"Carol Davila" University
of Medicine and Pharmacy Bucharest
DOCTORAL SCHOOL

Abstract
of
HABILITATION THESIS

Applicative research in microbiology for infection prevention and control

CANDIDATE

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Summary

Introduction

Habilitation thesis entitled ***"Applicative research in microbiology for infection prevention and control"*** is a synthesis of didactical and research activities that I performed after defending my PhD thesis.

The thesis is drawn up according to CNATDCU/"Carol Davila" UMP Senate recommendations and consists in 5 main chapters : I. Scientific activity ; II. Academic activity/Academic accomplishments ; III.Professional activities/Professional accomplishments ; IV. Plans of evolution and development of didactical activity; V. Bibliography.

I. Research activity

I have directed my research activity in the medical field, microbiology specialty, towards several directions derived from my PhD thesis subject. It may be structured like in Fig. 1.

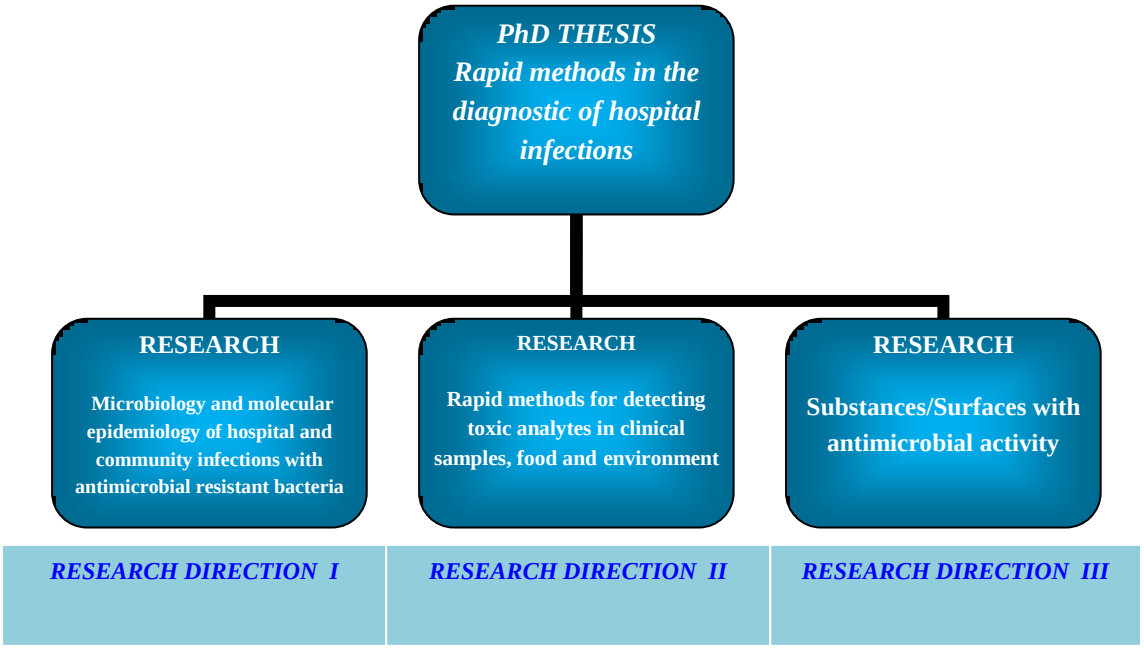

Fig. 1. Structure of research directions after defending my PhD thesis

RESEARCH DIRECTION I

Microbiology and molecular epidemiology of hospital and community acquired infections with antimicrobial resistant bacteria

Previous own studies and data from medical scientific literature led me to the conclusion that antimicrobial resistance and infections acquired during medical care represent a concerning public health emerging problem in Romania and worldwide.

After 2000 I successfully applied for several research projects dealing with nosocomial infections and antimicrobial resistance.

In 2001 I benefited of full support from Professor Andrei Aubert Combiescu, who by that time was the General Director of Cantacuzino Institute and encouraged me to contact the European System of Antimicrobial Resistance Surveillance (EARSS), established under the aegis of EC-DG SANCO and European Society of Clinical Microbiology and Infectious Diseases (ESCMID).

In 2010 I was nominated by the public health authority as National Focal Point for Antimicrobial Resistance for the European Centre for Disease Control (ECDC).

