Barbara Azzimonti

Curriculum vitae

PERSONAL DATA

BORN IN NOVARA

RESIDENT IN NOVARA

MAIL BARBARA.AZZIMONTI@MED.UNIUPO.IT

PHONE +39 0321 660870

MOBILE +39 347 5704862

SKYPE BABSMICRO

BIO AND EDUCATION

2008: Confirmation as Research assistant in Microbiology and clinical Microbiology (MED/07), Medical School, University of Piemonte Orientale (UPO), Novara;

2004: Research assistant in Microbiology and clinical Microbiology (MED/07), Medical School, UPO;

2003: Winner of a Research assistant position in Microbiology and clinical Microbiology, Medical School, UPO;

2003: Specialization in Clinic Pathology, UPO;

2003: Qualification to the profession of Biologist at the University of Milan, Italy;

1996: Degree in Biology, University of Milan;

Baccalaureate at the Liceo Scientifico A. Antonelli Novara.

ACADEMIC CAREER

Since 2011 Head of the Laboratory of Applied Microbiology (Center for the study of autoimmune and allergic diseases, CAAD), Department of Health Sciences, School of Medicine, UPO

Since 2004 University Researcher, SSD MED / 07 (Microbiology and Clinical Microbiology), UPO

2004 Fixed-term research contract at the Molecular Virology Laboratory (Prof. Gariglio M.), UPO

2001-2002 "Visiting scientist" at the Cancer Virology Laboratory (Prof. TommasinoM.), Deutsches Krebsforchungzentrum (DKFZ), Heidelberg, Germany

1999-2003 Research fellow, UPO

1997-1998 Fellow, UPO

1996-2011 Research activity at the Molecular Virology Laboratory (Prof. Gariglio M.), UPO

1996 Graduated from the Institute of General Pathology (Prof. Cairo G), University of Milan

1994-1996 Thesis internship at the Institute of General Pathology (Prof. Cairo G), University of Milan

ACADEMIC POSITION

From ay 2020-2021: Member of the Council of the Interdepartmental Library of Medicine, UPO

From ay 2020-2021: Secretary of the Board of the Degree Course in Biotechnology, UPO

Ay 2020-2021: Participating Member of the PhD School in "Food Health and Longevity", UPO

Ay 2019-2020: Member of the Academic Board of the PhD School in "Food Health and Longevity", UPO

2013-2018: Member of the teaching staff of the PhD School in "Medical Sciences and Biotechnologies", UPO

From ay 2019-2020: Coordinator of the Integrated Course: "Aetiopathogenesis of diseases"; Three-years Degree Course of Dental Hygiene, UPO

From ay 2019-2020: Member of the Board, School of Specialization in Clinical Pathology and Clinical Biochemistry

From ay 2014-2015: Coordinator of the Integrated Course "Fundamentals of Medical Immunology and Microbiology"; Three-years degree course in Biotechnology.

Since 2016: Member of the Board, School of Specialization in Hospital Pharmacy (Department of Pharmaceutical Sciences, DSF)

Since 2005: Member of the Academic Board for the Admission Exams for the Degree Courses in Medicine and Surgery, Biotechnology and Health Professions

Since 2005: Member of Graduate Commissions for Courses in Medicine and Surgery, Medical Biotechnology, Biotechnology, Biomedical Laboratory Technician, Dental Hygiene

Member of the Boards of the Degree Courses in Biotechnology, Biomedical Laboratory Technician, Radiologist Technician, Physiotherapy and Dental Hygiene

SCIENTIFIC POSITION

From November 2020: *Member of the Editorial Board* of "Journal of Cancer Metastasis and Treatment" (OAE Publishing Inc)

From October 2020: *Academic Editor* for "BioMed Research International" (Hindawi Publisher)

From September 2020: *Evaluator of FISR projects* (Special Integrative Fund for Research), established at the Ministry of Education, University and Research (MIUR)

2014: *Evaluator of SIR projects* (Scientific Independence of young Researchers) on behalf of MIUR

2013: *Evaluator of PRIN 2012 Projects* on behalf of MIUR

Since January 2017: *Member of the Editorial Board* of "EC Microbiology" (E-Cronicon)

