Institute of Research and Development for Microbiology and Immunology "Cantacuzino"

Research and Development and Innovation

Mission

Engaged in communicable disease surveillance, ensuring microbiological surveillance and training specialists in **microbiology and immunology**.

The main strategic directions of research and development in the medium term are:

- Fundamental Studies on the mechanisms of pathogenicity, body-pathogen interaction, coping mechanisms of pathogens (including antibiotic resistance)
- **Medical Microbiology**: etiology and pathogenesis of infectious disease study
- **Applied Microbiology**: characterization methods for microorganisms, study of interactions between organisms and their interaction with the host and the environment
- **Developing new diagnostics and control of infectious** diseases; development of new molecular tests to increase rapid response capacity in cases of microbiological alert
- study and **re-emerging infectious** diseases **emerging**
- medical **entomology and ecology of insects** as vectors
- **Developing new vaccines, adjuvants** for vaccination, , surveillance in vaccine-preventable diseases and post-vaccination monitoring
- fundamental and applied studies on the mechanisms of immune response and its adjustment in anti-infective and anti-tumor defenses, physiological and pathological role of inflammation, immune response mechanisms kick
- fundamental and applied studies in human **autoimmune pathologies** in order to elucidate the mechanisms involved in their etiopathogenesis, identify new markers for early diagnosis, the identification of new therapeutic targets
- Expanding the procedures for validating methods and laboratory accreditation

HR

- attracting students, residents and graduate (performing works of bachelor, master and doctoral temporary employment)
- increasing the number of PhDs, the number of scientific researchers Grades I and II
- providing a compelling motivation, intellectual and materials
- providing a stimulating and motivating local social climate

Laboratories

Enzymology and Applied Microbiology Laboratory - Director: Nadia Bucurenci, PhD, nadiab@cantacuzino.ro

Research fields:

- Basic activities: cloning, purification and physico-chemical characterization of proteins (enzymes) bacteria.

Major topics of study:

- The search for new therapeutic targets, nucleoside monophosphate kinase family in pathogenic bacteria resistant to antibiotics
- New methods of diagnosis mono- or polyclonal antibodies or coupled enzymatic reactions; obtaining and purifying the subunits of toxins, bacterial antigens etc.
- Methods of ATP or NADH regenerating enzyme for the synthesis of industrial enzymes phosphorylation reactions or oxidation / reduction
- Implementation and optimization technology of therapeutic sera active component F (ab ') 2 against highly pathogenic bacterial or viral agents

Scientific activities:

- Cloning and purification of toxins or bacterial antigens for diagnosis
    - **Shiga toxin B** subunit identical to Shiga-like toxin 1, was used to obtain monoclonal antibodies and B subunit of Shiga-like toxin 2 testing of possible cross reactions of monoclonal antibodies obtained.
- Toxoplasmosis detection of specific antigens, monoclonal antibody, in women with seroconversion
- Creating a new tuberculin skin test, using specific recombinant antigens for the diagnosis of tuberculosis (TB) and latent active
    - Collaboration with the laboratory of the Austrian institute.
- Implementation and optimization technology therapeutic sera active component F (ab ') 2 against highly pathogenic bacterial or viral agents.

Immunity Laboratory antiinfectives - Director: Aurora Sălăgeanu, immuno@cantacuzino.ro

Research area:

- Innate immunity, inflammation and immunomodulation.
    - Studying the properties and mechanisms of action of adjuvants and immunomodulators
    - Determining the profile of cytokines in certain physiological conditions
    - Investigate the relationship between cancer and inflammation

Scientific Activities

I. Experimental studies *in vivo* and *in vitro* bacterial immunomodulator Cantastim

- Cantastim (CS) is an immunomodulator bacterial generation-II, obtained alcoholic extraction from *Pseudomonas aeruginosa*.
- Treatment with CS is effective in improving the immune status of patients with chronic viral and bacterial infections, cancer patients and prevention of post-operative infection.

II. Tumor Immunology

- Highlighting immunosuppression in patients with breast and lung
- Profile of cytokines in cancer patients undergoing colorectal surgery
- "Interventional strategies modulating inflammation and immunosuppression involved in tumor progression

LABORATORY CELLULAR IMMUNITY - Director: Dr. Dorel Radu Lucian, dorel.radu@cantacuzino.ro.

Research directions:

Conducted studies of **autoimmunity** or **immune-infective conventional or transgenic murine models**, the main focus is on applied research.