Affiliation to EARSS of our research group from Cantacuzino Institute, together with several Romanian hospital laboratories which collaborated with us on a voluntary basis in the 2001-2010 interval, contributed to harmonizing the methods of antimicrobial susceptibility testing and facilitated our country's participation in EARSS satellit research projects, as well as the involvment of two researchers working in Cantacuzino Institute (Irina Codiță and Monica Străuț), as founder members, in the setting-up of the SeqNet (European Network of Laboratories for Sequence Typing of Microbial Pathogens http://www.seqnet.org/participants.html).

In 2005, as a continuation of these initatives and for supporting this research direction, I applied for and won funding for the national Excellence Project "Pathogenomics integrated network (platform) for translational research in biomedicine (microbiology of infectious diseases) – PATGEN-NET" CEEX 28/2005. Development of this project allowed us to reach two objectives of great interest:

- Validation of a network of partners from the public health system and of appropriate functional flows for the transfer of research results

- Introduction of European harmonized typing methods in the newly created Laboratory for Nosocomial Infections and Antimicrobial Resistance, with kind support from our colleagues from the Molecular Microbiology Laboratory

When, in 2010, EARSS became EARS.Net and was taken over by the ECDC, respectively The National Centre for Communicable Diseases Surveillance and Control at the national level, Romania was already prepared, including training of specialists working in hospitals participating in EARSS and a surveillance system validated by the applicative research projects developed in Cantacuzino Institute.

On the other hand, affiliation of Staphylococcus Reference Laboratory functioning inside the Laboratory of Nosocomial Infections and Antimicrobial Resistance from Cantacuzino Institute, to the European Network of Staphylococcus Reference Laboratories, created inside the European Society of Clinical Microbiology and Infectious Diseases has further expanded the prospects of collaborating in the European research.

The results of our research dealing with molecular epidemiology of bacterial strains involved in invasive infections evolving in hospital environment have been diseminated by national and international communications and/or published in national or international journals. In the case of European studies, I was involved mostly as co-author and principal investigator for Romania. These communications and publications are included in the bibliography of the habilitation thesis and/or in the list of publications.

This research direction was an opportunity for our laboratory to support a PhD fellow to complete the doctoral thesis "Genetic patterns of virulence and resistance in *Staphylococcus aureus* strains isolated in Romania", under the co-ordination of Professor Grigore Mihăescu, from the Biology Faculty, Bucharest University.

RESEARCH DIRECTION II

Rapid methods for detecting toxic analytes in clinical samples, food and environment

This direction has been developed in the 2009-2015 interval, in the frame of the Nucleu Project PN 09 22 01 05, „Rapid methods for detecting toxic analytes in clinical samples, food and environment", project responsible Irina Codiță.

We performed translational research aiming to introduce in the practice of the Reference Laboratory for Nosocomial Infections and Antimicrobial Resistance, rapid

methods for detection of staphylococcal enterotoxins, especially of enterotoxin B, recognized as dual-use biological agent (in microbiological diagnostic and/or in bioaggression).

This theme was valorized, between other means, by supporting the completion of the PhD thesis by Dr. Luminița Coldea, conducted by Professor Marian Neguț. She benefited of guidance from the Project responsible and of the material support needed for accomplishing her tasks.

RESEARCH DIRECTION III

Substances/Surfaces with antimicrobial activity

This direction has been approached in the frame of two projects developed in partnership in which I hold the position of Cantacuzino Institute Partner responsible (see Chapter 1.3).

The mentioned projects referred to:

- obtaining surfaces with antimicrobial activity covered with nano layers of Silver and/or Copper, for use in hospital environment to control infections
- developing and up-dating food package films based on biopolymers and natural antimicrobial agents (plant essential oils) to increase food biosafety

Developing of the second project led us to obtaining an invention patent to which I am a co-author.

Publications that disseminated the results are included in the thesis bibliography.

In the last 10 years I co-ordinated 4 national projects (1 as Project Director, 3 as responsible for Cantacuzino Institute Partner), I was responsible for Cantacuzino Institute in 4 international programs, of which one is in progress, I was involved in 4 Nucleu projects (1 project responsible, 3 scientific responsible), I was responsible for the Romanian partner in 2 structural programs with European funding.

I am the author or co-author of 26 scientific articles in ISI journals and 34 in BDI journals, of which 16, respectively 3 published in the last 5 years.

