STEPHAN ANGELOFF INSTITUTE OF MICROBIOLOGY

MEMBER OF THE BULGARIAN ACADEMY OF SCIENCES
MEMBER OF THE PASTEUR NETWORK

ANNUAL REPORT 2023

26, Georgi Bonchev street, Sofia 1113, Bulgaria
tel.: +359 2 979 31 57; +359 879 499 167
e-mail: micb@microbio.bas.bg
www.microbio.bas.bg

Information was collected and structured by
Assoc. Prof. Ekaterina Krumova
Assoc. Prof. Petya Dimitrova
Sofia, February 2024

OUR MISSION

Prof. Penka Petrova

The Director of the Stephan Angeloff Institute of Microbiology

„Our mission is to drive the excellence in microbiological research in Bulgaria and carry out scientific research in areas important to society.

Our priority is to support the career development of all researchers with high potential."

The mission of the Stephan Angeloff Institute of Microbiology is to address national and global challenges in health and industry and to contribute to problem-solving with innovation, research, and collaboration in microbiology, virology, immunology, and biotechnology.

Priorities

In microbiological research

- To consolidate research in the field of microbiology in Bulgaria by discovering and describing the diversity of non-pathogenic and pathogenic microorganisms.
- To identify food microbial contamination.
- To identify the mechanism of antibiotic resistance.
- To find a solution for soil pollution by studying the physiological response of microorganisms to heavy metals, phenol, and oil products.
- To identify sustainable anaerobic systems for efficient energy production.
- To study the impact of climate change on microbial diversity

In health

- To find solutions for maintaining a healthy microbiome with pre-, pro-, and post-biotics.
- To design novel therapeutic approaches to vaccination and to study the effect of new drugs on cancer, infectious and autoimmune diseases, acute and chronic conditions, and aging.
- To put forth new diagnostic tools for immunotherapy and disease pathogenesis.
- To identify new natural inhibitors with antiviral and antibacterial activity, and novel approaches to escape anti-microbial resistance and biofilm formation.

History of the Institute

In service to our society

We would like to contribute and help our society to overcome societal, national, and global challenges in climate and health with expertise, and theoretical and practical knowledge through collaborative and multidisciplinary research.

We adjust our research activity to National Priorities

REPUBLIC OF BULGARIA
Ministry of Education and Science

We adjust our activity according to the National Strategy for Scientific Research Development in Bulgaria in 2017-2030. The National Priorities are:

- **large-scale, rapid, and long-term development and modernization of research infrastructure;**
- **cutting-edge research innovation and technologies;**
- **improving the research ranking of Bulgarian scientists;**
- **increasing public trust in research and innovation;**
- **provide opportunities for young people to develop research careers.**

We adjust our research activity to EU priorities

We focus our activity on the priorities of "Horizon Europe" 2021-2027. We perform investigations on the following topics:

- **Health and quality of life;**
- **Prevention, early diagnosis, and therapy;**
- **Green, blue, and eco-technologies;**
- **Biotechnology and eco-foods;**
- **Environmental protection;**
- **Environmental monitoring;**
- **Utilization of raw materials and bioresources;**
- **Purifying and waste-free technologies.**

We align our research with the strategy of the Bulgarian Academy of Sciences

BULGARIAN ACADEMY of SCIENCES 1869

We value and align our strategy with the policy of the Bulgarian Academy of Sciences in:

- **Human resources;**
- **Infrastructure;**
- **Balance in scientific research - fundamental and applied;**
- **Regional strategy for research development.**

We adjust our priorities to the priorities of the Pasteur Network

INSTITUT PASTEUR

The role of the Pasteur Network is to help improve public health by dealing with infectious agents, through:

- **Biomedical research;**
- **Public health activities;**
- **Education;**
- **Innovation and technology transfer.**

The activities are performed by sustainable development and building up local capabilities while respecting human rights and the environment.

OUR STRUCTURE

Total employees: 155 persons
Governing body: 4 persons
Administrative body: 27 persons

- Human resources
- Accounting
- Public Relations
- IT Maintenance

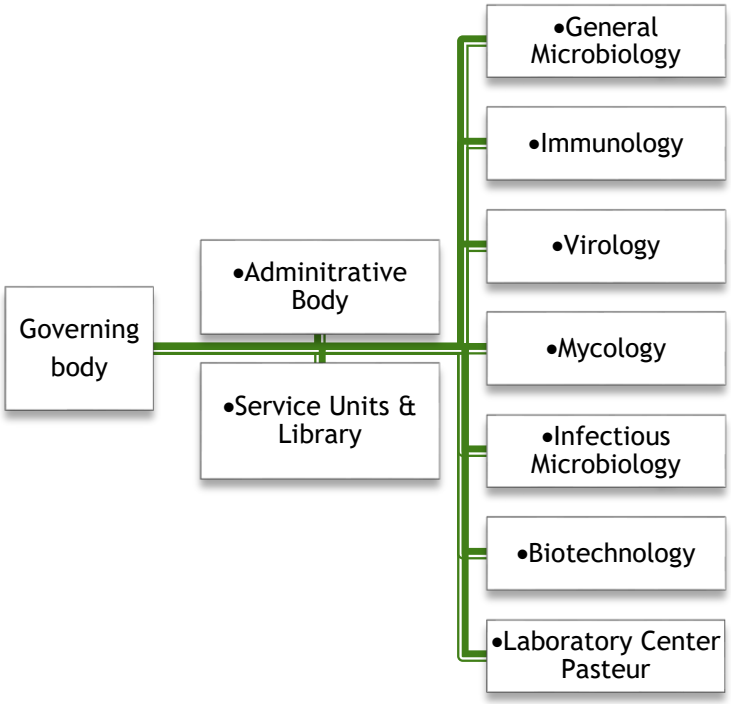
Scientific staff: 111 persons

- Departments
- Laboratory Center Pasteur

Library: 1 person
Service units: 12 persons

- Cell Culture Medium Lab
- Fermentation Lab
- Animal Facility
- Technical Service Unit

Associated Alumni Members: 14



CONTROL

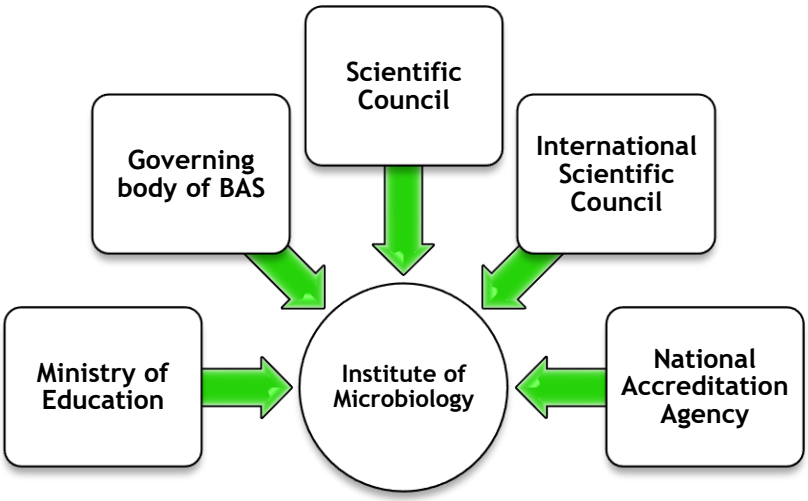
Scientific council: 20 members - Control over the Institute's mission and research goals

International Scientific Council: 11 members, Control over Research Excellence

Governing body of Bulgarian Academy of Sciences (BAS): Control over Financial policy, Human resources and Career Development

Bulgarian Ministry of Education: Control over National Regulations and Priorities in Science and Education

National Accreditation Agency: Control over the Quality of Education



POLICY-DRIVEN RESEARCH IN BULGARIA

The European Regional Development Fund (ERDF) and the Cohesion Fund (CF) support the economic social and territorial cohesion of the European Union. They contribute to reducing the disparities that still exist between European regions and countries. The European Social Fund + (ESF+) guides the implementation of the principles of the European Pillar of Social Rights.

Learn more about the priority

According to the draft Regulation of Common Provisions for the 2021-2027 programming period, the ERDF, the ESF+, the Cohesion Fund, and the EMFF support five policy objectives:

Policy objective 1: Smarter Europe by promoting innovative and smart economic transition (CP 1);

Policy objective 2: A greener, low-carbon Europe by promoting a clean and fair energy transition, green and blue investments, circular economy, climate change adaptation, and risk prevention and management (CP 2);

Policy objective 3: A better connected Europe by improving ICT mobility and regional connectivity (CP 3);

Policy objective 4: A more social Europe — realizing the European Pillar of Social Rights (CP 4);

Policy objective 5: Europe closer to citizens by promoting the sustainable and integrated development of urban, rural, and coastal areas and local initiatives (CP 5).

CENTERS OF COMPETENCE - PART OF POLICY CP1 AND CP2

ОПЕРАТИВНА ПРОГРАМА НАУКА И ОБРАЗОВАНИЕ ЗА ИНТЕЛИГЕНТЕН РАСТЕЖ

Project BG05M2OP001-1.002-0001 „Basic, translational and clinical research in the field of infections and infectious immunology“

PI for Institute of Microbiology: prof. Andrey Tchorbanov

clean circle

Project BG05M2OP001-1.002-0019 „Clean technologies for a sustainable environment - water, waste, energy for a circular economy" (Clean&Circle) for the construction and development of a Competence Centre

PI for Institute of Microbiology: prof. Penka Petrova

EU PROJECTS

PlantaSYST H2020 Widespread 2014-1 Teaming Establishment of a Center of Plant Systems Biology and Biotechnology (CPSBB) in Plovdiv, Bulgaria

PI for the Institute of Microbiology: Prof. Milen Georgiev

NATIONAL PROGRAMS

The National Scientific Program "Healthy Foods for a Strong Bioeconomy and Quality of Life" (NNP-FOOD)

PI for the Institute of Microbiology: Prof. Hristo Najdenski

The National Program "Healthy Foods for a Strong Bioeconomy and Quality of Life" (NNP-FOOD) has as its main goal to create adapted modern models and technologies for the production of healthy foods for a strong regional bioeconomy and to improve the quality of life of the population of the Republic of Bulgaria.