Scientific activities:

- Autoimmunity: Experimental **model of type 1 diabetes**
  - The investigation of cellular and molecular mechanisms involved in the onset of insulin-dependent diabetes mellitus in a double-transgenic mouse model.
  - Exploration and evaluation of complications induced type 1 diabetes using an animal model and different therapeutic modalities.
  - Preliminary study on experimental murine model of diabetic neuropathy
- Infective immunity:
  - Addressing the three research sections **influenza infection** and means of protection through **vaccination**
  - The study immune response in experimental models of infection with Gram positive and Gram negative.
- Nanotechnology**:**
  - Studies **in vitro toxicological and pharmacological profile** type fullerene compounds.

Immunomodulation Research - Director: Lidia Cremer - immunomod@cantacuzino.ro

Research Areas:

Aimed at developing experimental models in vivo and in vitro that provide information about immunomodulatory properties of natural compounds / purified synthetic:

- Involving the products analyzed in biological activities such as transport pumps modulation (Pgp, MRP) expressed on various normal and tumor cell lines.
  - Involved in the **development of resistance to antibiotics and chemotherapeutic** substances.
- Inhibiting the activity of enzymes involved in arachidonic acid metabolism (COX-2, 5-LO);
- Modulating NF-kB signaling through, PI3K, Akt / PKB or triggered by activating PPAR-γ Toll-like receptors (TLRs) and Dectin1.

Experimental Pathology Laboratory - Director: Dr. Bogdan Marinescu Veterinarian mbogdan@cantacuzino.ro

Industry: - Experimental Medicine

- Basic activities in achieving operational procedures performed in laboratory animals to undertake specific projects.
- Research in achieving experimental models for laboratory animals.
- Carrying out tests *"in vivo"* toxicity test abnormal (IV) hypersensitivity test in guinea pigs.

Laboratory cell receptors - Director: Cristiana Matache, PhD in biochemistry, CIS cristianamatache@cantacuzino.ro

The main scientific objectives:

- study cellular and molecular defects involved in connective tissue diseases etiopathology
- deciphering the cellular and molecular mechanisms that control the balance between immunity and tolerance in normal and pathological conditions (CTD)
- Identification of cellular processes or abnormal extracellular proteins that enter and potential targets of therapy for diseases of connective tissue.

Research projects:

- Genomics and proteomics research in the pathogenesis of **systemic sclerosis** in order to open new therapeutic perspectives
- Studies **in vitro induction of regulatory T cell expansion** - a new therapeutic approach in autoimmune diseases, allergy and to prevent graft rejection

Activity:

- Studies of Systemic **Lupus Erythematosus (SLE)** in order deciphering cellular and molecular mechanisms responsible for the status of hyperactivation of peripheral lymphocytes (PBLs)
- Studies conducted in order to regulate cellular and molecular mechanisms disrupted LES

Technological Platform - Director: Julian Radu TĂNASĂ, doctor, veterinarian, CS III - rtanasa@cantacuzino.ro

- Established to provide access Institute researchers in the **development of reagents and tests**.

Our main research interests include development:

- production of monoclonal antibodies against major zoonotic pathogens for public health (influenza virus)
- immunoassays based on monoclonal antibodies
- research in immunity and the pathogenesis of viral infections
- research on neonatal immunity
- Development of monoclonal antibody / recombinant human therapeutic potential.

Projects Categories:

- Projects Ideas
- Excellence Research Projects
- Biotech
- Microdm
- Renar
- Viasan : Partnerships Projects in Priority Areas ----- FP7
- EDENext : PCCA-II ----- Project Capacity ----- Structural Projects

Production

A. production of serums and other blood products which include:

- seruri microbiological diagnosis and immunochemically obtained from horses, sheep and rabbits
- seruri normal animals (ox, horse, rabbit)
- Other blood products (red ram, horse, rabbit, guinea pig, poultry etc.)

B. Production of laboratory animals:

- Soareci, rats and hamsters, specific pathogen-free (SPF) increase in animalerie Baneasa, unit increase special type.
- Cobai and rabbits bred and maintained in traditional terms, conventional.

C. Activities research is done mainly by performing experimental procedures on laboratory animals and creating experimental models

D. Production granulated fodder for animals provided by its own combined fodder factory and warehouse work needed raw materials and finished products.

E. household administrative activity, security, technical service, car compartment and diverse materials including storage of concentrated feed and fiber.

F. operating activities of agricultural land Comprises agricultural technologies cultivation of arable land and harvest of feed.

