Curriculum vitae Prof. MANUELA DONALISIO

<u>Personal details</u>

Born in: Savigliano, 04/07/1976 Nationality: Italy Email: manuela.donalisio@unito.it Website: https://www.dscb.unito.it/do/docenti.pl/Show?_id=mdonalis#tab-profilo ORCID ID: 0000-0001-7883-1523 Scopus ID: 11438958700 Researcher ID: AEZ-0214-2022

Educations

- Degree in Biological Sciences at the University of Turin in 2001 (110/110 cum laude)
- Master in Microbiology and Virology in 2005 (70/70 cum laude)
- PhD degree in Experimental Medicine and Therapy in 2014

Professional experiences and current position

- Visiting scientist at Robert Koch Institute in Berlin in 2008
- Internship at clinical laboratory (Microbiological Division) of San Giovanni Battista Hospital of Turin in 2003 and 2004
- Scientific consultant for ROTALACTIS, a start-up biotech company in 2009-2012 for the research and development of a peptide for the prevention of viral infections
- Assistant professor of Microbiology (MED/07) at the University of Turin from 2012 to 2019
- Associate Professor of Microbiology (MED/07) at the Department of Clinical and Biological Sciences at the University of Turin since November 2019
- Member of the Laboratory of Molecular Virology and Antiviral Discovery at Department of Clinical and Biological Sciences of Turin
- International Mobility Coordinator of the Medical School (San Luigi Gonzaga) of the University of Torino.

Teaching activity:

- Professor of Microbiology at the Degree course in Medicine and Surgery S. Luigi Gonzaga since 2013
- Professor of Microbiology at the School of Biotechnology since 2013
- Professor of Microbiology at the School of Nursing Science of University of Turin in Cuneo since 2014
- Professor of Microbiology at the School of Specialization in Hematology of University of Turin since 2021
- Professor of Microbiology at the Master in Environmental Virology of University of Turin in 2022
- Teaching Assistant of Microbiology at the School of Biotechnology of University of Turin from 2001 to 2012.
- Teaching Assistant of Microbiology at the school of Nursing Science of University of Turin since 2001 to 2012.
- Contract Professor of Bacterial Genetics at the Master Degree in Microbiology and Virology from 2006 to 2008
- Contract Professor of Microbiology at the Degree Course of Biological Sciences from 2004 to 2005
- Author of two student books of Medical Microbiology (Publishing Group: Edises) in 2006
- Editorial curator for the seventh Italian edition of the student book "Medical Microbiology" (Publisher: Sherris) in 2021

<u>Research main topics</u>

Her research interests have been focused mainly on virological experimental studies applied to a wide panel of viruses including respiratory viruses - responsible for annual large outbreaks - sexually transmitted viruses, emerging arthropod-transmitted viruses and viruses responsible for gastrointestinal infections. The main research topics are:

- The discovery and development of antiviral molecules and investigation of their mechanism of action and preclinical development
- Studies on virus-cell interactions in order to deepen the knowledge on the viral pathogenesis and to identify new pharmacological targets
- The research and development of innovative formulations based on nanocarriers for the delivery of known antiviral drugs to overcome the challenges associated with antiviral delivery
- Antiviral studies in the fields of Ethnomedicine, Phytomedicine and Nutraceuticals in order to discover bioactive compounds

These multidisciplinary studies were performed in collaboration with chemists, biochemists and biotechnologists of national and international Universities and with pharmaceutical and biotech companies.

<u>Main projects as PI</u>

• Identification and preclinical development of antiviral molecules against respiratory syncytial virus outbreaks

Respiratory syncytial virus (RSV) is the leading cause of respiratory infection in children, often with severe course and high mortality rate in the most fragile subjects such as preterm infants. Therefore, RSV is considered a major social and health problem against which specific antiviral drugs and vaccines are not available. In this context this project proposes the study and preclinical development of compounds effective against RSV thanks to the collaboration of virologists and pharmaceutical chemists. Starting from solid preliminary data, the research of new antiviral molecules takes place through different scientific approaches integrating techniques of virology, pharmaceutical chemistry and structural biology. The objective is the identification of the compounds endowed with greater antiviral efficacy on cell cultures by analyzing two libraries of molecules: the first consisting of known inhibitors against other viruses and the second generated by an analysis computational tool for the identification of RSV RNA polymerase inhibitors. The best molecules will be chemically optimized for their pharmacodynamic and pharmacokinetic properties respecting the principles of sustainability environmental. The mechanism of action of the selected anti-RSV candidates will be identified and formulations synthetized for inhalation administration. A preclinical study on epithelial respiratory tissue models will then be developed by validating antiviral efficacy and biocompatibility. This data will provide a solid foundation for conducting the advancement of the drug towards clinical trials.