The program builds the capacity and knowledge in leading priority areas "Food security, sustainable agriculture and forestry, marine and inland water research and the bioeconomy" under the European Union Framework for Research and Innovation "Horizon 2020".

The National Scientific Program "Innovative low-toxic biologically active agents for precision medicine" (BioActivMed)

PI for the Institute of Microbiology: Prof. Hristo Najdenski

The National Program "Innovative low-toxic biologically active agents for precision medicine" aims to conduct fundamental and applied scientific research on the discovery and development of new biologically active substances derived from Bulgarian natural sources and to investigate their application as remedies to overcome multidrug resistance.

Bulgaria, with its unique climatic and ecological niches, offers an amazing variety of plant and animal species extracts containing less toxic and better tolerated biologically active compounds than synthetic ones.

The National Program "Young scientists and postdoctoral fellows - 2".

The program aims to attract, retain, and develop highly qualified young scientists and postdoctoral fellows, thus ensuring a qualitative reproduction of the human potential for research work in Bulgaria.

„Up to BGN 3,000 per month can be received by young researchers in Bulgarian higher schools and scientific organizations“.

-Ministry of Education’s news portal

Approved proposals: 4 young scientists, 2 postdocs

AWARDS AND ACHIEVEMENTS IN 2023

Our young scientists receive awards and show research excellence

Young scientist Nikola Ralchev, a PhD student in the Department of Immunology received the prestigious Ivan Evtstiev Geshov award from the Bulgarian Academy of Sciences for achievements in the field of Biomedicine and Health.

Fourth Interdisciplinary Doctoral Students Forum with International Participation

The Ph.D. students, Vladislava Dishliyska from the Department of Mycology and Nikola Ralchev from the Department of Immunology received the award for the Best Oral Presentation at the IVrd Interdisciplinary International Ph.D. Forum, 16-19 May, Sandanski organized by the Training Center at the Bulgarian Academy of Sciences and the Career Center at the Central Academy of Sciences and Arts.

We receive awards for our collaborative efforts

The University of Chemical Technology and Metallurgy granted the Director, Prof. Penka Petrova, the Honor for long-standing partnership and contributions in the field of education and science.

Our scientists are awarded for their efforts to reach research excellence

Prof. Hristo Naydenski received the Award for High Scientific Achievements from the Union of Scientists in Bulgaria

Science and Business

BULGARIAN SMALL AND MEDIUM ENTERPRISES PROMOTION AGENCY (BSMEPA)

Over 200 representatives of business and academia took part in the event of the Bulgarian Small and Medium Enterprises Promotion Agency and the Bulgarian Academy of Sciences - „Science for Business“ on the 27th of April 2023

Stephan Angeloff Institute of Microbiology presented the developments, prototypes, and new technologies, ready to turn into a successful business.

Assist. Prof. Venelin Hubenov, Ph.D. gave a talk on "Waste bio sludge treatment agent for the cultivation of microalgae". Assoc. Prof. Galina Stoyancheva, PhD, presented the synbiotic product containing selected strains of *Lactic acid bacteria*. Assist. Prof. Nikolina Atanasova showed how microorganisms can be used in the fight against plastic waste.

The Bulgarian Antarctic Expedition

The microbiologist and biotechnologist Assoc. Prof. Snezhana Rusinova from the Laboratory of "Cellular Biosystems" at the Stephan Angeloff Institute of Microbiology, participated in the 31st Bulgarian Antarctic Expedition to Livingston Island.

Her project "Biotechnological approach for obtaining biologically active molecules from Antarctic yeasts" aims to track the biodiversity of Antarctic yeasts and to explore their potential for synthesizing biologically active molecules with pharmaceutical applications.

COLLABORATION FOR EXCELLENCE

RESEARCH NETWORKS

Networking is a key factor for our growth as researchers

- PN - Pasteur Network
- OCUVAC - Center of Ocular Inflammation and Infection
- MED-VET-NET - Network for Prevention and Control of Zoonoses
- FLAG ERA - DeGraph - Bacterial degradation of GRMs
- Global Initiative to Promote the Study of Fungal Biodiversity
- Global Mountain Biodiversity Assesment
- World *Mycobacterium bovis* Characterization Project
- FATE - Fight Against Tuberculosis

COST ACTION

Open to all science and technology fields, including new and emerging fields; COST Actions offers an inclusive, pan-European environment for individuals of all levels of seniority to grow their professional research networks and boost their careers

- **COST Action CA18101**
  SOURDOugh biotechnology network towards novel, healthier and sustainable food and bioprocesses
- **COST Action CA1713**
  Implementing nature based solutions for creating a resourceful circular city
- **Cost Action CA18127**
  International Nucleome Consortium
- **COST Action 21164**
  Towards an improvement in diagnostics and treatment strategies for TB control (ADVANCE-TB)
- **COST Action CA20121**
  Bench to bedside transition for pharmacological regulation of NRF2 in noncommunicable diseases
- **COST Action CA21145**
  European Network for diagnosis and treatment of antibiotic-resistant bacterial infections (EURESTOP)

NEW COLLABORATIONS

南京理工大学
NANJING UNIVERSITY OF SCIENCE & TECHNOLOGY

National Science Fund supported the bilateral cooperation between Bulgaria and China

The researchers from Stephan Angeloff Institute of Microbiology built a strong collaboration with Nanjing University of Science and Technology

The researchers from The Stephan Angeloff Institute of Microbiology participate in a Bulgaria - China - research project: “Experimental studies, modeling, observation, and extremum seeking optimal intelligent control technology research of two-phase anaerobic digestion process of lignocellulosic wastes with the production of hydrogen and methane”.

During its implementation, two-stage anaerobic digestion processes for optimization and control performance using mathematical models and automatic control theory for bioenergy production were achieved and the overall energy conversion efficiency with high yields of hydrogen and methane was realized with stable microbial consortia. New data on anaerobic digestion mediated by novel microbial consortia could be widely used to utilize wastes for green energy production in a sustainable way. The developed biotechnology can be successfully incorporated into the circular economy concept.

PROOF OF CONCEPT INTERNATIONAL PROJECTS

PI: Assist. Prof. Milena Leseva	m6A_RAIAV The lung epitranscriptome and chromatin accessibility landscape in rheumatoid arthritis complicated by the flu. Institut Pasteur International Network, 2020-2023
PI: Prof. Andrey Tchorbanov	VacciNanoCor Generation of Humanized NSG transfer mouse model for coronavirus SARS-CoV-2 vaccine testing. Institut Pasteur International Network, 2020-2022
CoPI: Prof. Svetla Danova	JINR Nuclear Regulatory Agency (NRA): Effect of ionizing radiation on probiotic strains of bacteria and yeast. International Institute for Nuclear Research Dubna, 2021 – 2022
CoPI: Prof. Hristo Najdenski, DVM, DSc	Technology model for microbial degradation of cellulose containing wastes in life support systems for manned space flights, contract No 4000126327/18/NL/SC – 09.01.2019, 2019-2021.
CoPI: Assist. Prof. Diliana Simeonova	FLAG-ERA: DeGraph – Bacterial degradation of GRMs. Universite de Strasbourg, CNRS, Helmholtz-Institut Freiberg für Ressourcentechnologie, 2021-2024

FINANCIAL POLICY

At the national level, our research is a part of the national resilience plan potential

National Plan For Recovery And Sustainability Of The Republic Of Bulgaria

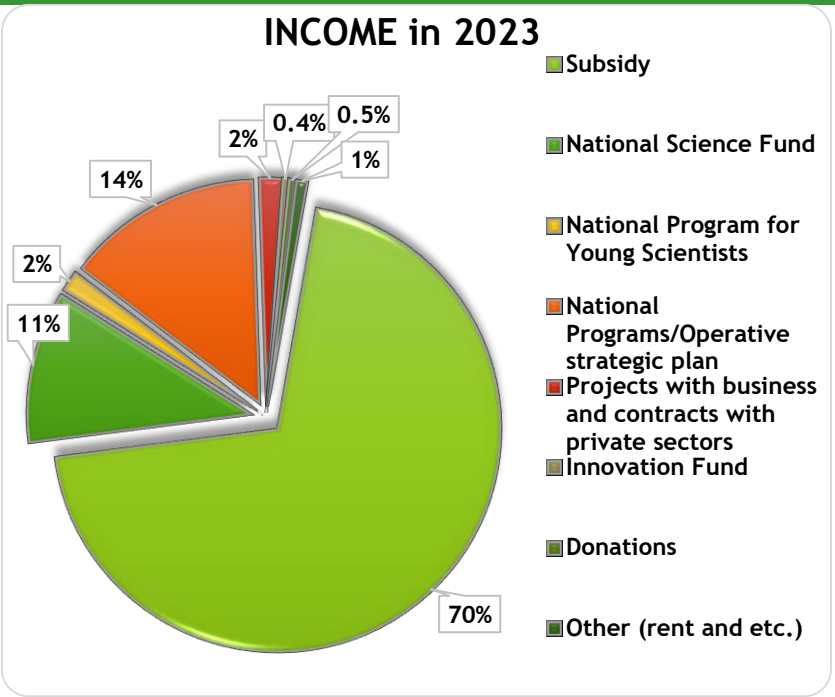
The Recovery and Resilience Facility is part of the Next Generation EU (2021-2024) instrument of the Recovery and Resilience Plan (RSP). The main objective of the PVA is to facilitate economic and social recovery from the crisis caused by the COVID-19 pandemic.