Since 2017: *Member of the Management Committee* for European Cooperation in Science and Technology (COST Action: CellFit CA16119, "In vitro 3-D total cell guidance and fitness")

Since 2015: *REPRISE Official Referee*, established at the Ministry of Education, University and Research (MIUR)

Since 2011: *Researcher accredited for ANVUR* (VQR 2015-2019, 2011-2014, 2004-2010)

She is also an *ad hoc* scientific Reviewer for the international journals "Molecules", "Emergency Medicine, Trauma & Surgical Care", "Biotechnology Journal", "Journal of Applied Biomaterials & Functional Materials", "Functional Foods", "Critical Review in tissue engineering "

MAIN FIELDS OF INTEREST

1. **Role of probiotics in non-melanoma skin cancer (NMSC)**
2. **Probiotics, microbiota and metabolome**
3. **Role of microbiota and vitamin D in oropharyngeal cancer**
4. **Analysis of risk factors for oral autoimmune precancerous lesions and oropharyngeal tumors**
5. **Human papillomaviruses and DNA damage**
6. **Use of 3D models for the study of epithelial pathologies with microbial involvement**
7. **Development of strategies for the prevention and control of infectious risk induced by multi-resistant bacteria**

CURRENT ISSUES OF RESEARCH

1. **Role of probiotics in non-melanoma skin cancer (NMSC).** Research has recently focused on the role of the microbiota in a number of diseases affecting the skin or other organs. What is well established is that its deregulation promotes various skin disorders, such as psoriasis and atopic dermatitis. To date, little is known about the composition of the skin microbiota, its mediators and their role in the genesis, progression and response to therapy of NMSC. What is emerging is how they present a greater prevalence of *Staphylococcus aureus, Streptococcus pyogenes, Pseudomonas aeruginosa*, Human papillomaviruses belonging to the beta genus such as the 38 genotype, Epstein Barr virus, Malassezia or some Candida spp., which can contribute to the induction of a state of a chronic inflammation and the genesis of epithelial cancer. Among the bacterial species, the contribution of *S. aureus* appears to be prevalent. In this context, specific probiotics, such as *Lacticaseibacillus rhamnosus GG*, *Lactobacillus johnsonii NCC 533* and Bifidobacteria spp., seem to play a selective protective role. Based on the evidence obtained, we we are evaluating the effect of

secretomes produced by selected probiotics, characterized with Maldi-TOF technology, on the pathogen *S. aureus,* by means of culturomic and molecular analyzes.

2. Probiotics, microbiota and metabolome. The existence of beneficial interactions between the host and its microbiota is essential for the proper functioning of the organism, since alterations in its microflora can contribute to the development of many diseases. In this context, probiotics are able to favor the restoration and / or maintenance of a microbial balance, exerting a substantial health promoting effect.

Based on this knowledge, in collaboration with the Magnetic Resonance Center (CERM) of Florence, we evaluated, through a metabolomic approach, the modulation of the intestinal microflora following specific probiotic treatment, analyzing the serum and urinary metabolic profiles of healthy subjects.

Probiotic treatment is able to profoundly influence the urinary metabolic profiles of volunteers; despite it doesnt' significantly alter their individual phenotypes, it reduces metabolic differences between individuals.

This analysis has allowed us to lay the foundations for carrying out the same investigation by applying it to a category of immunosuppressed patients characterized by a high predisposition to the development of NMSC.

3. Role of the microbiota and vitamin D in oropharyngeal cancer. Emerging literature is revealing the fundamental involvement of the microbiota in determining the health or disease status of different human niches and that of vitamin D in extra-skeletal regions. Much of the impact of the oral microbiota and vitamin D on oropharyngeal squamous cell carcinogenesis is still largely unknown.

An in-depth analysis of the scientific literature revealed significant differences in the quantity and variety of oral microbial species of patients with squamous cell tumor of the oropharynx (OPSCC); in particular, mainly Human papillomaviruses at high risk of transformation, *Fusobacterium nucleatum, Porphyromonas gingivalis, Pseudomonas aeruginosa* and Candida spp. seem to be highly represented. Regarding vitamin D, it is able to prevent and fight the infections promoted by the pathogens identified above, thus confirming its homeostatic function on the microbiota balance. However, its antimicrobial and antitumor actions, well described for the intestine, have not yet been fully documented for the oropharynx.

