

**"VICTOR BABEȘ" UNIVERSITY OF  
MEDICINE AND PHARMACY TIMIȘOARA  
DOCTORAL SCHOOL  
MEDICINE**



# **HABILITATION THESIS**

**ANTIMICROBIAL RESISTANCE:  
GENETIC MARKERS,  
RISK FACTORS, DRIVERS**

**A B S T R A C T**

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**Timișoara  
2022**

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# ABSTRACT

## Scientific achievements

The topic of multidrug resistant organisms (MDROs) represents in recent years one of the biggest challenges facing our society, in terms of morbidity, mortality, life expectancy, length of hospitalization, costs. There are cases when resistance extends to the entire range of available therapeutic agents (the so-called pan-drug-resistant phenotypes), which represents a real challenge in terms of antimicrobial therapy. Starting with 1996, when I finished my doctoral thesis, my entire research activity was focused on the study of MDROs and their role in the etiology of the community but especially healthcare associated infections (HCAI). I also focused my research activity on genetic, risk factors, triggers and antimicrobial consumption correlated with MDROs. Actually even prior to finalising my doctoral studies, in 1995, I had the opportunity to obtain a scholarship from the Organisation Medecins Sans Frontieres (MSF) and to specialise in clinical microbiology and HCAI prevention by completing a training programme at OLVG Clinical Microbiology Laboratory from Amsterdam, Netherlands, under the supervision of Dr. Peter Rietra.

In 1998, I've participated in a second training programme, this time at the CHU Bicetre Clinical Microbiology Laboratory from Paris, under the supervision of Prof. Patrice Nordmann, a globally well-known personality, mainly due to his studies in the field of molecular diagnosis of Gram-negative bacilli (GNB) resistance genes. In this lab I've learned how to classify pathogens based on their resistance phenotypes and using this experience, on my return to Timisoara, I was able to train my students and younger colleagues and to publish a series of research papers, courses and books.

*National and international grants.* Throughout my entire professional career, I've earned multiple national and international grants, in which I held the position of project manager or member.

Thus, in 2001 I've obtained and led, based on a competition, the **Grant CNCSIS 42612**, financed by the World Bank and the Romanian Government. In 2004, I've obtain by competition and led a second research project: **Viasan no. 310/2004** with a similar topic, but this time, with molecular diagnostic added: "The

evaluation of the antimicrobial resistance of the *E coli* and *Klebsiella* strains and highlighting the presence of SHV and TEM genes in the extended-spectrum beta-lactamase-producing strains isolated in the western region of the country". Between 2008 and 2011, following competition, I had the opportunity to lead a third research project, **Partnerships for Priority Areas Programme PNII, nr.42121/01.10.2008**, with the theme: "Study of the multidrug resistance molecular determinants in the hospital and community acquired bacterial strains in south-western Romania".

In terms of my participation as a **member to national projects**, I was involved in 4 projects. In 2018, I've participated in an **international consortium** that applied for and obtained the **cross-border grant**: "Romanian-Hungarian cross-border project with a wider focus on diagnostics related to infertility, healthy pregnancy and newborn care". **ROHU339 / HEALTH-PREGN-RO -HU / 2019**. In perspective, together with an international team we would like to **re-submit the HORIZON project** called "TAILOR; Transmission prevented by Tailored Interventions" and we are looking forward to the outcome of our submission.

*Clinical trials.* During my academic career, I've also actively participated in a series of **clinical trials**. Through the results obtained in all these clinical trials, I contributed together with the team I worked for to the improvement of antimicrobial therapy, leading to the development of new compounds or new combinations of therapeutic agents.

*Invited speaker and organizer of many national and international conferences and workshops.* Following my PhD degree, my entire research activity was focused on the study of bacterial resistance, etiology, risk factors and methods for prevention of HCAI. But I also was involved in collaboration with other groups of researchers, in scientific research activities in the evaluation of various bioactive molecules for their antimicrobial activity.

Thus, I had the opportunity to share the results of my research as an invited speaker to many national and international conferences and workshops.

### **Publishing research and didactic activity**

I have disseminated my research work in 44 papers indexed in Clarivate's Web of Science (40 *in extenso* papers and 2 proceeding papers and 2 meetings abstracts). 7 of these research papers have been awarded by UEFISCDI. In February 2022 I had a Hirsch index of 12 in Web of Science (with a total of 656

citations without self-citations) an index of 20 in Google Academic (with 1600 citations) and respectively 10 in Scopus (with 624 citations). My research work was published in more than 29 distinct journals (at least 18 indexed in Clarivate's Web of Science) with high impact on the scientific community, this statement being demonstrated by the fact that my cumulated impact factor of the published manuscripts is higher than 90, while the cumulated impact factor of the published papers in which I am the main author is **43.61**. My work, counting more than 200 papers, was published in numerous journals, most notable being: 20 *in extenso* papers indexed in Clarivate's Web of Science, main author, 20 *in extenso* papers indexed in Clarivate's Web of Science, co-author, 11 *in extenso* papers indexed in international scientific databases, main author, 33 *in extenso* papers indexed in international scientific databases, co-author, 14 abstracts after conferences in supplements of journals indexed in Clarivate's Web of Science, main author, 29 abstracts after conferences in supplements of journals indexed in Clarivate's Web of Science, co-author, 57 posters at international scientific meetings, 22 posters at national scientific meetings.