2. Academic activity/Academic accomplishments*:*

Academic activity in „Carol Davila" University of Medicine and Pharmacy in the field of medical microbiology can not be conceived without taking into consideration the relationship with Cantacuzino Institute.

So, until 2012 Cantacuzino Institute hosted the unique Microbiology Chair and most of the courses for medical students in the General Medicine Faculty and residents stages. Since 2012, Cantacuzino Institute functioned as didactic facility for Microbiology II Discipline and provided practical work didactical materials needed for curricular activities of students and residents in laboratory medicine, and since 2017 of residents in clinical microbiology, in collaboration with other disciplines functioning in "Carol Davila" University of Medicine and Pharmacy, Bucharest.

On the other hand, Cantacuzino Institute is offering the main research platform in the microbiology domain for UMP Carol Davila microbiology and infectious diseases teaching staff, taking into consideration that in order to reach scientific requirements to publish in ISI journals you need to accomplish advanced research studies like sequencing, including whole genome sequencing, Pulse Field Gel Electrophoresis, Real Time PCR and/or RT Real Time PCR, proteomics etc., available nowadays in the institute.

I performed teaching activities for microbiology specialists on a voluntary basis starting with 1980 years, when I was hired as research associated physician and then as a researcher in Cantacuzino Institute, in the Reference Laboratory for Staphylococcus, being invited to give lectures for medical students at the Microbiology Chair functioning by that time. My field of didactic activities has widened starting with 2002, when I won the position of Assistant Professor (Șef de lucrări) and afterwards of Associate Professor in 2007.

I always brought into the education process my experience into the research field and all I learnt as a professionist fully involved in activities of reference public health microbiology and I combined teaching with continuous personal education. I also tried to continuously adapt the discipline Curriculum to the objective requirements of the health system.

My deep involvement in the antimicrobial resistance domain has set up an opportunity that I capitalized by introducing in my courses and/or practical works with students and residents concrete notions and examples on this public health issue of high relevance. In this respect, I up-dated Chapters dealing with antimicrobial resistance testing in the Microbiology Treatise (Buiuc D, Neguț M – Coordinators), currently considered the leading book of microbiologists in Romania.

My experience and involvement in the work of the reference laboratories as well as the good professional and interpersonal relationship with all the heads of the Reference Laboratories in Cantacuzino Institute contributed to better train students and residents both in theoretical activities and in the practical works, thus contributing to facilitate assimilation of notions and skills in close relation with realities of medical and public health microbiology laboratories.

Teaching activities in "Carol Davila" University of Medicine and Pharmacy:

- Medical microbiology courses and practical works for students, in Romanian and English
- Courses and practical works for residents in laboratory medicine (I am an official residency coordinator for Cantacuzino Institute stages in microbiology and mycology since 2007 and I started to hold informally this activity since 2002)
- Courses and stages for specialists in microbiology, epidemiology etc.

I was also involved as an institutional responsible for international programs to participate in organizing training courses for microbiology specialists from County Public Health Authorities and hospital laboratories, such as: International training course "Microbiological investigation of communicable diseases under surveillance in Romania" (2 courses of 2 weeks duration each in 2004); WHO/Bichat Hospital Paris/Cantacuzino Institute course on AST testing for Romanian specialists (2005) - organizer; WHO/Cantacuzino Institute international course on dangerous pathogens and biosafety (2004) etc.

Since 2013, I am a superviser for fellows admitted at the European School of Public Health Microbiology (EUPHEM) of the European Center for Disease Control (ECDC), nominated for the Cantacuzino Institute EUPHEM site, following the endorsement visit of ECDC.

I have guided 8 licensing papers in our laboratory under the coordination of the Head of the Discipline and prepared, together with residents, publications and / or communications at National Microbiology Conferences.

The subjects of the Bachelor degree theses were chosen taking into account the graduates' preferences, but also the temporal configuration of the significant epidemic events.

I have been asked several times to participate in the jury for awarding prizes in the student sessions of scientific communications.

As a Head of Nosocomial Infections and Antimicrobial Resistance Laboratory from Cantacuzino Institute, and using the possibilities offered by the participation of this laboratory in research programs, I facilitated and guided the completion of at least four doctoral theses coordinated by doctoral supervisors from Carol Davila UMF or the University of Bucharest, Faculty of Biology, dealing with molecular microbiology of MRSA strains involved in hospital or community infections, staphylococcal toxinoses, antibiotic resistance in *Klebsiella*, etc.