INCOME

70% of the income in the Institute is due to a subsidy that covers mainly salary.

Our Institute received **14%** of its total budget as co-funding from the National Programs.

Only **2%** of the income is from the collaborations with private sector.

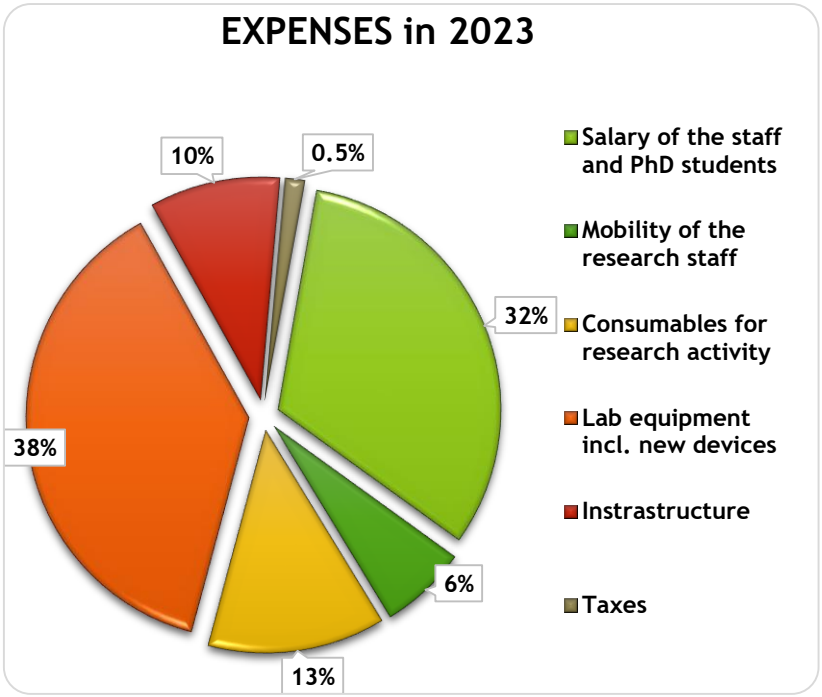


EXPENSES

32% of the expenses of the subsidy are for the salary of the staff and PhD students.

Only **10%** of the income (incl.subsidy) are for maintaining the infrastructure.

38% of the income from research project projects is for lab equipment and new devices and **13%** for lab consumables.

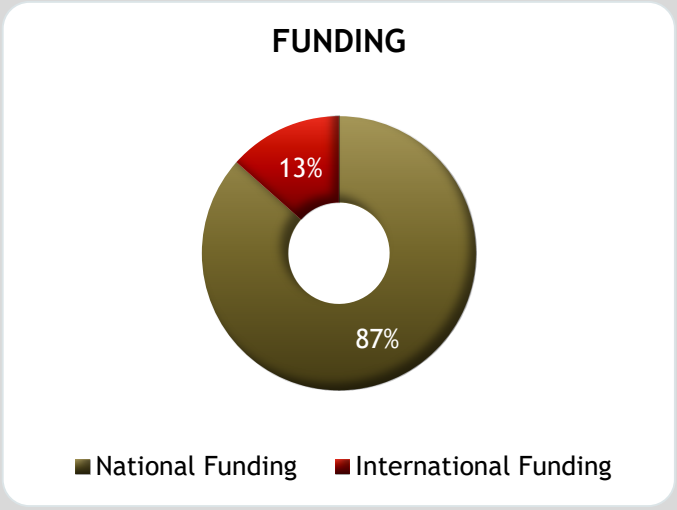


GRANTS

National Funding: 67 grants

- Bulgarian National Science Fund: 41 projects
- Other funding at the national level: 26

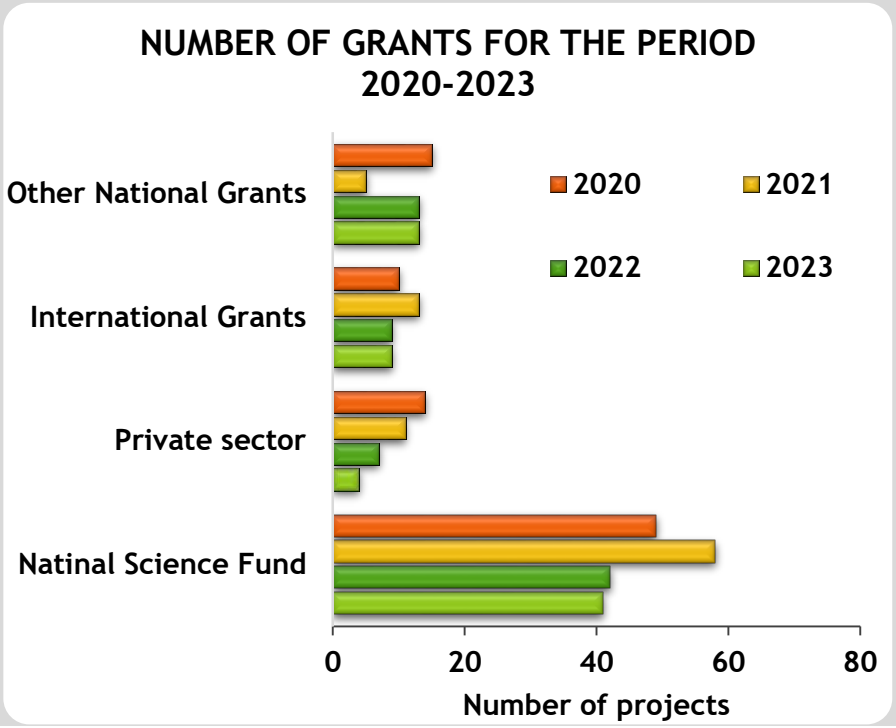
International Funding: 9 grants



TRENDS IN FUNDING

Project > 150 000 BGN: 20

Project < 150 000 BGN: 47



RESEARCH ACTIVITIES IN NUMBERS

PUBLISHED ARTICLES

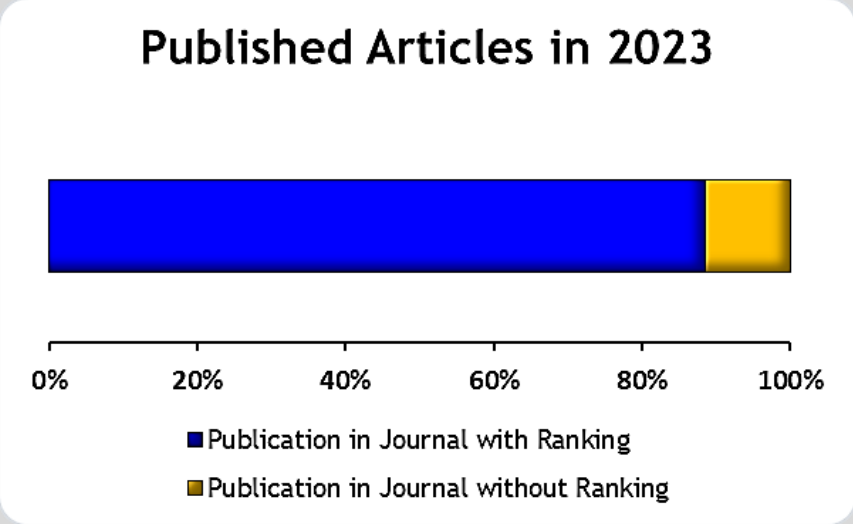
Published articles:119

Publications in Scopus/Web of Science Database:101

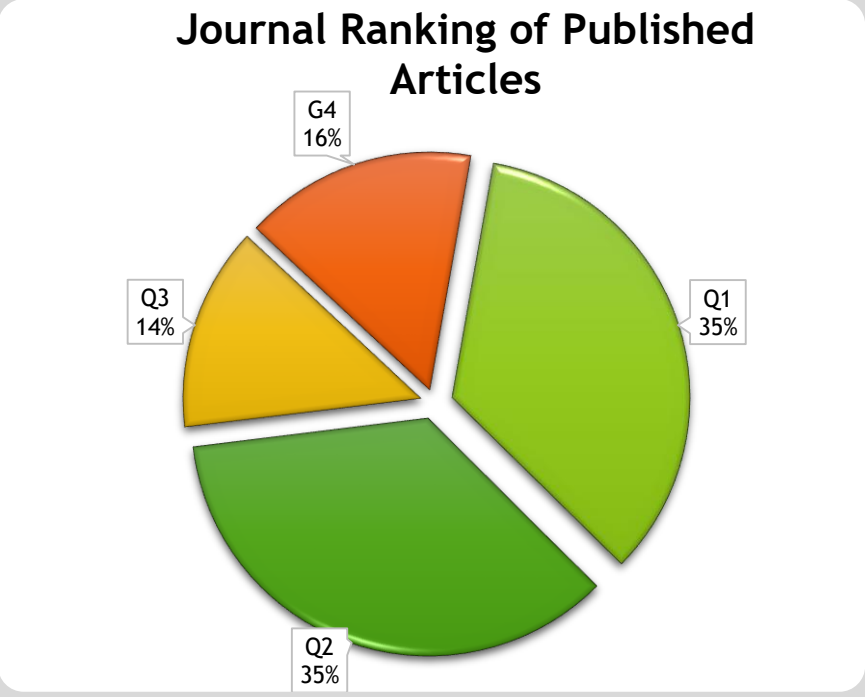
Other publications: 18

***Q - Quartile rankings upon Journal Citation Report**

85% of published articles in 2023 are in Journals with a Ranking

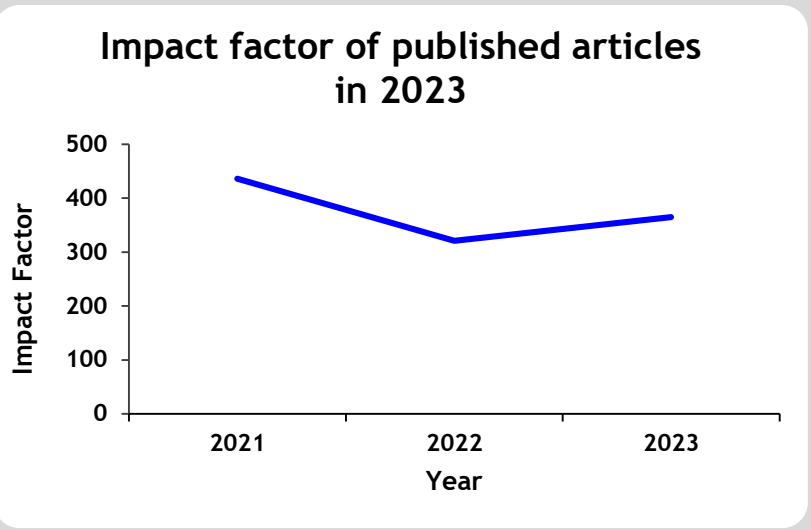


49% of published articles are in a category of the High Ranked Journals



The number of published articles decreased with 1.13 times compared to 2022.