The project was funded by Intesa San Paolo in 2023.

• Valacyclovir-loaded nanodroplets for the treatment of HSV-2 infections

Valacyclovir is an approved drug for herpes simplex virus type 2 (HSV-2) infection treatment. Therapy with valacyclovir is hampered due to its poor bioavailability, low retention at the vaginal mucosa, thus requiring high doses and frequent administrations. Nanocarriers have been proposed to overcome the challenges associated with antiviral delivery. This project aims at developing a novel formulation consisting of β -cyclodextrin decorated nanodroplets for valacyclovir topical delivery to improve its antiviral effectiveness. The project will pave the way for the development of a future nanomicrobicide for the HSV-2 infections.

• Investigation of bovine milk components as broad-spectrum antiviral agents.

Solid reports show presence of antiviral substances in human milk, however there is a lack of knowledge in a bovine context. In collaboration with Aarhus University, Denmark the antiviral activity against emerging arthropod-transmitted (ZIKV) and respiratory viruses (RSV, FluV) of bovine milk components is being investigated.

Bibliometry (2004-present)

Number of papers on international journals with IF: 57 H-index (Scopus): 23 Total citations: 1951

10 best publications

1: Arduino I, Calvo J, Rittà M, Cabeza S, Llobera M, Lembo D, Gayà A, **Donalisio M.** Impact of time-temperature combinations on the anti-Cytomegalovirus activity and biological components of human milk. *Pediatr Res.* 2023 Apr 14. doi: 10.1038/s41390-023-02606-1.

2: Milani M, **Donalisio** M, Bonotto RM, Schneider E, Arduino I, Boni F, Lembo D, Marcello A, Mastrangelo E. Combined in silico and in vitro approaches identified the antipsychotic drug lurasidone and the antiviral drug elbasvir as SARS-CoV2 and HCoV-OC43 inhibitors. *Antiviral Res.* 2021 May; 189:105055. doi: 10.1016/j.antiviral.2021.105055.

3: Donalisio M, Argenziano M, Rittà M, Bastiancich C, Civra A, Lembo D, Cavalli R. Acyclovir-loaded sulfobutyl ether-β-cyclodextrin decorated chitosan nanodroplets for the local treatment of HSV-2 infections. *Int J Pharm.* 2020 Sep 25;587:119676. doi: 10.1016/j.ijpharm.2020.119676.

4: Donalisio M, Cirrincione S, Rittà M, Lamberti C, Civra A, Francese R, Tonetto P, Sottemano S, Manfredi M, Lorenzato A, Moro GE, Giribaldi M, Cavallarin L, Giuffrida MG, Bertino E, Coscia A, Lembo D. Extracellular Vesicles in Human Preterm Colostrum Inhibit Infection by Human Cytomegalovirus In Vitro. *Microorganisms*. 2020 Jul 21;8(7):1087. doi: 10.3390/microorganisms8071087.

5: Cagno V, Andreozzi P, D'Alicarnasso M, Jacob Silva P, Mueller M, Galloux M, Le Goffic R, Jones ST, Vallino M, Hodek J, Weber J, Sen S, Janeček ER, Bekdemir A, Sanavio B, Martinelli C, **Donalisio M**, Rameix Welti MA, Eleouet JF, Han Y, Kaiser L, Vukovic L, Tapparel C, Král P, Krol S, Lembo D, Stellacci F. Broadspectrum non-toxic antiviral nanoparticles with a virucidal inhibition mechanism. *Nat Mater.* 2018 Feb;17(2):195-203. doi: 10.1038/nmat5053.