I was involved twice in Carol Davila University of Medicine and Pharmacy examination for admission in the Medicine Bachelor degree studies and I participated in more than 10 commissions for specialist positions, PhD disertations, didactic promotion examination etc.

In 2013 I was appointed through the vote of my discipline colleagues as a Delegate of Microbiology II Discipline at the level of University Department II.

3. Professional activity/ Professional accomplishments

I am a graduate of Carol Davila IMP (currently Carol Davila UMP), Faculty of General Medicine since 1977, with the completion of studies thesis entitled "Anatomical and Clinical Correlations in Hepato-Cellular Carcinoma and Hepatic Cirrhosis". In 1976 I obtained the pre-clinical resident post by contest (ranked second of 14 candidates), in 1979 I was hired by competition at the Cantacuzino Institute (ranked the 1st from 4 candidates), in 1982 I took the specialty examination in microbiology and since 1991 I am a primary physician in

clinical laboratory and microbiology (exam completed with grade 10). Since 2001 I hold the position of Senior Scientific Researcher I at Cantacuzino Institute.

I am a PhD since 1997, when I defended my PhD thesis entitled "Rapid methods in the diagnostic of hospital infections".

I have attended several training courses in Romania and abroad, participating both as a fellow and as an organizer in some of them.

Between these, I mention:

- **9/10/2016 – 20/10/2016: Advanced course on antimicrobial resistance** - Pasteur Institute Paris/ Merieux Fondation, Les pensieres, Veyrier Du Lac (Annecy), France;
- **June 2013 (5 days) : ECDC** Summer school, Stockholm, Sweden;
- **Sept./Oct. 2008 (4 days) :** Seminar on communicable diseases prevention and control **INT MARKT TAIEX 30085**, Sofia, Bulgaria;
- **Oct. 2007 (3 days):** Seminar on communicable diseases prevention and control **INT MARKT TAIEX 24654**, Zagreb, Croația;
- **2004 (3 weeks) :** EPIET-like international course of epidemiology "Field epidemiology: Information for action", Sinaia, Romania – EPIET Program, PHARE program "Technical assistance for strengthening the capacity of epidemiologic surveillance and control of communicable diseases in Romania" EuropAid/113121/D/SV/RO;
- **Dec. 2003 (10 days):** Study visit on public health microbiology: London - Basildon Hospital and Colindale Public Health Agency; Cambridge - Department of Public Health - PHARE Program "Technical assistance for strengthening the capacity of epidemiologic surveillance and control of communicable diseases in Romania" EuropAid/113121/D/SV/RO;
- **2002 – 2 months and 2003 – 3 weeks** - participation in Strengthening laboratory capacities in outbreak/epidemic detection and response – theoretical knowledge and practical work – WHO CSR/Lyon Office Program, Lyon, France (nominated by Ministry of Health based on selection process);
- **2001 - 5 days**: Antimicrobial resistance – Basis and laboratory determination – Warsaw, Poland - Central Sera and Vaccines Laboratory, Warsaw, Poland and the European Society for Clinical Microbiology and Infectious Diseases etc.

I have gained experience in institutional management, helding the following positions:

- **2007-2013** and **2016-present: Head of Nosocomial Infections and Antimicrobial Resistance Laboratory,** INC Cantacuzino,
- **2002-2007: Chief of Public Health Microbiology Department**, Cantacuzino Institute. In this capacity, I coordinated at the institutional level the rehabilitation and reorganization of reference laboratories within the PHARE Program "Technical Assistance for the Improvement of the Epidemiological Surveillance System and Control of Communicable Diseases in Romania" EuropAid / 113121 / D / SV / RO engaged by the Romanian Ministry of Health, in collaboration with the international and national experts responsible for the program.
- **2013-2016:** Coordinator of the National Reference Laboratories in Cantacuzino Institute during the most severe crisis in the history of the institute. With few exceptions, the laboratories have responded to all major requests and microbiological diagnosis emergencies in the public health system and have obtained remarkable research results.
- **2015-2016:** Founding Director of the National Interest Instalation "National Center for Expertise and Intervention in Microbiology, Parasitology and Medical Entomology" in INCDMI Cantacuzino http://erris.gov.ro/CNEIMPEM
- **1979-2002:** Staphylococcus reference laboratory, Cantacuzino Institute (since 1982 coordinator)