The quality of published articles was similar to 2022.



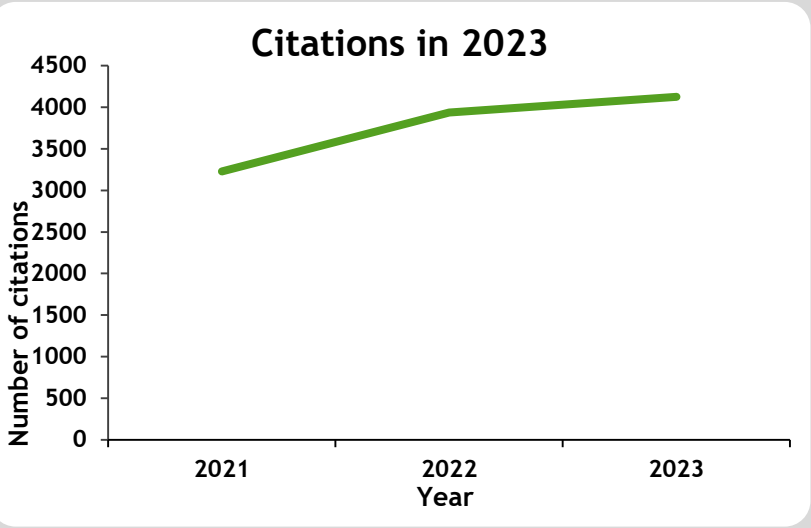
Citations

Total citations: 4128

Citations in Scopus/Web of Science Database: 3471

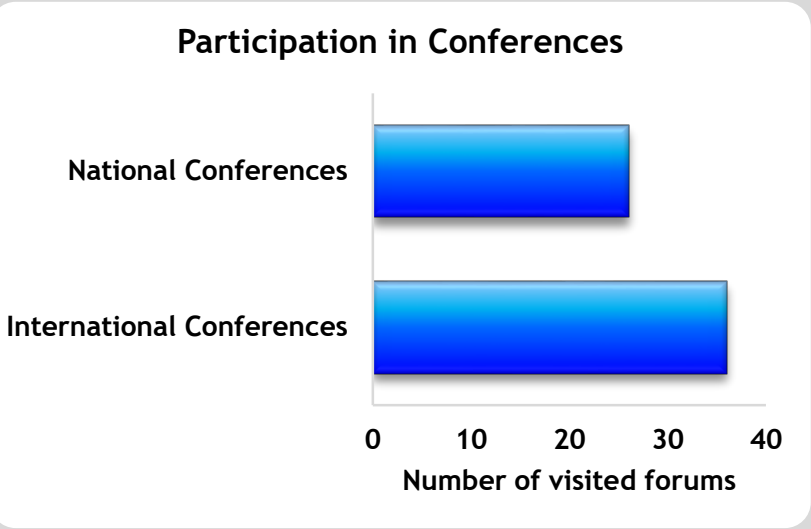
Cited articles: 757

The number of citations increased 1.56 times compared to 2019.



Scientific conferences

We want to get to know other people and use the benefits and opportunities at each conference for networking.



WHAT WE HAVE ACHIEVED IN 2023..

Department of General and Applied Microbiology

Head:
Prof. Penka Petrova, PhD, DSc
Tel.: +359 2 979 31 79
E-mail: pepipetrova@yahoo.com

Laboratories:

- Cellular Microbiology
- Microbial Genetics
- Microbial Biochemistry
- Extremophilic Microorganisms

1. We boost research in microbiology

- We studied the nutritional value and food safety of microbial enzymes, vitamins, exopolysaccharides, probiotics, prebiotics, postbiotics, or antimicrobial compounds.
- We identified specific probiotic strains with anti-infectious and immunostimulatory activity.
- We used a biotechnological approach to produce valuable low-molecular-weight compounds (butanediol, butanol, organic acids) through the valorization of agricultural waste and the utilization of renewable natural resources.
- We investigated a novel therapeutic strategy to target the escape mechanisms of bacterial biofilm formation and antimicrobial resistance.
- We optimized ecological technologies based on microbial degradation or transformation

Department of Biotechnology

Head:
Prof. Lyudmila Kabaivanova, PhD
Tel.: +359 2 979 31 67
E-mail: lkabaivanova@yahoo.com

Laboratories:

- Metabolomics
- Cellular Biosystems
- Bioremediation and biofuel

2. We create new platforms for plant biotechnology research

- We create a biotechnological platform to study plant-derived metabolites.
- We used a biotechnology approach to culture endemic medicinal plants.
- We used innovative methodologies like genomics, transcriptomics, proteomics, and metabolomics to investigate the potential of plants in pharmacy, medicine, industry, and agriculture.
- We discovered the method for detoxification of water ecosystems by algae.

Department of Infectious Microbiology

Head: Professor Hristo Najdenski, DVM, DSc, Corresponding Member of BAS
Tel.: +359 2 979 31 61
E-mail: hnajdenski@abv.bg, hnajdenski@gmail.com

Laboratories:

- Bacterial Virulence, Resistance, and New Antimicrobial Agents
- Molecular Biology of Mycobacteria
- Cytotoxicity and Signal Transduction

3. We elevate the research in Infectious Microbiology

- We identified foodborne pathogens in agricultural farms, food products (meat, milk, etc.), drinking, natural and waste waters, soils and treatment plants.
- We determined antimicrobial resistance in bacterial isolates from various sources.
- We studied the pathogenesis of coronavirus infections with a focus on the interaction at the cellular and host level.
- We performed screening of plant and microalgae extracts, fractions and biologically active substances, microbial metabolites, synthetic compounds, and nanoscale systems loaded with active ingredients with antimicrobial and/or antineoplastic activity for the prevention of infectious diseases, chemoprevention and control of

- Ecology of Pathogenic Bacteria

multidrug resistance in infectious and antineoplastic chemotherapy.
- We investigated the virulence mechanisms in bacterial pathogens and the pathogenesis and carcinogenesis in conditions of bacterial colonization.
- We performed toxicology analyses of new drug candidates and nutritional supplements with antimicrobial and/or antineoplastic activity.
- We discovered the genetic diversity and genealogy of *Mycobacterium caprae* strains isolated from goats of different Bulgarian geographic regions.

Department of Immunology

Head: Prof. Andrey Tchorbanov, PhD
Tel.: +359 2 979 63 57
E-mail:
tchorban@microbio.bas.bg

Laboratories:

- Experimental Immunology
- Experimental Immunotherapy
- Infectious Immunology and Inflammation
- Immunohistochemistry and Immunopathology

4. We investigate the pathological mechanisms of immune response

- We investigated how flu infections affect the host epitranscriptome in arthritic conditions.
- We studied how epigenetic and metabolic modifications by pharmacological agents promote discrete fine-tuning of neutrophil function.
- We discovered a new paradigm and diagnostic algorithm to study the repertoire of natural IgM antibodies.
- We designed new vaccines against SARS-CoV2.
- We studied novel therapeutic approaches to target osteoarthritis.
- We exploited murine and humanized models of melanoma to study novel anti-tumor vaccines.
- We studied the effect of saffron extract in a murine model of osteoarthritis.
- We investigated the role of folate in murine and human lupus models.
- We developed specific protein-engineered molecules for therapy in Hashimoto's models and dust allergy.
- We showed fertility loss and complications in spontaneous and induced lupus models.

Department of Mycology

Head: Assoc. prof. Ekaterina Krumova, PhD
Tel.: +359 2 979 31 26
E-mail:
e_krumova@microbio.bas.bg

Laboratories:

- Biodiversity and Molecular Biology of Micromycetes
- Metabolism and its Regulation In Micromycetes

5. We strive to be a leader in fungal research in Bulgaria

- We studied the cellular response against oxidative stress induced by various stimuli.
- We investigated the mycetes biodiversity in extreme habitats - habitats with high and low temperatures, habitats polluted with heavy metals, and habitats with increased salinity.
- We isolated endophytic fungi and their potential in biotransformation processes.
- We studied filamentous fungi as producers of biologically active substances and enzymes, incl. temperature-sensitive enzymes.
- We purified and characterized enzymes produced by filamentous fungi.
- We investigated the antifungal activity of various natural and synthetic substances.
- We discover the role of filamentous fungi in the degradation process of cellulose-containing waste.