Areas addressed

- Preclinical in vivo pharmacological tests
- Testing new components of compound feed granules used in laboratory animal feed
- Study of the effect of modulators on tumor cells
- Study of stem cells on regeneration of the sciatic nerve
- The study immunological effects of leptin
- Study of the effect of drugs regulating estrus
- The use of biomaterials in bone regeneration

- Production of serum diagnosis for the detection of toxins in food
- Developing a test method inflammatory activity of pharmaceutical products, in vivo

Medical services

INTERNAL CONTROL LABORATORY – head of laboratory: **dr. Denissa-Manuela Michael**,MD

The Laboratory tests are carried out to control **biological products**, in vitro **diagnostic reagents**, decontaminating products / disinfectants / antiseptics, the European Pharmacopoeia and ISO standards, applying their own procedures validated

Functional structure laboratory

I. Compartment: Microbiology – Sterility - RESPONSIBLE: DR. Deniss MIHAI - primary health laboratory medicine

Methods applied:

1. Sterility 2. Microbial load 3. *Microbiological testing of non-sterile products* 4. *Microbiological efficacy tests*

5. "Potency" bacterial vaccines 6. *Safety tests (microbiological) Vaccines*

II. Compartment: laboratory tests on small animals, embryonated hens' eggs. RESPONSIBLE: DR. Mihai Perescu

Methods applied:

1. Tests on laboratory animals small 2. Tests on embryonated chicken egg

III. Compartment: Tests on cell systems - RESPONSIBLE: Biol. PR. MARIA Orăşanu

Methods applied:

1. Testing of virus concentration by titration of infectivity in cell culture

2. Testing hemadsorbanţi foreign agents in viral vaccines for human use

3. Testing in cell culture of foreign agents in viral vaccines for human use

4. Test for intact cells

5. Testing Equine Immune cell cultures for contaminating viruses

6. Bacterial endotoxins

IV. Compartment: Physico-chemical - RESPONSIBLE: GABRIELA GHERGANU, research assistant CHIMIST

Methods applied:

1. General Tests 2. Analytical Biochemistry 3. Enzymatic 4. Biological methods - Binding Assays

National Reference Laboratories

1- Medical entomology lab - Head of laboratory: Dr. Biol. Gabriela Nicolescu, entomol@cantacuzino.ro

Participation in national programs:

- National surveillance program of vector insects, including studies and Environmental epizootological

Participation in international programs:

- European Surveillance Program vector-borne infections

Research activities (for details see section "Research"):

- internal research programs funded by the Ministry of Education and Research and other internal financiers
- programs funded by the European Commission (collaboration with laboratories vector-borne infections and parasitology)
- Participation in research programs funded by the Pasteur Institutes and Associated 9 Reteaua RIIPIA)

2- Molecular Epidemiology Laboratory - Director: Dr. Biol. **Maria DAMIAN** SC I, mdamian@cantacuzino.ro

Area of work

- Development and implementation of molecular methods in **medical diagnostic** and **laboratory surveillance** of communicable diseases.
- In the transfer of technology, Molecular Microbiology lab conducts training.
- Participant in national public health programs providing diagnosis and molecular typing of infectious agents involved in epidemics.

Specific objectives of research activity

- Molecular studies on virulent pathogen and / or condition of pathogenic and opportunistic involved in infectious diseases
- Genetic and molecular mechanisms of **antibiotic resistance**
- Improving laboratory methods for diagnosis, epidemiology and treatment of infectious diseases
- Molecular **diagnosis of microorganisms non cultivable**
- Typable Molecular characterization of microorganisms by classical methods of microbiology
- Studies on microbial variability impact on the methods of diagnosis and pathogenesis of infections
- Preparation laboratory for a **quick response** in case of microbiological alert.

3- Laboratory hepatitis -

- National programs: National program of surveillance and control of infections with hepatitis viruses
- International programs:
    - DG-SANCO programs (European Commission)

- ESSENTIAL 2 - European seroprevalence study for vaccine-preventable diseases (**hepatitis A and B** immune status)
- PHARE programs (European Commission):
- Technical Assistance for Improving the System for Epidemiological Surveillance Romanian and Control of Communicable Diseases

WHO programs:

- WHO Lyon Office Program for Strengthening Capacities for Communicable Diseases Laboratory Detection and Response
- Participation in external quality control programs International

4- Laboratory Anaerobic infections - Head of Laboratory: Dr. Daniela Lemeni (dlemeni@cantacuzino.ro)