I have worked in the following **specialized committees and / or expert groups of the Health Ministry:**

- Member of the **National Influenza Committee**: 2004-2007 (Order MS 861/2004);
- Member of the **Subcommittee on Antibiotic Resistance of the Commission for Infectious Diseases 2013 - present** (currently committees are being reorganized): Participation in the elaboration of 3 guides on the control of the spread of antibiotic resistance; participation in the elaboration of consultative documents at the request of the Ministry of Health (Order MS 398/2013 modified by MS Order no 1406/2014),
- Member of the **Expert group responsible for drawing up technical points on the documents under discussion at Community level and insuring**

representation at the meetings of the working structures of the European Union institutions (Order MS 1173/2010).

I participated as senior doctor and then as teaching staff in examination boards for occupying specialized positions at the Cantacuzino Institute with the approval of the Ministry of Health.

I also hold the following positions:

- Member of the **Executive Committee of the Romanian Society of Microbiology** - since 1997
- **Vicepresident of the Executive Committee of the Romanian Society of Microbiology** - since 2013,
- Member of the **Scientific Council of the Cantacuzino Institute** (2001-2002),
- Member of the **Association of Laboratory Medicine** - since 2009
- Member of the **European Society of Clinical Laboratory and Infectious Diseases** - since 2003,
- Member of the **European Federation of Microbiology Societies** - since 2002,
- Member of the **Laboratory Commission of the Romanian College of Physicians** (2000 – 2005).
- Member of the **European Joint Initiative Program Coordination Committee** - Antimicrobial Resistance (JPI AMR) 2012 – present
- Member of the Organizing Committees of the Annual Microbiology Conferences from 1990 to present.

Experience in editing medical journals - Member of editorial teams

- Secretary responsible for the Bacteriology, Virology, Parasitology, Epidemiology journal of the Romanian Society of Microbiology: 1992 - 2013
- Member of the editorial staff of the journal Bacteriology, Virology, Parasitology, Epidemiology: 2013- present
- Member of the editorial staff of the Cantacuzino Institute's journal Romanian Archives of Microbiology and Immunology: since 2010 - present
- **Referrent for:** Revista Română de Medicină de Laborator, Roumanian Archives of Microbiology and Immunology; Bacteriologia, Virusologia, Parazitologia, Epidemiologia; *Maedica – a Journal of Clinical Medicine*

I held the position of National Representative of EARSS / EARS.Net (European Antibiotic Resistance Surveillance System) - 2001-2007; 2009 - present

Distinctions and prizes:

I received "The merit award granted in 2015 by the National Center for Communicable Disease Surveillance and Control for her contribution 10 years ago to the establishment and operation of the National Center for Communicable Disease Surveillance and Control at the National Institute of Public Health".

I participated as invited lecturer and/or invited event organizer in national and international trainings.

4. Academic Career Development and Evolution Plans

The academic career in microbiology at UMP Carol Davila Bucharest can only be conceived in close correlation with the practice in the field of microbiology and the research activity, which I continue to carry out at the Cantacuzino Institute as Senior Scientific Researcher I.

The challenges I have faced during my over 37 years of activity have required a positive attitude towards modern approaches and an intellectual, physical, mental and emotional adapting capacity that I consider beneficial for the difficult period of time the medical profession in general, the Cantacuzino Institute and medical education, in particular, are crossing over, as a result of staff and funding crisis in a vital area such as health care.

In order to outline the strategy and objectives of my academic career development and further evolution plans, I have undertaken a SWOT analysis, which is reproduced below:

Strong points

• Didactic experience for more than 15 years, at Carol Davila UMP, of which 10 as Associate Professor
• University studies of psychology and pedagogy untertaken
• Informal experience in guiding PhD thesis
• Continuous training and education in the field of microbiology, in Romania and abroad, during a professional career of over 37 years
• Experience in coordinating reference laboratories for microbiology
• Access to research platforms and national interest facilities at INC Cantacuzino
• Integration into national networks of collaboration in various fields as public health, nanomaterials etc.
• Participation in European networks in the field of public health microbiology and antibiotic resistance
• Honorable Hirsch index (10) and international visibility, under the conditions of institutional crisis and under-funding of national research