Department of Virology

Head: Assoc. Prof. Ivanka Nikolova, PhD
Tel.: +359 2 979 31 09
E-mail:
inikolova@microbio.bas.bg

Laboratories:

- **Experimental Chemotherapy of Enteroviral Infections**
- **Experimental Chemotherapy of Influenza**
- **DNA Viruses and Oncolytic Viruses**
- **Biological Response Modifiers and Pathogenesis of Viral Infections**

6. We extensively study the biology of viruses and novel antiviral therapies

- **We studied how Bi-polar ionizers for air and surface purification affect various human viruses.**
- **We performed screening for antiviral and virucidal effects of various chemically synthesized substances or plant-derived metabolites.**

TOP RESEARCH ARTICLES AND HIGHLIGHTS

In General Microbiology

Microorganisms in food and healthy nutrition

The researchers from the Department of General Microbiology have described the nutritional value of the microorganisms' diversity and postbiotics in various fermented food and bio-resources and **Bulgarian yogurt used in astronaut missions.**

Bartkiene, E., Starkute, V., Jomantaite, I., Zokaityte, E., Mockus, E., Tolpeznikaite, E., Zokaityte, G., Petrova, P., Santini, A., Rocha, J.M., Özogul, F., Klupsaite, D. Multifunctional Nutraceutical Composition Based on Fermented Spirulina, Apple Cider Vinegar, Jerusalem Artichoke, and Bovine Colostrum. Foods, 12, 1690, 1-17, MDPI, 2023, DOI:10.3390/foods12081690. SJR (Scopus):0.771, JCR-IF (Web of Science):5.2.

Shopova, I., Bogueva, D., Yotova, M., Danova, S. Can Bulgarian Yogurt enhance astronauts' performance during the Mars Missions?. Journal of Ethnic Foods, 10, 46, 2-16, Elsevier, 2023, ISSN:2352-619X, DOI:10.1186/s42779-023-00211-5.SJR (Scopus):0.544, JCR-IF (Web of Science):4.4.

Danova, S., Yankov, D., Dobreva, L., Dobreva, A., Armenova, N., Apostolov, A., Mileva M. Postbiotics Production of Candidate-Probiotic Lactiplantibacillus plantarum AC131 with Renewable Bio Resources. Life, 13, 10, MDPI, 2023, DOI:10.3390/life13102006, SJR (Scopus):0.634, JCR-IF (Web of Science):3.2

Using microorganisms to create ecological solutions

The researchers from the Department of General Microbiology showed the potential of microbial detoxification for the elimination of the residual pesticides **in fermented food.**

Armenova, N., Tsigoriyna, L., Arsov, A., Petrov, K., Petrova, P. Microbial Detoxification of Residual Pesticides in Fermented Foods: Current Status and Prospects. Foods, 12, 6, 1163, MDPI, 2023, ISSN:2304-8158, DOI:10.3390/foods12061163. SJR (Scopus):0.73, JCR-IF (Web of Science):5.561.

The researchers from the Laboratory Center Pasteur have summarized **the** knowledge on **the role of bacteria in the plausible degradation pathways of nanomaterial graphene oxide and other potentially toxic compounds.**

Simeonova, D. D., Pollmann, K., Bianco, A., Lievremont, D. Graphene oxide and bacteria interactions: What is known and what should we expect? mSphere, 9, 1, ASM, 2024, DOI:10.1128/msphere.00715-23, SJR (Scopus):1.29, JCR-IF (Web of Science):5.03.

The researchers from the Laboratory of Extremophilic Microorganisms **have described the diversity of microorganisms in the Bulgarian extreme niches and their potential for the synthesis of exopolymers as well as their various applications to solve ecological problems.**

Yıldız, Y.S.& Radchenkova, N. Exploring Extremophiles from Bulgaria: Biodiversity, Biopolymer Synthesis, Functional Properties, Applications. Polymers 2024, 16, 69. DOI: 10.3390/polym16010069. SJR (Scopus):0.72, JCR-IF (Web of Science):5.0.

Highlights in General Microbiology

The researchers from different Laboratories of the Department of General Microbiology have characterized the i**nsecticidal activity** of *Bacillus thuringiensis* strains. They identified the genes encoding 12 different crystal (Cry) endotoxins in the *B. thuringiensis* strain and characterized the strain-specific crystal morphology of spores and toxins.

Arsov, A., Gerginova, M., Paunova-Krasteva, T., Petrov, K., Petrova, P. Multiple cry Genes in *Bacillus thuringiensis* Strain BTG Suggest a Broad-Spectrum Insecticidal Activity. International Journal of Molecular Sciences, 24, 13, MDPI, 2023, DOI:10.3390/ijms241311137, 11137. SJR (Scopus):1.154, JCR-IF (Web of Science):5.6.

New approaches to target biofilm formation

Highlights in General Microbiology

The researchers have characterized the potential of mixed polymeric micelles to detach pre-formed bacterial biofilms and to reduce significantly their biomass via suppression of bacterial metabolic activity indicative of successful drug delivery and release without evidence of epithelial cell destruction or morphological signs of cell death.

Stancheva, R, Paunova-Krasteva, T, Topouzova-Hristova, T, Stoitsova, S., Petrov, P., Haladjova, E.. Ciprofloxacin-Loaded Mixed Polymeric Micelles as Antibiofilm Agents. Pharmaceutics, 15, 4, 1147, MDPI, 2023, DOI:10.3390/pharmaceutics15041147. SJR (Scopus):0.8, JCR-IF (Web of Science):6.525.

In Infectious Microbiology

Novel anti-tuberculosis agents

Within the frame of a Ph.D. thesis, the scientists from the Department of Infectious Microbiology have elucidated the prevalence of pathogenic Yersinia enterocolitica in pig farms in Bulgaria and described their genetic profiles. New detection methodology is also involved in laboratory practice.

Angelovska, M.; M.M. Zaharieva, L.L. Dimitrova, T. Dimova, I. Gotova, Z. Urshev, Y. Ilieva, M.D. Kaleva, T.C. Kim, S. Naydenska, Z. Dimitrov, H. Najdenski. Prevalence, Genetic Homogeneity, and Antibiotic Resistance of Pathogenic Yersinia enterocolitica Strains Isolated from Slaughtered Pigs in Bulgaria. Antibiotics, 2023, 12, 716. DOI: 10.3390/antibiotics12040716, IF-4.8.

The researchers from the Department of Infectious Microbiology in collaboration with the scientists from the Department of Virology have shown the strong antimycobacterial activity of novel 2-nitrofuranyl amides, hydrazide hydrazones, and thiadiazoles.

Dimitrov, S., Slavchev, I., Simeonova, R., Mileva, M., Pencheva, T., Philipov, S., Georgieva, A., Tsvetanova, E., Teneva, Y., Rimpova, N., Dobrikov, G., Valcheva, V. Evaluation of Acute and Sub-Acute Toxicity, Oxidative Stress and Molecular Docking of Two Nitrofuranyl Amides as Promising Anti-Tuberculosis Agents. Biomolecules, 13, 8, 1174, MDPI, 2023, DOI:10.3390/biom13081174. JCR-IF (Web of Science):5.5.

Teneva, Y., Simeonova R., Valcheva V., Angelova V. Recent Advances in Anti-Tuberculosis Drug Discovery Based on Hydrazide–Hydrazone and Thiadiazole Derivatives Targeting InhA. Pharmaceuticals, 16, 4, 484-508, MDPI, 2023, DOI:10.3390/ph16040484. SJR (Scopus):0.8, JCR-IF (Web of Science):4.6.

Highlights in Infectious Microbiology

The researchers from the Department of Infectious Microbiology have provided the first insight into the VNTR diversity of animal *Mycobacterium bovis/Mycobacterium caprae* isolates in Bulgaria with a focus on the local transmission within the country versus an emphasis on a detection of imported strains.

Terentieva, D., Savova-Lalkovska, T., Dimitrova, A., Bonovska, M., Mokrousov, I., Valcheva, V. First Insight into Diversity of Minisatellite Loci in Mycobacterium bovis/M. caprae in Bulgaria. Diagnostics, 13, 4, 771, MDPI, 2023, DOI:10.3390/diagnostics13040771. SJR (Scopus):0.658, JCR-IF (Web of Science):3.992.

In Immunology

Tools to target innate immunity in degenerative diseases and infection

In collaboration with the Laboratory of Metabolomics, the researchers from the Department of Immunology demonstrated a

Amirova, K.M., Dimitrova, P.A., Leseva, M.N., Koycheva, I.K., Dinkova-Kostova, A.T., Georgiev, M.I. The triterpenoid Nrf2 activator, CDDO-Me, decreases neutrophil senescence in a murine model of joint damage. International Journal of Molecular Sciences, 24, 10, 8775, MDPI, 2023, DOI:10.3390/ijms24108775. SJR (Scopus):1.07, JCR-IF (Web of Science):5.6.

novel tool to decrease neutrophil senescence in osteoarthritis.

Highlights in Immunology

The researchers from the Department of Immunology have added new insight for the regulation of host-pathogen interactions using current approaches of N6-Methyladenosine mRNA modification strategies.

Leseva, M.N. Buttari, B., Saso, L., Dimitrova P.A. Infection Meets Inflammation: N6-Methyladenosine, an Internal Messenger RNA Modification as a Tool for Pharmacological Regulation of Host-Pathogen Interactions. Biomolecules (Special Issue: Advances in RNA as Diagnostic Biomarkers), MDPI, 2023, DOI:10.3390/biom13071060, SJR (Scopus):1.07, JCR-IF (Web of Science):5.5.

Machine learning models in tumor diagnostics

Highlights in Immunology

The researchers from the Department of Immunology have postulated that in tumor diagnostics, high-throughput peptide binding assays can be augmented by graph theory approaches to yield useful machine-learning models.