I also published 19 professional books and 2 chapters in collective volumes. These are courses and practical works for students from the different study programs of our university, as well as diagnostic guidelines, monographs related to HCAI and antimicrobial resistance, for doctors and resident doctors specializing in laboratory medicine and medical microbiology. It is worth mentioning that all of the research work was done within multidisciplinary teams, mainly including pharmacists, doctors specialised in epidemiology, intensive care, internal medicine or diabetes, urologists, surgeons, dentists, biostatisticians, biochemists, biologists, etc. Part of the research was possible due to the financial support provided by the national scientific grants obtained by competition. Finally, but not least, I am involved in the academic publishing activity, being currently **reviewer at 8 journals**, all indexed in Clarivate's Web of Science (e.g., World Academy of Sciences Journal, Spandidos Publications; Journal of Antimicrobial chemotherapy; Romanian review of laboratory medicine; Journal of hospital infections; Journal of Infection in Developing Countries; etc.). At the same time, I am a member in 2 editorial boards of scientific medical journals: Bacteriology, Virology, Parasitology, Epidemiology Journal and Journal of hospital infections. **In conclusion**, my entire research activity was

focused on studying the determinants of antibiotic resistance and addressed the research directions set out below.

Throughout my professional career I have followed the following research directions: Phenotypic characterization of MDROs; Molecular characterization of MDROs; The study of antibiotic use correlated with the costs and resistance patterns; The study of particular species and / or resistance patterns; Evaluating the local trend of MDROs; The study of risk factors associated with acquired multidrug resistance to antimicrobials.

### **Academic achievements**

I've graduated from Timisoara Institute of Medicine – Faculty of Medicine in 1988, obtaining a grade of 10 out of 10 at the bachelor's exam. Currently, I am a professor, position held in the Discipline of Microbiology-Virology, XIV Department of Microbiology, “Victor Babeș” University of Medicine and Pharmacy from Timișoara. I hold this position since October 2009 (designated on this position following a public examination). Presently I am involved in the academic activity of the Faculty of Medicine, providing lectures of Microbiology to students in the first and second year of study. Prior to this position, I held the positions of associated assistant professor (1992-2001), assistant professor (2001-2002) and lecturer (2002-2009) at the same discipline. During my 29 years of academic career I was involved in continuous update of my courses and academic materials in accordance with highest European standards. In 1993, I started my PhD in the Hygiene specialty at the same university. The title of my PhD thesis was " Contributions to the evaluation of microbial pollution and the risk of acquiring nosocomial infections in pediatric departments". Thesis was publicly presented in 1996 and I've obtain the PhD degree in medicine. From 2010 to date I became a PhD supervisor. Since 2017 I started to involve students in VADA volunteer program at the level of Microbiology Department. I am the author of 15 courses and practical workbooks for students (being the main author in 14 of them), for all the study programs I work with: Medicine for Romanian, English, French programs, nursing, dentistry for English programs, etc. Other 8 books were published for specialist and resident physicians specializing in laboratory medicine or medical microbiology (5 of them being dedicated to the study of antimicrobial resistance and detection and MDROs). Throughout my career, I participated as a lecturer in more than fifteen postgraduate courses, all having the central topic of

classifying pathogens based on resistance phenotypes or novelties in the etiology and treatment of community and HCAI. I am also member of the UMFT Senate since 2012. I was president of the Department of Educational Quality Assurance (DEACE) of our university during 2013-2016 and vice dean of the Faculty of Medicine during 2016-2020. During my last position I participated in: the equivalence and disciplinary commissions, the team for drawing up the ARACIS accreditation files, curricular reform committee, etc. I also participated as head of the admission commission or member of the central commission of the university in the bachelor's or residency exams. I currently hold the position of director of the XIV Department of Microbiology, which includes the Discipline of Microbiology-Virology, Hygiene and Dermatology. In the last 20 years I was also a referent / member or president in numerous doctoral and competition commissions organized by our university or other prestigious universities in the country.