6: Pelliccia M, Andreozzi P, Paulose J, D'Alicarnasso M, Cagno V, **Donalisio M**, Civra A, Broeckel RM, Haese N, Jacob Silva P, Carney RP, Marjomäki V, Streblow DN, Lembo D, Stellacci F, Vitelli V, Krol S. Additives for vaccine storage to improve thermal stability of adenoviruses from hours to months. *Nat Commun.* 2016 Nov 30; 7:13520. doi: 10.1038/ncomms13520.

7: Donalisio M, Quaranta P, Chiuppesi F, Pistello M, Cagno V, Cavalli R, Volante M, Bugatti A, Rusnati M, Ranucci E, Ferruti P, Lembo D. The AGMA1 poly(amidoamine) inhibits the infectivity of herpes simplex virus in cell lines, in human cervicovaginal histocultures, and in vaginally infected mice. *Biomaterials*. 2016 Apr; 85:40-53. doi: 10.1016/j.biomaterials.2016.01.055.

8: Donalisio M, Ranucci E, Cagno V, Civra A, Manfredi A, Cavalli R, Ferruti P, Lembo D. Agmatinecontaining poly(amidoamine)s as a novel class of antiviral macromolecules: structural properties and in vitro evaluation of infectivity inhibition. *Antimicrob Agents Chemother*. 2014 Oct;58(10):6315-9. doi: 10.1128/AAC.03420-14.

9: Donalisio M, Massari S, Argenziano M, Manfroni G, Cagno V, Civra A, Sabatini S, Cecchetti V, Loregian A, Cavalli R, Lembo D, Tabarrini O. Ethyl 1,8-naphthyridone-3-carboxylates downregulate human papillomavirus-16 E6 and E7 oncogene expression. *J Med Chem.* 2014 Jul 10;57(13):5649-63. doi: 10.1021/jm500340h.

10: Donalisio M, Rusnati M, Cagno V, Civra A, Bugatti A, Giuliani A, Pirri G, Volante M, Papotti M, Landolfo S, Lembo D. Inhibition of human respiratory syncytial virus infectivity by a dendrimeric heparan sulfatebinding peptide. *Antimicrob Agents Chemother*. 2012 Oct;56(10):5278-88. doi: 10.1128/AAC.00771-12.

15 more relevant pubblication in the last 5 yrs (2018-2022)

1: Francese R, **Donalisio M**, Rittà M, Capitani F, Mantovani V, Maccari F, Tonetto P, Moro GE, Bertino E, Volpi N, Lembo D. Human milk glycosaminoglycans inhibit cytomegalovirus and respiratory syncytial virus infectivity by impairing cell binding. *Pediatr Res.* 2022 May 5. doi: 10.1038/s41390-022-02091-y.

2: Sureram S, Arduino I, Ueoka R, Rittà M, Francese R, Srivibool R, Darshana D, Piel J, Ruchirawat S, Muratori L, Lembo D, Kittakoop P, **Donalisio M.** The Peptide A-3302-B Isolated from a Marine Bacterium Micromonospora sp. Inhibits HSV-2 Infection by Preventing the Viral Egress from Host Cells. *Int J Mol Sci.* 2022 Jan 15;23(2):947. doi: 10.3390/ijms23020947.

3: Gayà A, Rittà M, Lembo D, Tonetto P, Cresi F, Sottemano S, Bertino E, Moro GE, Calvo J, **Donalisio M.** Analysis of Thermal Sensitivity of Human Cytomegalovirus Assayed in the Conventional Conditions of a Human Milk Bank. *Front Pediatr.* 2021 Jul 27;9:640638. doi: 10.3389/fped.2021.640638.

4: Milani M, **Donalisio** M, Bonotto RM, Schneider E, Arduino I, Boni F, Lembo D, Marcello A, Mastrangelo E. Combined in silico and in vitro approaches identified the antipsychotic drug lurasidone and the antiviral drug elbasvir as SARS-CoV2 and HCoV-OC43 inhibitors. *Antiviral Res.* 2021 May; 189:105055. doi: 10.1016/j.antiviral.2021.105055.

5: Donalisio M, Argenziano M, Rittà M, Bastiancich C, Civra A, Lembo D, Cavalli R. Acyclovir-loaded sulfobutyl ether- β -cyclodextrin decorated chitosan nanodroplets for the local treatment of HSV-2 infections. *Int J Pharm.* 2020 Sep 25;587:119676. doi: 10.1016/j.ijpharm.2020.119676.