Ferdinandov, D., Kostov, V., Hadzhieva, M., Shivarov, V., Petrov, P., Bussarsky A., Pashov, A.D. Reactivity Graph Yields Interpretable IgM Repertoire Signatures as Potential Tumor Biomarkers. International Journal of Molecular Sciences 24, 3,2597, 2023, MDPI, DOI: /10.3390/ijms24032597, JCR-IF (Web of Science):5.6.

Immune response and new therapies against viral infections

The researchers from the Department of Immunology have constructed DNA and protein-generated chimeric molecules for the delivery of Influenza viral epitopes in Mouse and Humanized NSG transfer models.

Mihaylova, N.M., Manoylov, I.K, Nikolova, M.H, Prechl, J., Tchorbanov A. DNA and protein-generated chimeric molecules for delivery of Influenza viral epitopes in Mouse and Humanized NSG transfer models. Human Vaccines & Immunotherapeutics, 20, 1, 2024, DOI:10.1080/21645515.2023.2292381, JCR-IF (Web of Science):4.8.

For the first time, it provided insight into the role of CD74 and D-DT in the immune response to SARS-CoV-2 infection and highlighted the potential for these proteins to be targeted in the development of new therapies for COVID-19.

Ralchev N.R., Bradyanova, S.L, Doneva, Y.V., Mihaylova, N., Elefterova-Florova, E.V., Tchorbanov, A.I., Munoz-Valle, J.F., Petralia, M.C., Checconi, P., Nicoletti, F., et al. Exploring the Role of CD74 and D-Dopachrome Tautomerase in COVID-19: Insights from Transcriptomic and Serum Analyses. Journal of Clinical Medicine 2023, 12, 5037. DOI: 10.3390/jcm12155037; SJR (Scopus): 0.935, JCR-IF (Web of Science): 3.9.

In Biotechnology

New strains of microorganisms converting different wastes to green energy

The researchers from the Department of Biotechnology and the Department of General

Stoyancheva, G., Kabaivanova, L., Hubenov, V., Chorukova, E.. Metagenomic Analysis of Bacterial, Archaeal and Fungal Diversity in Two-Stage Anaerobic Biodegradation for Production of Hydrogen

Microbiology have identified the microbial communities (bacterial, archaeal, and fungal) in a two-stage system of anaerobic bioreactors used for the production of hydrogen and methane from the waste substrate, corn steep liquor. The study demonstrated the anaerobic digestion by the novel microbial consortia.

and Methane from Corn Steep Liquor. Microorganisms, 11, 5, 2023, 1263. Q2 JCR-IF (Web of Science):4.926.

Stoyanova, K., Gerginova, M., Peneva, N., Dincheva, I., Alexieva, Z. Biodegradation and Utilization of the Pesticides Glyphosate and Carbofuran by Two Yeast Strains.. Processes, 11, MDPI, 2023, ISSN:2227-9717, DOI:doi.org/10.3390/pr11123343, 3343. SJR (Scopus):0.53, JCR-IF (Web of Science):3.5.

Rusinova-Videva, S. V., Ognyanov, M, Georgiev, Y, Petrova, A, Dimitrova, P, Kambourova, M. Chemical characterization and biological effect of exopolysaccharides synthesized by Antarctic yeasts Cystobasidium ongulense AL101 and Leucosporidium yakuticum AL102 on murine innate immune cells. World Journal of Microbiology and Biotechnology, 39, 2023, DOI:doi.org/10.1007/s11274-022-03477-0, JCR-IF (Web of Science):4.253

Plants as a source of biologically active metabolites

The researchers of the Laboratory of Metabolomics have summarised the systemic approach to studying plant physiology.

Ali, K., Georgiev, M.I. Omics and its integration: A systems biology approach to understand plant physiology. Frontiers in Plant Science, 14, 1324901, Frontiers, 2023, DOI:10.3389/fpls.2023.1324901. JCR-IF (Web of Science):5.6.

Highlights in Immunology

The researchers of the Laboratory of Metabolomics have characterized novel palnt-derived metabolites targeting signaling pathways in obesity.

Savova, M.S., Mihaylova, L.V., Tews, D., Wabitsch, M., Georgiev, M.I.. Targeting PI3K/AKT signaling pathway in obesity. Biomedicine and Pharmacotherapy, 159, 114244, Elsevier, 2023, DOI:10.1016/j.biopha.2023.114244. JCR-IF (Web of Science):7.5.

In Virology

Novel drugs with anti-viral activity

The researchers from the Department of Virology have investigated the anti-coronavirus potential of a series of novel tetrahydroisoquinoline derivatives on human coronavirus strains 229E and OC-43 replication cycle.

Kandinska, M., Burdzhiev, N., Cheshmedzhieva, D., Ilieva, S., Grozdanov, P., Vilhelmova-Ilieva, N., Nikolova, N., Lozanova, V., Nikolova, I. Synthesis of Novel 1-Oxo-2,3,4-trisubstituted Tetrahydroisoquinoline Derivatives, Bearing Other Heterocyclic Moieties and Comparative Preliminary Study of Anti-Coronavirus Activity of Selected Compounds. Molecules, 28, 3, 2023, DOI:10.3390/molecules28031495, JCR-IF (Web of Science):4.6.

Highlights in Virology

The collaborative efforts of the researchers from the Department

Ivanova, N., Ermenlieva, N., Simeonova, L., Kolev, I., Slavov, I., Karashanova, D., Andonova, V. Chlorhexidine–Silver Nanoparticle Conjugation Leading to Antimicrobial Synergism but Enhanced Cytotoxicity. Pharmaceutics, 15, 9, 2298, MDPI, 2023,

of Virology with other groups have demonstrated the potential synergism within chlorhexidine-silver nanoparticle conjugates on Influenza virus replication.

DOI:10.3390/pharmaceutics15092298. SJR (Scopus):0.795, JCR-IF (Scopus): IF 5.4.

Improving the anti-viral activity of the tissue environment

Highlights in Virology

The researchers from the Department of Virology have shown the antiviral activity of the metal-peptide complexes immobilized on cotton fibers and emphasized the protection of the immobilization environment by these complexes as well as their implication for biological structure-activity relationship studies in the future.

Georgieva, S., Todorov, P., Staneva, D., **Grozdanov, P.**, **Nikolova, I.**, Grabchev, I.. Metal-Peptide Complexes with Antimicrobial Potential for Cotton Fiber Protection. Journal of Functional Biomaterials, 14, 2, 2023, DOI:10.3390/jfb14020106, JCR-IF (Web of Science):4.8.

In Drug's Toxicology

Studying the exogenous manipulation of the endogenous cannabinoid system *in vivo*

Highlights in Drug's toxicology

The team from the Department of Virology evaluated how the exogenous manipulation of the endogenous cannabinoid system and the NO-ergic system can affect the cold-restraint stress response in an experimental model on male Wistar rats by the approaches of supplementation of different combinations of cannabinoid receptor type 1 agonist anandamide or antagonist AM251 along with an NO donor, NO precursor, or inhibitor of NO synthase.

Nocheva, H., Krastev, N., Krastev, D., Mileva, M. The Endogenous Cannabinoid and the Nitricoxidergic Systems in the Modulation of Stress Responses. International Journal of Molecular Sciences 24, 3, 2886, MDPI, 2023, DOI: 10.3390/ijms24032886, JCR-IF (Web of Science): IF 5.6.

In Mycology	
	Antartic fungial strains – distribution and application in medicine and biotechnology
The researchers from the Department of Mycology have identified the gene-encoded catalase enzyme and have shown the role of catalase in the survival strategy of filamentous fungi in extremely cold habitats. Research on catalases produced by Antarctic fungal strains is attractive for consideration in future potential applications in both medicine and biotechnology.	Dishliyska, V., Stoyancheva, G., Abrashev, R., Miteva-Staleva, J., Spasova, B., Angelova, M., Krumova, E. Catalase from the Antarctic Fungus Aspergillus fumigatus I-9–Biosynthesis and Gene Characterization. Indian Journal of Microbiology, 1-8, 2023, JCR-IF (Web of Science):3.00
In a multi-disciplinary collaboration, the researchers from the Department of Biotechnology, Microbiology, and Immunology have characterized the exopolysaccharides isolated from Antarctic yeast and their application for modulation of innate response.	Rusinova-Videva, S. V., Ognyanov, M, Georgiev, Y, Petrova, A, Dimitrova, P, Kambourova, M. Chemical characterization and biological effect of exopolysaccharides synthesized by Antarctic yeasts *Cystobasidium ongulense* AL101 and *Leucosporidium yakuticum* AL102 on murine innate immune cells. World Journal of Microbiology and Biotechnology, 39, 2023, DOI:10.1007/s11274-022-03477-0, JCR-IF (Web of Science):4.253.
	Antimicrobial and antimycotic activity of geopolymer paints
Highlights in Mycology **The Stephan Angeloff Institute of Microbiology researchers have shown novel insight into the** novel geopolymer paints based on copper and silver-modified zeolite with a stable antimicrobial potential. It seems promising antimicrobial coating material that can be implemented in the global fight against the spread of diseases and pathogens.	Nikolov, A., Dobreva, L., Danova, S., Miteva-Staleva, J., Krumova, E., Rashev, V., Vilhelmova-Ilieva, N., Tsvetanova, L., Barbov, B. Antimicrobial geopolymer paints based on modified natural zeolite. Case Studies in Construction Materials, Elsevier, 2023, e02642. JCR-IF (Web of Science):6.2.

EDUCATION AND TEACHING

National Evaluation and Accreditation Agency

The mission of NEAA is to encourage higher education institutions to ensure and enhance the quality of education they offer by sustaining high academic standards and good education traditions in Bulgaria.

Ph.D. students graduate by fulfilling the common credit system of the Bulgarian Academy of Sciences and ensuring high research quality.