Weak points

• Difficulties in attracting quality human resources to ensure continuity and success at the level of laboratories and in education
• Excessive bureaucracy in the establishment of inter-institutional relations between Carol Davila UMP and Cantacuzino Institute
• The costs of media and reagents required for practical works and demonstrations are not but with few exceptions covered by the faculty
• Incomplete capitalization of research results through ISI publications in journals with significant impact factor, mainly because of using excessive time for surpassing chronic transition problems in Cantacuzino Institute
• Organizational problems faced by Cantacuzino Institute, which is a basis of education and research for Carol Davila UMP and a second employer of Carol Davila UMP didactic staff, are affecting the time available for effective education and research activities

Oportunities

- Cantacuzino Institute is an institution which crosses a full recovery process, which could be beneficial for developing and improving medical microbiology teaching activity,
- New calls in the PNCD III national program are or will be available soon
- New EU ERA-NET and Horizon 2020 calls available

Threats

- Excessive competition at the public health system level and in the scientific field caused by chronic under-financing
- Poor funding of research at national level
- Human resource shortage from a quantitative and qualitative point of view

General objectives for developing my didactic career and further evolution plans are:

1. continuing daily training for the maintenance and improvement of knowledge, skills and competences in the field of medical microbiology and public health and related fields

2. capitalization of the accumulated theoretical and practical knowledge, skills and competences through the continuous updating of the microbiology courses content and of other didactic activities, in line with the fast track progress in the medical microbiology field

3. modernizing the forms of teaching by improving the training and information in the pedagogical field in order to increase the performance and attractiveness of didactic and research activities
In this respect, I mention that I am a graduate of the Faculty of Psychology in 2009 and hold a Graduation Certificate from the Department for Teacher Training granted by Spiru Haret University in the same year.

4. improved use of intra and inter-institutional collaboration opportunities at national and international level in order to increase the quality of the educational process in the field of medical microbiology

Evolution and career development plan for teaching activity

1. ⇒ Continuing professional development and updating of specialized knowledge by attending conferences, congresses, symposiums, webinars, individual training, etc.
2. ⇒ Continuing the practice of including notions and skills harmonized with real-time specialties developments in the faculty courses and the practical works.
3. ⇒ Improvement of the teaching methods – setting-up of an interactive digital course model
4. ⇒ Participation in the elaboration of a unitary course for residents at the level of Microbiology Discipline of UMP Carol Davila, in collaboration with the other teachers working in this Discipline, as discussed at the level of the discipline at the end of this academic year

Proposed personal contribution to develop topics of the curriculum:

- The normal microbiota of the human host
- Sampling, processing and microbiological investigation of biological probes
- Chapters from special microbiology such as gram positive pathogens, enterobacteria etc. depending on the needs identified at the Discipline level
- Antibiotics - basics and updates on new antibiotics
- Resistance to antibiotics - theoretical knowledge regarding the resistance mechanisms and their detection in the practice of the microbiology laboratory
- Hard version of microbiology course and practical works in English that I prepared in digital format

5. ⇒ Continuing the activity of guiding the Bachelor studies termination theses
6. ⇒ Exploitation of existing possibilities in the Nosocomial Infections and Antimicrobial Resistance Laboratory for supporting doctoral students in completing their PhD thesis, with the approval of Cantacuzino Institute coordinating body
7. ⇒ Improving student and resident evaluation process and continuing to integrate feedback from learners through interactive approaches in order to optimize the content and format of teaching materials and of the teaching process.

Evolution and career development plan for research activity

1. ⇒ Continuing and deepening the research in the field of molecular microbiology and molecular epidemiology of hospital and community infections with antibiotic resistant bacteria (1 complex project in which we are partners is under the Phase II evaluation, with high success chance)
2. ⇒ Continue and deepen research on nanomaterials with antimicrobial activity (2 national applications and 2 international applications under evaluation)
3. ⇒ Participation in other applications for obtaining national and / or international funding for studies and research in the field of resistance to antibiotics, nanomaterials, toxic microbial analytes, etc.

4. ⇒ Increase of the research value and visibility by publishing in high impact factor journals - target: at least one ISI article per year.

5. ⇒ Expanding the relationship with partners in the public health sector or with third parties in the economic field in order to become aware about the need of research studies and to accelerate the transfer of research results in biomedical and / or economic environments