The mechanisms by which vitamin D and selected probiotic strains can affect oral pathogens implicated in the inflammatory processes leading to the development of OPSCC are currently under study.

4. Risk factor analysis of oral autoimmune precancerous lesions and tumors of the oropharynx. Oral lichen planus is an autoimmune precancerous disease for which a unique and globally recognized classification criterion has not yet been identified. In fact, the histopathological and clinical findings

are often discordant; for this reason, patients at high risk of neoplastic progression are often not recognized correctly.

The purpose of the study is to propose a new classification hypothesis, devised by dividing the lesions into low and high grade on the basis of the different tissue expression of some parameters known for their correlation with the disease.

Much research has been conducted over the past decade to improve the diagnosis, therapy and prognosis of oropharyngeal squamous cell carcinomas (OP-SCC). Since they arise in an area rich in lymphoids, while intense lymphocytic infiltration has been related to a better prognosis, a presumed function of TREM-1 in the progression and worse prognosis of this type of HPV related tumor has been hypothesized.

5. Human papillomaviruses and DNA damage. Although there are many epigenetic alterations in the papillomavirus (HPV) genome and its cell host in infection-induced carcinogenesis, and although chromatin plays a crucial role in HPV-induced carcinogenesis, little is known of the mechanisms adopted by this virus in the induction of chromatin remodeling and of the molecular actors underlying these changes. The project, carried out in collaboration with the Molecular Biology Laboratory of the Swiss Federal Institute of Technology (ETH) in Zurich, and the Dermatology Unit - University Hospital of Novara, aimed at i) gaining an in-depth understanding of the interactions between HPV and host DNA damage sensors; ii) understand how HPV reprograms infected cells and how these modifications participate in the multiple aspects of the virus life cycle. To achieve these objectives, a three-dimensional (3D) epithelial co-culture model was developed and used, made with human primary keratinocytes expressing HPV oncoproteins E6 / E7 at high risk of transformation and HPV positive keratinocytes deriving from cancerous anogenital lesions.

6. Use of 3D models for the study of epithelial pathologies with microbial involvement. The incidence of diseases with epithelial involvement is constantly increasing in the world. Despite advances in the therapeutic field, the prognosis for some of them is still poor or in any case still associated with a reduced quality of life. One of the most important reasons for the failure of traditional drug therapies seems to be represented by the use of preclinical models that are not always adequate (immunocompromised animals, two-dimensional cell cultures). Improved isolation protocols and culture conditions have enabled the development of various three-dimensional (3D) *in vitro* culture systems, which, despite their promising premises and cutting-edge results, still lack the complexity typical of *in vivo* conditions. Four fundamental conditions are required to develop new preclinical predictive models: i) the possibility for healthy and pathological epithelial cells to grow in a three-dimensional context; ii) the presence of components of the Extra Cellular Matrix (ECM) iii) the availability of primary cells derived from the patient. While the importance of using 3D models

that take into account cell-cell and cell-matrix interactions has been established, the use of cells entirely derived from the patient opens the door to the development of truly personalized therapeutic treatments. In this regard, one of the most promising preclinical models is represented by the cutaneous equivalents, structurally and functionally similar to the *in vivo* epithelia, in which the keratinocytes stratify on a dermal support and completely differentiate into squamous epithelia in about 2 weeks through the production of specific cytokeratins. The implementation of these models is an essential tool for understanding the stages of progression of epithelial pathologies and laying the foundations for the development of personalized therapies.

7. Development of strategies for the prevention and control of infectious risk induced by multi-resistant bacteria. In recent decades, there has been a progressive increase in morbidity and mortality due to multi-resistant germs (MDR). The general purpose of the research is to identify alternative strategies to antibiotics able to i) prevent infections promoted by the pathogenic bacteria defined "ESKAPE", such as *E. coli, S. aureus, K. pneumoniae, A. baumannii and P. aeruginosa* and, ii) cause their death and / or iii) prevent their hyperproliferation, through the use of quantitative assays (count of Colony Forming Units, CFU; bacterial viability, XTT and live / dead), morphological (Microscopy Scanning Electronics, SEM), direct and indirect cytocompatibility assays in 2D and 3D models (primary human keratinocyte cells, fibroblasts, osteoblasts), viability assays (MTT), measurement of reactive oxygen species and nitric oxide (ROS and NOS), pro-inflammatory cytokines (TNFα, TGFβ, IL1β, -6, -8) and apoptosis (annexin V and caspases 3 and 8).