- Isolation of anaerobic microorganisms sporulated and nesporulaţi of biological taken by classical bacteriological methods.
- Identification / confirmation anaerobic microbial strains isolated in laboratories in the field.
- **Presence of botulinum toxin** in the serum, food, fragments necropsy, the mouse lethality test.
- Determination of the presence of ***Clostridium perfringens* toxin** serum food autopsy fragments by intraperitoneal inoculation in mice.
- Antibiotic susceptibility testing of anaerobic microorganisms by diffusion method.
- Presence of **Clostridium difficile toxins** in the stool sample amended (diarrhea).
- Test Ehrlich tetanus antibody identification.
- Jensen Test to identify antibodies against diphtheria.

National programs:

- National surveillance program of nosocomial infections
- National Epidemiological Surveillance Program for botulism

5- Vector-transmitted laboratory infections and medical entomology - Laboratory Director Dr. Med. Daniela Badescu - danielab@cantacuzino.ro

Activities:

1. Diagnosis and microbiological expertise vector-borne infections and also in infections caused by *Coxiella burnetii, Ch. Psittacii, Mycoplasma pneumoniae and Legionella pneumophila* for :

- National **surveillance program arboviral meningitis**
- Surveillance of *Legionella pneumonia*
- ENIVD European program: European Network for Diagnostics of Imported Viral Diseases

2. Research programs

3. Preparation residents and specialist's laboratory medicine and epidemiology

6- Laboratory bacterial enteric infections - Director: Dorina Tatu-Chitoiu, MD, dtatu@cantacuzino.ro / enterobact@cantacuzino.ro

Three **bacterial enteric** infections:

- CNR for: Salmonella- E. coli and enteric Fagi (responsible dr. Dorina Tatu-Chitoiu)
- Shigella CNR (responsible Dr. Lucia Ciudin)
- Vibrio CNR (responsible Dr. Anca Michaela Israel)

National programs:

- National surveillance program of acute diarrheal diseases (BDA)
- National surveillance program and antibiotic-resistant nosocomial infections (IN).

International programs:

- European Surveillance Program Foodborne Infection and hydrate (ECDC / TESSy)
- European Program for Antimicrobial Resistance Surveillance (EARSS)

7- Laboratory viral enteric infections –Director Dr. Baicus Anda, MD, PhD, lecturer, CSIII, abaicus@cantacuzino.ro

Objectives:

- Examination by classical and molecular diagnostic techniques in the field of **enteroviruses and rotavirus infections**.
- Harmonisation of the molecular analysis of isolates to participate in the international competitive research

International / national programs:

- accredited within the Global Polio Laboratory and participating in the WHO Programed Global Polio Eradication
- studying the genetic variability of strains of poliovirus and enterovirus nonpolio isolated on Romanian territory
- The national program of surveillance of cases of acute flaccid paralysis (PAF)
- National surveillance program acute viral meningitis
- The national program with rotavirus diarrheal disease surveillance

8- Laboratory nosocomial infections and antibiotic resistance - Director: Irina Codita, CS I (icodita@cantacuzino.ro)

Nosocomial infections and antibiotic resistance in national programs:

- Program for sentinel surveillance of nosocomial infections
- National program of **antibiotic resistance surveillance**: including surveillance of microorganisms isolated from invasive infections, according System protocols European Antimicrobial Resistance Surveillance (EARSS) etc.

- Participate in conducting external quality control in the EARSS and receives strains for characterization in the context of external quality control schemes for antibiotic susceptibility testing and / or identification of bacterial microorganisms.

Nosocomial Infections Laboratory and resistance to antibiotics *is composed of two National Reference Centre:*

- National Reference Centre for **Staphylococcal**
  - The investigation of pathogenicity and circulation various staphylococcal species and clones
  - Identification of species and subspecies to establish the **prevalence** of different taxa in infections and healthy carriers required for interpreting results of microbiological investigation
  - **Typing strains** in epidemiological investigations by phenotypic methods and / or molecular detection of epidemic strains and / or endemic species and sources and transmission pathways of epidemic or endemic infections.
  - Study of **antibiotic resistance**: study of phenotypic characters of strains circulating resistance and genetic mechanisms
  - Objectives taking **quality assurance and reliability** of laboratory analyzes in the microbiological diagnosis of staphylococcal infections.