6: Donalisio M, Cirrincione S, Rittà M, Lamberti C, Civra A, Francese R, Tonetto P, Sottemano S, Manfredi M, Lorenzato A, Moro GE, Giribaldi M, Cavallarin L, Giuffrida MG, Bertino E, Coscia A, Lembo D. Extracellular Vesicles in Human Preterm Colostrum Inhibit Infection by Human Cytomegalovirus In Vitro. *Microorganisms*. 2020 Jul 21;8(7):1087. doi: 10.3390/microorganisms8071087.

7: Rittà M, Marengo A, Civra A, Lembo D, Cagliero C, Kant K, Lal UR, Rubiolo P, Ghosh M, **Donalisio M.** Antiviral Activity of a Arisaema Tortuosum Leaf Extract and Some of its Constituents against Herpes Simplex Virus Type 2. *Planta Med.* 2020 Mar;86(4):267-275. doi: 10.1055/a-1087-8303.

8: Francese R, Civra A, Rittà M, **Donalisio M**, Argenziano M, Cavalli R, Mougharbel AS, Kortz U, Lembo D. Anti-zika virus activity of polyoxometalates. *Antiviral Res.* 2019 Mar;163:29-33. doi: 10.1016/j.antiviral.2019.01.005.

9: Donalisio M, Rittà M, Francese R, Civra A, Tonetto P, Coscia A, Giribaldi M, Cavallarin L, Moro GE, Bertino E, Lembo D. High Temperature-Short Time Pasteurization Has a Lower Impact on the Antiviral Properties of Human Milk Than Holder Pasteurization. *Front Pediatr.* 2018 Oct 16;6:304. doi: 10.3389/fped.2018.00304.

10: Donalisio M, Rittà M, Tonetto P, Civra A, Coscia A, Giribaldi M, Cavallarin L, Moro GE, Bertino E, Lembo D. Anti-Cytomegalovirus Activity in Human Milk and Colostrum From Mothers of Preterm Infants. *J Pediatr Gastroenterol Nutr*. 2018 Nov;67(5):654-659. doi: 10.1097/MPG.00000000002071..

11: Toujani MM, Rittà M, Civra A, Genovese S, Epifano F, Ghram A, Lembo D, **Donalisio M**. Inhibition of HSV-2 infection by pure compounds from Thymus capitatus extract in vitro. *Phytother Res.* 2018 Aug;32(8):1555-1563. doi: 10.1002/ptr.6084

12: Donalisio M, Leone F, Civra A, Spagnolo R, Ozer O, Lembo D, Cavalli R. Acyclovir-Loaded Chitosan Nanospheres from Nano-Emulsion Templating for the Topical Treatment of Herpesviruses Infections. *Pharmaceutics*. 2018 Apr 10;10(2):46. doi: 10.3390/pharmaceutics10020046.

13: Cagno V, Andreozzi P, D'Alicarnasso M, Jacob Silva P, Mueller M, Galloux M, Le Goffic R, Jones ST, Vallino M, Hodek J, Weber J, Sen S, Janeček ER, Bekdemir A, Sanavio B, Martinelli C, **Donalisio M**, Rameix Welti MA, Eleouet JF, Han Y, Kaiser L, Vukovic L, Tapparel C, Král P, Krol S, Lembo D, Stellacci F. Broadspectrum non-toxic antiviral nanoparticles with a virucidal inhibition mechanism. *Nat Mater.* 2018 Feb;17(2):195-203. doi: 10.1038/nmat5053.

14: Donalisio M, Cagno V, Civra A, Gibellini D, Musumeci G, Rittà M, Ghosh M, Lembo D. The traditional use of Vachellia nilotica for sexually transmitted diseases is substantiated by the antiviral activity of its bark extract against sexually transmitted viruses. *J Ethnopharmacol.* 2018 Mar 1;213:403-408. doi: 10.1016/j.jep.2017.11.039.

15: Lembo D, **Donalisio M**, Civra A, Argenziano M, Cavalli R. Nanomedicine formulations for the delivery of antiviral drugs: a promising solution for the treatment of viral infections. *Expert Opin Drug Deliv.* 2018 Jan;15(1):93-114. doi: 10.1080/17425247.2017.1360863.

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