CURRENT FUNDED PROJECTS

From 01-07-2019 to 31-12-2021. Funding "FAR 2017", UNIVERSITY RESEARCH FUNDS" (UPO) on a project entitled "Contribution of the oral microbiota and vitamin D in the development of cardiovascular diseases in patients with head and neck tumors". Resolutions 3.4 and 6.4.1 Department of Health Sciences (UPO) 04-06-2019. **Role: PI**

From 01-05-2020 to 31-07-2020. Funding from "FASTMED ITALIA SRL" on a project entitled "Evaluation of the biocidal activity of COMVIR, non-woven fabric for medical use". **Role: PI**

From 01-11-2020: Funding from "PROBIOTICAL RESEARCH SRL" on a project entitled: "" Impact of a selected blend of probiotics and vitamin D on head and neck tumorigenesis: an integrated approach ". **Role: PI**

From 01-03-2019: Funding from "PROBIOTICAL RESEARCH SRL" on a project entitled: "Characterization of microbiota, microbiome and metabolome of control and immunocompromised patients with NMSC before and after supplementation with probiotics". **Role: PI**

TOP FIVE PAPERS

1. Squarzanti DF, Zavattaro E, Pizzimenti S, Amoruso A, Savoia P and **Azzimonti B**. Non-Melanoma. Skin Cancer: news from microbiota research. *Critical reviews in Microbiology* **2020,** doi: 10.1080/1040841X.2020.1794792.
2. Squarzanti DF, Sorrentino R, Landini MM, Chiesa A, Pinato S, Rocchio F, Mattii M, Penengo L, **Azzimonti B**. Human papillomavirus type 16 E6 and E7 oncoproteins interact with the nuclear p53-binding protein 1 in an in vitro reconstructed 3D epithelium: new insights for the virus-induced DNA damage response. *Virol J.* **2018** Nov 16;15(1):176. doi: 10.1186/s12985-018-1086-4. PubMed PMID: 30445982; PubMed Central PMCID: PMC6240266.
3. **Azzimonti B**, Zavattaro E, Provasi M, Vidali M, Conca A, Catalano E, Rimondini L, Colombo E, Valente G. Intense Foxp3+ CD25+ regulatory T-cell infiltration is associated with high-grade cutaneous squamous cell carcinoma and counterbalanced by CD8+/Foxp3+ CD25+ ratio. *Br J Dermatol*. **2015** Jan;172(1):64-73. doi: 10.1111/bjd.13172.
4. **Azzimonti B**, Cochis A, Beyrouthy ME, Iriti M, Uberti F, Sorrentino R, Landini MM, Rimondini L, Varoni EM. Essential Oil from Berries of Lebanese Juniperus excelsa M. Bieb Displays Similar Antibacterial Activity to Chlorhexidine but Higher Cytocompatibility with Human Oral Primary Cells. *Molecules*. **2015** May 21;20(5):9344-57. doi: 10.3390/molecules20059344.
5. **Azzimonti B,** Dell'oste V, Borgogna C, Mondini M, Gugliesi F, De Andrea M, Chiorino G, Scatolini M, Ghimenti C, Landolfo S, Gariglio M. The epithelial-mesenchymal transition induced by keratinocyte growth conditions is overcome by E6 and E7 from HPV16, but not HPV8 and HPV38: characterization of global transcription profiles. *Virology*. **2009** Jun 5;388(2):260-9. doi:10.1016/j.virol.2009.03.033.

During her career, Dr. Barbara Azzimonti has published in peer-reviewed international scientific journals, for a total of over 1419 citations and an h-index = 23 on Google Scholar and 1040 citations and an h-index = 21 on Scopus.

