemistry, Department of Biochemistry, section Science, University of Pavia and Genova, Italy. Supervisor prof. M.E. Tira, discussing the thesis "Interactions of Leucine-rich proteoglycans with fibrillar collagens".

2001-2002      Research fellowship in "Role of decorin in platelets function" Department of Biochemistry, section Science.

1998:      M.S. degree in Biological Sciences at the University of Pavia, Italy, Department of Biochemistry, "A. Castellani" section. Sciences, discussing the thesis " A study of the binding between Decorin and collagen type I using CNBr peptides"; mark 108/110.

1993:      High School degree at Liceo Scientifico Statale "A. Avogadro" (Biella)

## PERSONAL SKILLS

Publications 62 publications on Extracellular Matrix (ECM).

h-index (Hirsch index) = 28 (SCOPUS)

Editorial activity editorial board member of Biomolecules

<https://www.mdpi.com/journal/biomolecules/editors>

Conference Committee member of 1st International Electronic Conference on Biomolecules: Natural and Bio-Inspired Therapeutics for Human Diseases - 01/12/2020 - 13/12/2020

Publishing and expert activities: Referee of international journals including "Molecular Cancer Therapeutics" PlosONE, Food and Chemical Toxicology etc.

Editor of the special Issue 2011 "Glycosaminoglycans Metabolism" of International Journal of Biochemistry Research

As expert of the extracellular matrix referee of the projects PRIN 2008 granted by MIUR (Ministry of Education, University and Research) and of VQR 2004-2010 for ANVUR

Prizes Poster award at the "8th International Conference on proteoglycan", 25-29th August 2013 Frankfurt/Main Germany

Languages: English Listening: Upper-Intermediate - B1 / Reading Intermediate B2 / Spoken interaction: Upper-Intermediate - B1 / Spoken production. B2 / Writing: B2

## ADDITIONAL INFORMATION

Scientific societies SIB - Società Italiana Biochimica e Biologia Molecolare – from 2003

2005 member of the organizer committee of the annual National SIB Meeting

SISC - Società Italiana per lo Studio del Connettivo – from 1999

2011 member of the organizer committee of the annual National SISC Meeting

ISMB- International Society for Matrix Biology – from 2015

## Teaching

A.A 2019/2020 -present: professor of chemistry in undergraduate course of Dentistry

AA. 2016-present: Professor of Chemistry and biochemistry in undergraduate course of Obstetrics

A.A. 2011-present: professor of Biochemistry in undergraduate course of Biomedical Laboratory Techniques, School of Medicine, Faculty of Medicine and Surgery; university of Insubria

A.A. 2011-present: professor of Chemistry and Biochemistry in undergraduate course of Cardiocirculatory Physiopathology and Cardiovascular Perfusion and Dental Hygiene, School of Medicine, Faculty of Medicine and Surgery; university of Insubria

A.A. 2017-2018: present: professor of Chemistry and Biochemistry in undergraduate course of Physiotherapy, School of Medicine, Faculty of Medicine and Surgery; university of Insubria

2005-present: tutor of Biomedical Laboratory Techniques students.

2003-2011: professor of Biochemistry in undergraduate course in: Nursing, Cardio circulatory Physiopathology and Cardiovascular Perfusion, Biomedical Laboratory Techniques; Imaging and Radiotherapy techniques; School of Medicine, Faculty of Medicine and Surgery; university of Insubria.

### Research interest:

The main research interest is the metabolism of glycosaminoglycans (GAG), and in particular, hyaluronan (HA) and heparan sulphate (HS) polysaccharides. The synthesis of those two chains are quite different: the first, HA, being polymerized by means of a family of HAS (hyaluronan synthases) on the plasma membrane and immediately extruded in the extracellular matrix; the HS chains, on the contrary, are synthesised in the ER and Golgi on the core protein of specific proteoglycans (PG). The molecular mechanism involved the overexpression of the synthetic enzymes responsible for the HA polymerization, named HASs. Among the 3 HA synthases, HAS1-3, whose genes are located on different chromosomes, and located on the cell membrane in order to produce and extrude the HA, oxLDL doubled the expression of both HAS2 ( $\approx$  30-fold higher of HAS3) and HAS3.

HA and HSPGs, i.e. Syndecans, are altered in their metabolism during inflammation or in cancer. The cytokines alter both HASs expression and syndecans or HS sulfation pattern. In in vitro experiment using inflammatory cytokines and oxidised LDL, we demonstrated that HA metabolism can be altered both in ECs and SMCs, indicating the modifications of EC glycocalyx and SMC ECM as pivotal steps of the disease progression and as potential therapeutic targets. In our study on SMCs using oxidised LDL, we showed that these particles were able to increase the synthesis of HA, in agreement with the in vivo data of the thickening of the intima layer. The entrance of oxLDL in SMC was proved to be effect of the upregulation of the scavenger receptor LOX1 and the effect on HA metabolism was a consequence of ER stress due to oxysterols load.

For what it concern cardiovascular disease, the relationship between the high cholesterol and the onset of pathologies of the vascular system are still largely unknown, even though several data point at a pivotal role of the alteration of the extracellular matrix (ECM) organization ; for this reason, the research is focused the onset the atherosclerotic plaque, in which the glycosaminoglycan (GAG) hyaluronan, HA, is highly increased, causing the arterial wall thickening. The HA increase completely changes the organization of the ECM within the wall layers, the tunica intima, the tunica media, and the tunica adventitia.

Given the effect on HA metabolism and their central role in the onset of CVD, we are interested in the effect of LDL/cholesterol on ECs glycocalyx. During inflammation, both HA and HS syndecans are altered and this new ECM induce an increment of monocytes recruitment and activation.

The last research interest is therefore to investigate the role of PCSK9 since it was published that this protein can interact with HS on the cell membrane, speculating that this GAG could sequestrate PCSK9 having a role in its systemic effect.

Scientific collaborations:

1. – Dr Sherif Ibrahim, PhD, Cancer Biology Research Laboratory Zoology Department, Faculty of Science; Cairo University: Exchange of Researcher “Mobility Grant” with the project “Glycocalyx importance in cellular behaviour”

2 - Dr M. Götte at the University of Muenster (Germany): collaboration regarding the mechanisms of synthesis regulation of the of GAGs HS/HE

3 - Collaboration with Prof. Raspanti (Department of Surgical and Morphological Sciences, University of Insubria) and Prof. Tira (Department of Biochemistry, University of Pavia): study of interactions between molecules of the extracellular matrix with special attention to the effect of PG and GAG on the formation of supramolecular structures of collagens.

4 - Collaboration with Dr. L. Alaniz, of the “Universidad Austral, Argentina.” The collaboration aim is the definition of HA (hyaluronan) molecular size in various diseases (e.g. fibrosis or liver cancer) since it is known that HA has different biological effects depending on its length.

Consento il trattamento e la comunicazione dei miei dati secondo le modalità e le finalità della Legge 675/96.