### **Professional activity**

In parallel with the academic activity, I am a medical doctor, specialized in the field of Laboratory Medicine and Medical Microbiology. Following graduation (starting with 1989) I was employed as an intern at County Hospital Arad, where I completed the paediatrics and gynaecology rotations. From 1990, I continued my internship working in internal medicine at Timisoara Clinical County Emergency Hospital (TCCEH). In 1992, following the competition for the position of assistant professor in Microbiology at the University of Medicine and Pharmacy Victor Babes Timisoara, which was successful, I also started my residency training in Microbiology. The name of the specialty changed during my training, from Microbiology into Laboratory Medicine. In 1994, after the final specialty examination, I became specialist doctor in the field of Laboratory Medicine, and in 1999 I obtained the title of senior doctor in this specialty. Currently, I am a senior doctor in Laboratory Medicine and Medical Microbiology (in this second specialty, starting from 2017). In relation to my **clinical activity** in the Public Health sector, between 1995 and 2015, I was employed at The Public Health Institute "Dr. Leonida Georgescu", Regional Center for Public Health from Timisoara. From 2009 until 2010, I held the position of Deputy Coordinating Director of the Control in Public Health employed by the Public Health Department in Timis county. From 2015 to date, my role implies being responsible for the Microbiology-Parazitology Department of the Clinical Laboratory from "Pius Brinzeu"

County Clinical Emergency Hospital Timisoara (TCCEH). Starting with 2017, once the Medical Microbiology specialty was re-established, I became a residency training coordinator in this specialty. During my medical and academic activity I attended numerous **post-graduate courses** in the field of microbiology, laboratory medicine, epidemiology, public health or clinical topics. In 2014, in order to gain new abilities and competencies in research project management, I graduated the courses organized by the Public Health and Healthcare Management National School from Bucharest and in 2014 I've obtained the **competency diploma in healthcare system management**. In the last 20 years I have held the position of member or president in numerous specialty or senior doctor commissions in Laboratory Medicine or Medical Microbiology specialties. I am also vice-president of the Romanian Society of Microbiology (SRM) and member of the Medical Microbiology Commission of the Ministry of Health.

### **Academic and scientific perspectives**

My academic career involves the academic titles obtained during teaching, as well as peers professional recognition and a number of competencies like good communication skills, ability to disseminate information to students and research results to experts in the field, continuous medical education, teamwork, interdisciplinary collaboration, leadership skills, critical thinking and dedication. Although I am a medical graduate, the special interest in teaching goes hand in hand with my skills as a doctor due to the fact that I am a good communicator, I want to train future generation of doctors, I want to contribute to the development of society and the wellbeing of others and I have a strong motivation for personal and professional development.

All the research activity carried out as part of my university career was in the context of my scientific interests and in the Microbiology department that I coordinate. This created a good premise for the integration of both, my research and teaching activities and this represents a personal goal that I plan to pursue in connection with my teaching activity. To this end, my immediate goals include: updating the student courses according to new developments in the subjects that I teach: medicine, medicine in French, general nursing program; updating the teaching methods, all the more so as the classical way of teaching has changed, making room for online teaching; foundation of student research centers on the topic "Antimicrobial



resistance and HCAI prevention and therapeutic options"; continuing to involve students in VADA volunteer programs; coordinating the scientific papers of the students at the national and international conferences, as well as the workshops at the student conferences; further coordination of the bachelor's theses of our graduates and the doctoral theses in the field of medical microbiology and other related specialities; drafting and permanent updating of lecture books and practical tutorials manuals, and also collaborating with prestigious authors for the updates of multiple national and international books and book chapters; organizing and leading postgraduate courses for resident physicians and specialist doctors; participation in organizing committees and as invited lecturer at national and international conferences; continuing the activity of peer-reviewer at prestigious journals in my area of expertise.

As the role of diagnostic and therapeutic guidelines is currently indisputable, I intend to further contribute to the development of guidelines under the auspices of the Romanian Society of Microbiology, especially those related to antimicrobial resistance and HCAI prevention and therapeutic options. Also one of the indicators of the research grants in which I participate or will participate is represented by the elaboration of books and monographs in the field of research, I propose the writing of such monographs.

**I will strengthen my professional relationships** based on high quality scientific papers and I will try to expand my professional network with the aim of higher research standards and better funding opportunities. I would like to continue the activities related to the investigation of microbial biofilm in several directions: the study of biofilm microorganisms, the mechanisms for antimicrobial resistance of biofilm microorganisms, the potential of medical procedures to disrupt the flora of the local biofilm and to disseminate, etc. I also intend **to expand the collaboration with researchers from other Romanian universities.**

In the long run, according to these research topics, I will continue to work on the main directions established by the Department of Microbiology and by the MULTI – REZ research group of our department. In the future I also intend to apply for both, national and international research projects. The credibility of these projects and therefore their chance to receive funding, increases with the diversity of the fields of activity of the research team of the members, as well as with the addition of new specialties and fields of intervention to the researched topics. I also aim to publish

my scientific results in ISI-rated journals, in order to gain higher international scientific recognition, and I will use all my skills to train future generations of dedicated researchers.

Finally, having the premises of my previous education and experience and considering my future plans, I hope that by achieving the above-mentioned objectives I will fulfill the expectations of UMFVBT academic staff.

## LIST OF 10 REPRESENTATIVE SCIENTIFIC PAPERS

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