The career center at the Bulgarian Academy of Sciences helps Ph.D. students to plan their research steps.

ОПЕРАТИВНА ПРОГРАМА
НАУКА И ОБРАЗОВАНИЕ ЗА ИНТЕЛИГЕНТЕН РАСТЕЖ

We help Bulgarian Universities to consolidate and increase their education capacity.

We devoted more than 1500 hours to training students.

Accreditation to train Ph.D. students in 4 research fields

- Microbiology
- Immunology
- Virology
- Biotechnology

Ph.D. students: 10

Ph.D. credit system: 2 components

1. Education program: min 130 credits
   - Common specialization courses: 2 courses
   - Individual education: 2 exams
   - Common education courses in English and Computer Science
2. Credits for individual research activity: min 70 credits
   - Published articles
   - Participation in conferences and schools
   - Participation in projects
   - Other research activities

Total credits: min 250 credits

National Programs to support students and young scientists

- National program "Young scientists and postdoctoral fellows - 2" - 4 persons
- The national program „Evropeiski Praktiki“ - training of more than 20 master and bachelor students

The teaching activity of the Scientific Staff

- Lectures: 19 Methodological Programs
- Courses: 2 Specialization Courses
- Practical training: 21 Training Courses in our Labs
- Seminars: 1 Research Seminar

We provide our expertise in education to:

- Sofia University St. Kliment Ohridski
- Plovdiv University Paisii Hilendarski
- New Bulgarian University - Sofia
- South-West University - Blagoevgrad
- University of Food Technology (UHT) - Plovdiv

EXPERT ACTIVITIES

- **We are members of 35 Research Organizations….**
- **We are Editorial Board members in 48 Journals….**
- **We took part in 20 Expert Committees consolidating opinions to solve society's challenges….**

ACTIVITIES IN PASTEUR NETWORK

ACIP PROJECTS

- **ACIP m6A_RAIAV 2020-2023:** The lung epitranscriptome and chromatin accessibility landscape in rheumatoid arthritis complicated by the flu. PI: Milena Leseva, CoPI: Dr. M. Hasan, Institute Pasteur-Paris, France, CoPI: C. Barbezange, Sciensano, Belgium.
- **ACIP VacciNanoCor 2020-2022:** Generation of Humanized NSG transfer mouse model for coronavirus SARS-CoV-2 vaccine testing.
- **ACIP/A-05_13, 2013-2015:** Viral Antigen Targeting by Genetically Engineered Chimeric Molecules, PI: Assoc. Prof. Andrey Tchorbanov, Institute of Microbiology – Sofia.
- **ACIP A-07-2012, 2012-2014**: Therapeutic potential of modified IgM and IgG preparations in inflammatory respiratory syndrome and sepsis. Supervisor: Prof. Tchavdar Vasilev.
- **ACIP/A05_11, 2011-2013:** The role of neutrophils and NK cells in the development of collagenase-induced osteoarthritis, PI: Assoc. Prof. Petya Dimitrova, Institute of Microbiology-Sofia, CoPI: Prof. Angela Santoni, University La Sapienza-Rome, CoPI: Crina Stavaru, Cantacuzino Institute-Bucharest.
- **ACIP A-08-2010, 2010-2013:** Role of migrating birds and their feeding ticks on the dissemination of some medically important zoonotic pathogens along the East-European flyway. PI: Prof. Hristo Najdenski, CoPI: 21 | www.microbio.bas.bg Prof. Elizabeth Carniel, Institut Pasteur-Paris, CoPI: Nikolay Tokarevich, Saint-Petersburg Pasteur Institute
- **ACIP A/7/2005, 2005-2007:** Macrophage dependent immunoprotective action of Candida albicans DNA, PI: Prof. Nina Ivanovska, Institute of Microbiology-Sofia, CoPI: Prof. Dr. Jean-Mark Cavaillon, Institute Pasteur-Paris, CoPI: Prof. Dr. Aurora Salageanu, Cantacuzino Institute – Bucharest.

PTR PROJECTS	
	• PTR-43-16: 2017-2018: The Role of ExoY nucleotidyl cyclase toxin in Pseudomonas aeruginosa infections" (1917-1918), PI: Prof. U. Mechold, Institute Pasteur, Paris; Co-PI Institute of Microbiology: Assoc. Prof. Stoyanka Stoitsova.
TRAVEL GRANTS	
	• 2008: Lora Simeonova - Vaccinology course, Institut Pasteur, Paris (course) • 2013: Maya Hadjieva - 6th HKU Pasteur Immunology Course, Hong Kong (travel grant) • 2013: Lora Simeonova - 11th International Virology Course on Influenza and Viral Zoonozes, Institut Pasteur Hong Kong (travel grant) • 2014: Violeta Valtcheva - International Scientific Symposium Institut Pasteur International Network (2014), Institute Pasteur, Paris • 2015: Nikola Kerekov - Vaccinology course, Institut Pasteur, Paris (course) • 2018: Violeta Valtcheva – Introduction to Molecular Phylogenetics – Institute Pasteur Hong Kong (course) 2016: 3rd Institut Pasteur International Network Symposium "From Basic Sciences to Biomarkers & Tools in Global Health" • 2017: Violeta Valtcheva – Transgenic technologies in modeling the human diseases – principles and technologies, Hellenic Insitute Pasteur, Athens (course) • 2018: Violeta Valtcheva – 2nd St. Petersburg Symposium on Tuberculosis and Mycobacteria: Molecular Approach, St. Petersburg Pasteur Institute (travel grant) • 2019: Violeta Valtcheva – Next-generation sequencing and bioinformatic tools for M. tuberculosis drug resistance detection and epidemiological analysis, St. Petersburg Pasteur Institute. • 2021: Iliyan Manoylov – Calmette and Yersin Grant – Vaccinology course, Institute Pasteur, Paris • 2023: Simeon Dimitrov - Training Course- High Content Screening for Therapeutics Discovery.
INTERNSHIP	
	• 2015: Rositsa Tropcheva – Calmette and Yersin Grant, 2 months, Hellenic Institute Pasteur, Athens; • 2019: Iliyan Manoylov – Calmette and Yersin Grant – Regulatory course for project designers (rodents and lagomorphs), Institute Pasteur, Paris • 2022: Iliyan Manoylov – Calmette and Yersin Grant, 1 month, Animalerie Centrale, Institute Pasteur, Paris.

ERASMUS+	
	• 2023: Marieta Belceva, PhD • 2023: Venelin Hubenov, Post-Doc (Séjours scientifiques de haut niveau) • 2018-2019: Venelin Hubenov, PhD

PLATFORMS: USE AS PUBLIC HEALTH TOOLS

PLATFORM: PROKARYOTES AND EUKARYOTES IN HEALTH AND DISEASES

Probiotics and postbiotics v/s microbiome - nutrition-health

Expertise:

- probiotics from different ecological niches
- mode of action of lactic acid bacteria and postbiotics
- new functional foods related to the beneficial bacteria in traditional fermented dairy products and sourdough
- novel bio-therapeutic potential

Analyses:

- human microbiome - biodiversity of lactobacilli from vaginal samples and breast milk;
- probiotic potential and beneficial effects

Contact persons:

Department of General Microbiology
Prof. Svetla Danova, DSc - stdanova@yahoo.com

Development of new functional foods based on probiotic/prebiotic interactions

Expertise:

- Biodiversity and probiotic potential of Bulgarian yogurt strains
- Galactooligosaccharides production by *Lactobacillus bulgaricus*

Analyses:

- Selection of lactic acid bacteria displaying β-fructosidase activity
- Metagenomics of Bulgarian LAB fermented foods

Contact persons:

Department of General Microbiology
Prof. Penka Petrova, DSc - ppetrova@microbio.bas.bg

Development of novel foods, food supplements and cosmeceuticals based on cellular agriculture by using plant in vitro systems

Expertise:

- Development, characterization and cultivation of plant in vitro systems with different levels of differentiation;
- Optimization, analyses, downstream processing and standardization of plant biomass with improved qualityes;
- Bioreactor cultivation, scale-up and production of target bioactive metabolites by using plant in vitro systems:
- Development of nutraceuticals based on plant in vitro systems.

Contact persons:

Department of Biotechnology
Assoc. Prof. Vasil Georgiev: vasgeorgiev@gmail.com

PLATFORM: WHOLE ORGANISM DISEASE MODELS	**Murine models use and refinement for evaluation of immune response and drug efficacy**
	Expertise:
	• Experimental models of acute inflammation
	  ○ LPS-induced inflammation and shock (lung, kidney, and liver injury)
	  ○ Zymosan-induced inflammation and multiple organ dysfunction syndrome
	  ○ Polymicrobial sepsis model (cecal ligation and puncture, CLP)
	  ○ Carrageenan-induced and zymosan-induced paw inflammation
	• Models of rheumatoid arthritis (RA)
	  ○ Collagen antibody-induced arthritis
	  ○ Zymosan-induced arthritis
	• Models of osteoarthritis (OA)
	  ○ Collagenase-induced OA
	  ○ Surgical model of anterior cruciate ligament transection
	  ○ Ovariectomy – post-menopausal model
	• **Analyses:**
	  ○ Clinical evaluation
	  ○ Phenotyping, homing, and distribution of immune cells - flow cytometry
	  ○ Cell functional analysis – flow cytometry, In cell kits
	  ○ Histology – knee/ankle joints, lung, liver, kidney
	  ○ Immunohistochemistry for catabolic and metabolic pathways
	  ○ MMPs, cytokines, chemokines
	Contact persons:
	Department of Immunology
	Assoc. Prof. Petya Dimitrova: petya_dimitrova@web.de
	Assoc. Prof. Nikolina Mihailova: mihaylova_n@microbio.bas.bg

PLATFORM: SCREENING, CHEMICAL BIOLOGY, CHEMICAL LIBRARIES	**Biodiversity of extremophilic microorganisms – archaea, bacteria, and fungi, and investigation of their biosynthetic potential** **Expertise:** • Characterization of microbial diversity in extreme niches is carried out by applying modern and classical molecular and microbiological methods. • The investigations provide new information on the microbial biodiversity in these habitats, as well as their biotechnological potential • **Plastics degrading strains and consortia** **Analyses:** • isolation of thermophilic and halophilic microorganisms • taxonomical identification of isolated strains • Investigation of the biotechnological potential of microorganisms **Contact persons:** Prof. Penka Petrova: ppetrova@microbio.bas.bg **Natural and synthetic products as a drug lead and screening for anti-viral, anti-microbial, anti-tumor, and anti-inflammatory activity.** **Comprehensive plant metabolite profiling** **Expertise:** • Production of pharmaceutically valuable plant molecules.