PUBMED: https://www.ncbi.nlm.nih.gov/pubmed/?term=Azzimonti+B

GOOGLE SCHOLAR https://scholar.google.it/citations?user=KWBMMLgAAAAJ&hl=it

SCOPUS https://www.scopus.com/search/form.uri?display=basic

AWARDS

1. Special prize "Biotec Notopharm", II EDITION - START CUP TORINO PIEMONTE; 2006;

2. Scholarship bannedby the "Italian League for the Fight Against Cancer" (LILT) for cancer research, University of Piemonte Orientale; 2003;

3. Scholarship financed from 'Italian Fundation for Research on Cancer (FIRC) with a project on "Cutaneous HPV and skin cancer" held at the Laboratory of Virology of the tumors (Prof. Tommasino), Deutsches Krebsforchungzentrum (DKFZ), Heidelberg (Germany); 2002;

4. Scholarship banned by the "Italian League for the Fight Against Cancer" (LILT), University of Piemonte Orientale; title of the project: "Biological characterization of interferon-inducible HIN200" genes; 1997-1998.

FURTHER INFORMATION

Member of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID);

Member of the European Society for Dermatological Research (ESDR);

Member of Associazione Internazionale Ricercatori Italiani (AIRIicerca);

Member of the National Interuniversity Consortium for Material Science (INSTM)

OTHER ACTIVITIES

TEACHING ACTIVITY

She holds the following courses:

Since 2011: Discipline: Medical Microbiology and Microbiology Laboratory; Integrated course: "Fundamentals of Immunology and Medical Microbiology"; Three-year Degree Course in Biotechnology, University of Eastern Piedmont UPO); (Integrated Course Coordinator)

Since 2005: Discipline: General Microbiology; Integrated course: "The molecular basis of diseases"; Three-year Degree Courses of Health Professions (Biomedical Laboratory Technician, Radiologist Technician, Physiotherapy);

Since 2005: Discipline: General Microbiology; Integrated course: "Aetiopathogenesis of diseases"; Three-year Degree Courses of Health Professions (Dental Hygiene,); (Integrated Course Coordinator from ay 2019-20)

Since 2016: Discipline: Microbiological Analysis; Training area: "Analytical Methodologies and Clinical Diagnostics", School of specialization in Hospital Pharmacy,

From 2019: Discipline: Clinical monitoring of the needs and analysis of the consumption of antibiotics and antivirals, School of Specialization: Hospital Pharmacy,

From 2020: Discipline: Internship in virological diagnostics, School of Specialization: Clinical Pathology and Clinical Biochemistry,

From 2020: Discipline: Internship in fundamentals of microbiological diagnostics, School of Specialization: Clinical pathology and clinical biochemistry,

He is thesis supervisor for students of the three-year degree courses in medical and three-year biotechnology, medicine and surgery and biomedical laboratory technician.

Supervisor of the research activity of Post-docs, PhD students and students belonging to the Degree Courses in Medicine and Surgery, Medical Biotechnology, Biotechnology, Biomedical Laboratory Technician and participants in the "Erasmus" "Erasmus plus" and Free mobility program mover of the European Union.

From ay 2018-2019: Holder of the optional teaching activity (ADO) entitled "Culturomics and microbiota: importance of cultural conditions for the growth and identification of anaerobic, microareophilic and aerobic bacteria" for students of the Degree in Biotechnology

He actively participated in the "Researchers' Night"

In 2015-2018 and in the academic year 20-21: proposes Laboratory Internships as part of the "Path of Excellence" project for students of the Degree Course in Medicine and Surgery

Since 2014: Lecturer in the National Science Degree Plan: High School Educational Laboratories

She actively participated in public events

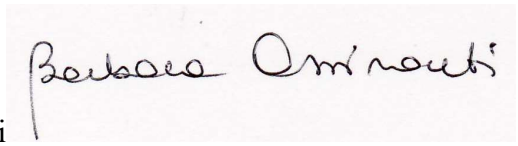
2019 Researchers' Night, UPO (Alessandria): “Infectious diseases and climate change”.

2018 Researchers' Night, UPO (Alessandria): “The human microbiota”.

2019 UPO Junior 2019, UPO (Novara): “The microbiota at the table: good appetite bacteria!

Novara, 27th November 2020

Yours faithfully,



Dott.ssa Barbara Azzimonti