- National Reference Centre for **Pseudomonas**
  - Making microbiological diagnosis for determining the **prevalence** of different taxa in infections and healthy carriers.
  - Orientation surveillance and control measures Pseudomonas infections by determining phenotypic markers epidemiological and /or molecular
  - The study of **antibiotic resistance** by detecting new phenotypes of antibiotic resistance genes and the mechanisms involved, especially multidrug-resistant bacteria.
  - Objectives taking quality assurance and reliability of laboratory analyzes in the microbiological
  - Contribution to continuing education programs to support bacteriology laboratories nationwide to detect emerging resistance mechanisms.

9- Laboratory bacterial respiratory infections - Director: Vasilica Ungureanu, MD, vungureanu@cantacuzino.ro

Respiratory bacterial infections: streptococcal infection, pneumococcal infections, meningococcal infections, whooping cough, Haemophilus infections, diphtheria, etc.

Work on these National Reference Centre:

- National Reference Center for Streptococci, Enterococci and Meningococcal - Center Director Dr. Vasilica Ungureanu
- National Reference Centre for corynebacteria - Center Director Dr. Angela Diaconescu
- National Reference Centre for pertussis and Haemophilus - Center Director Veronica Alecu
- National reference centers provides highly specialized services for microbiological diagnosis of infectious diseases.

National programs:

- National surveillance program streptococcal infections
- Diphtheria national surveillance program
- National surveillance program of pertussis

- National surveillance program meningitis
- National surveillance program of nosocomial infections
- National program of surveillance of antibiotic resistance

International programs:

- DG-SANCO programs (European Commission)
- ESSENTIAL 2 - European seroprevalence study for vaccine-preventable diseases (diphtheria, tetanus)
- DIPNET: European Network for diphtheria surveillance
- EARSS: The European Antimicrobial Resistance Surveillance
- The European Group of meningococcal disease study
- International quality external programs streptococcus, enterococcus, diphtheria, haemophilus
- PHARE programs (European Commission):
- Technical Assistance for Improving the System for Epidemiological Surveillance

WHO programs:

- WHO Lyon Office Program for Strengthening Capacities for Communicable Diseases Laboratory Detection and Response

Research activities:

- internal research programs funded by the Ministry of Education and Research and other internal financiers (3 projects)
- Research programs funded by the European Commission (FP5 program: Severe *Streptococcus pyogenes* disease in).
- Programs Ripi (Pasteur and Associated Institutes Network) - diphtheria study and supervision.

10- Laboratory vector-borne infections - Head : Daniela Badescu MD, PhD., danielab@cantacuzino.ro itv@cantacuzino.ro

In the laboratory works:

- National Reference Centre for Rickettsia - Center Director Dr. Med. Daniela Badescu
- National Reference Centre for Borrelia - Center Director Dr. Med. Daniela Badescu
- National Reference Centre for Viral vector-borne infections (infections with West Nile virus, hantavirus, v. Encephalitis tick)

National programs:

- National surveillance program arboviral meningitis
- Surveillance of *Legionella pneumonia*

International programs:

- Contact ENIVD: European Network for Diagnostics of Imported Viral Diseases
- Training CDC Atlanta

11- Laboratory parasitosis – Director: Professor Dr. Biol. Dan Steriu, CS II (parazit@cantacuzino.ro)

National Reference Centre for parasitic infections - Center Director Prof. Dr. Biol. Dan Steriu

Participation in international programs, in collaboration with similar institutes and / or other institutions

12- Laboratory sexually transmitted infections - Dr. Dan Ionescu - e-mail.: bts@cantacuzino.ro

Work on:

- Syphilis,
- N. gonorrhea infections,
- HIV
- Chlamydia,
- HPV

National programs:

- National Program for Sexually Transmitted Infections Surveillance with the following duties:
  - Current Diagnosis and diagnostic reference
  - Development of diagnostic methodology
  - Educational activity for specialists in the field
  - Epidemiological and antibiotic resistance
  - Research Activity
  - Production of diagnostic reagents

International programs:

- Global Fund Program - HIV / AIDS surveillance
- NAMRU 3 - (USA) genotyping HIV

13- Laboratory of Microbial Culture Collection - Director: Rodica Oancea, Biol. Pr. (microcult@cantacuzino.ro)

- Maintenance activity setting collection of reference strains and delivery to beneficiaries
- determining the **fungicidal activity of disinfectants and antiseptics** in collaboration with the Laboratory fungal standards
- Research Activity

National programs:

- National surveillance program of nosocomial infections
- National surveillance program for the antifungal resistance