- Unraveling the regulatory codes and metabolic pathways that govern plant development, stress physiology, and production of valuable metabolites.

Analysis:

- Collection of medicinal and aromatic plants
- Isolation and structure elucidation
  - 1H NMR or 13C NMR spectroscopy
  - 2D NMR spectroscopy (J-resolved; 1H-1H COSY; TOCSY; 1H-13C HMBC; HSQC)
  - 3D NMR spectroscopy (HSQC-TOCSY)
- Data processing
  - Metabolomics and metabolite profiling (In-house database)
  - Bucketing (AMIX, MestReNova)
  - Multivariate data analysis (SIMCA-P)

Contact persons:

Department Biotechnology
Prof. Milen Georgiev–milengeorgiev@gbg.bg

Large-scale screening for antiviral activity

Expertise:

Viruses: entero-, toga-, flavi-, orthomyxo-, paramyxo-, rhabdo-, adeno-, herpes, poxviruses.

Analyses:

- Anti-viral activity
- Mode of action
- Combination of applications
- New approaches for alternative applications
- Resistance
- Biological response modifiers
- Double-blind study (adenovirus)

Contact persons:

Department of Virology and Laboratory Center Pasteur
Acad. Angel Galabov - galabov@microbio.bas.bg
Assoc. Prof. Ivanka Nikolova - vanianik@mail.bg
Assoc. Prof. Neli Vilhelmova nelivili@gmail.com
Assist. Prof. Lora Simeonova - losimeonova@gmail.com
Assist. Prof. Peter Grozdanov - grozdanov@microbio.bas.bg

Screening for drug effects on immune cell functions

Expertise:

- Multi-parametric analysis of immune cell function.
- Anti-inflammatory activity of novel drugs.

Analysis:

- JAK kinase inhibitors
- Anti-proliferating drugs
- HDAC inhibitors
- Sirtuin activators
- NRF2 activators
- Modifiers of neutrophil functions
- Modifiers of bone cell functions
- Modifiers of B-cell functions
- Methylation agents – folic acid

Contact persons:

Department of Immunology
Prof. Andrey Tchorbanov - tchorban@microbio.bas.bg
Assoc. Prof. Petya Dimitrova - petya_dimitrova@web.de

Analysis of the antibody repertoire in its complete diversity

Expertise:

- Diagnostic tool for evaluation of IgM repertoire.
- The implication in glioblastoma multiforme, non-tumor patients, lung cancer brain metastasis, and breast cancer metastasis.
- Topological data analysis for biological big data.

Analysis:

- Design of mimotope-based repertoire profiles.
- Defining predictors based on repertoire profiles.
- Data processing implementing machine learning techniques.

Contact persons:

Department of Immunology
Assoc. Prof. Anastas Pashov - a_pashov@microbio.bas.bg

Screening for anti-microbial activity (antibacterial and antifungal) of natural and synthetic products

Expertise:

- Defining antimicrobial activity of novel drugs extracts and compounds thereof.
- Defining antimicrobial activity of proteins and antibodies.
- Defining antimicrobial activity of nano-formulations with new or existing compounds, incl. clinically approved chemotherapeutics and antibiotics.
- Exploring the mechanisms of action of extracts and compounds (bioactive and synthetic) in comparison with known clinically applied chemical structures.

Analysis:

- Implementation of microbiological approaches for the determination of MIC, CFU counts, and MBC.
- Biochemical approaches for enzyme activity and investigation of interference with the quorum sensing system of sensitive bacteria.
- Molecular-biology approaches for evaluation of the effects of active compounds and extracts on the bacterial quorum sensing system.
- Microscopic approaches for evaluation of the effects of active extracts and/or compounds on the bacterial cell wall.

Contacts:
Department of Infectious Microbiology
Prof. Hristo Najdenski - hnajdenski@abv.bg
Department of Mycology
Assoc. Prof. Ekaterina Krumova e_krumova@microbio.bas.bg
Department of General Microbiology
Assoc. Prof. Tsvetelina Paunova-Krasteva, PhD, pauny@abv.bg

Screening for antineoplastic activity

Expertise:

- Evaluation of the antineoplastic activity of plant extracts, compounds thereof, synthetic chemical structures, and microbial products on tumor cell lines originating from tissues that are in contact with the environment and suggest the involvement of bacterial infections in the disease. pathogenesis: effects on cell growth and proliferation
- Evaluation of mechanisms of action of active plant extracts, compounds thereof, synthetic chemical structures, and microbial products in terms of:
  - effects on induction of programmed cell death;
  - influence on the cell cycle and signal transduction;
  - epigenetic modulation potential.

Analysis:

- Pathomorphological evaluation of cytopathic effects on treated cell lines.

	• Determination of median inhibitory concentrations and in vitro cytotoxicity based on biochemical methods for cell proliferation and cytotoxicity. • Evaluation of clonogenicity and genotoxicity. • Biochemical evaluation, fluorescent methods and immunoassays of apoptosis induction, and determination of apoptosis and other types of cell death. • Implementation of PCR-based molecular biology methods (real-time PCR, digital droplet PCR) for evaluation of effects on gene activation and/or silencing. • Epigenetic approaches for determination of epigenetic DNA modulation as a consequence of exposure to test substances. **Contacts:** Department of Infectious Microbiology Assoc. Prof. Maya Zaharieva, zaharieva26@yahoo.com **Investigations of cell's oxidative stress events** **Expertise:** Investigations of oxidative stress events in eukaryotic cells: Assay of stress biomarkers and evaluation of the antioxidant activity. **Analysis:** • Determination of stress biomarkers in cells • Determination of antioxidant activity **Contacts:** Department of Mycology Assoc. Prof. Ekaterina Krumova e_krumova@microbio.bas.bg **Studying molecular epidemiology and evolutionary genetics for mycobacteria** **Expertise:** • Molecular epidemiology and evolutionary genetics for mycobacteria, including species from *Mycobacterium tuberculosis* complex. • Genomic bioinformatic tools for analysis of mycobacteria. • Screening of new molecular markers for drug resistance in mycobacteria. **Analysis:** • Molecular genetic and population structure analysis of *Mycobacterium tuberculosis*. • Molecular phylogeny and bioinformatic analysis of mycobacteria. • Evaluation of new molecular markers for drug resistance in mycobacteria. **Contact persons:** Department of Infectious Microbiology Assoc. Prof. Violeta Valcheva-violeta_valcheva@mail.bg
PLATFORM: IMAGING TECHNIQUES	**Morphology of microorganisms and electron microscopy** **Expertise:** • Biofilms – structure, development and control. • In situ interaction of bacteria with cultured cells. • Ultrastructure and cytochemistry of microorganisms from diverse phylogenetic groups – viruses, prokaryotes (bacteria, actinomycetes) and eukaryotes (yeasts, fungi). **Analysis:** • Transmission electron microscopy: processing and sectioning of resin-embedded samples, negative staining.

	• Immunocytochemistry – immuno-gold labeling of ultrathin sections and negatively stained samples. • Scanning electron microscopy. **Contacts:** Department of General Microbiology Assoc. Prof. Tsvetelina Paunova-Krasteva, PhD, pauny@abv.bg
PLATFORM: ANTIMICROBIAL RESISTANCE	**Antimicrobial resistance in agricultural areas in the light of the one health concept** **Expertise:** • Biodiversity of pathogenic bacterial strains in animals and environment, incl. farms, farm lagoons, water sources, and agricultural fields around farms. • Resistance pattern in pathogenic and non-pathogenic bacterial species in agricultural areas (collaboration with Hellenic IP (Greece). • Types of resistance – biochemical, genetically determined, etc. • Genes of resistance – chromosomal and R plasmids, pharmacological groups of antibiotics involved. • Possibilities for transmission of resistance carriers between non-pathogenic and pathogenic bacterial species within bacterial communities in agricultural areas. **Analysis:** • Identification of pathogenic bacteria – according to microbiological ISO standards, biochemically (Phoenix BD system). • AST testing using microbiological approaches recommended by EUCAST. • biochemically (Phoenix BD system). • Agar-diffusion test for determination of zone inhibition (automates counter SCAN1200). • Genetic analysis of resistance carriers collaboration with ILVO (Melle, Belgium). • Determination of genes of resistance (R plasmids or chromosomal located) – PCR-based techniques (conventional and real-time PCR), LAMP assay. • Determination of point mutations (existing and new) that could be related to antibiotic resistance – digital droplet PCR and NGS. • Screening for antibiotic residuals in samples from agricultural areas using chemical analytical methods such as HPLC and mass spectrometry. **Contacts:** Department of Infectious Microbiology Prof. Hristo M. Najdenski, DSc, Corr.-member of BAS, hnajdenski@abv.bg, hnajdenski@gmail.com Assoc. Prof. Maya Zaharieva, zaharieva26@yahoo.com