



Federal State Budget Institution “National Medical Research Center of Obstetrics, Gynecology and Perinatology named after Academician V.I. Kulakov” of the Ministry of Health of Russia Moscow

CREMLIN PLUS

Connecting Russian and European Measures
for Large-scale Research Infrastructures



This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 871072



Main building



Perinatal Center



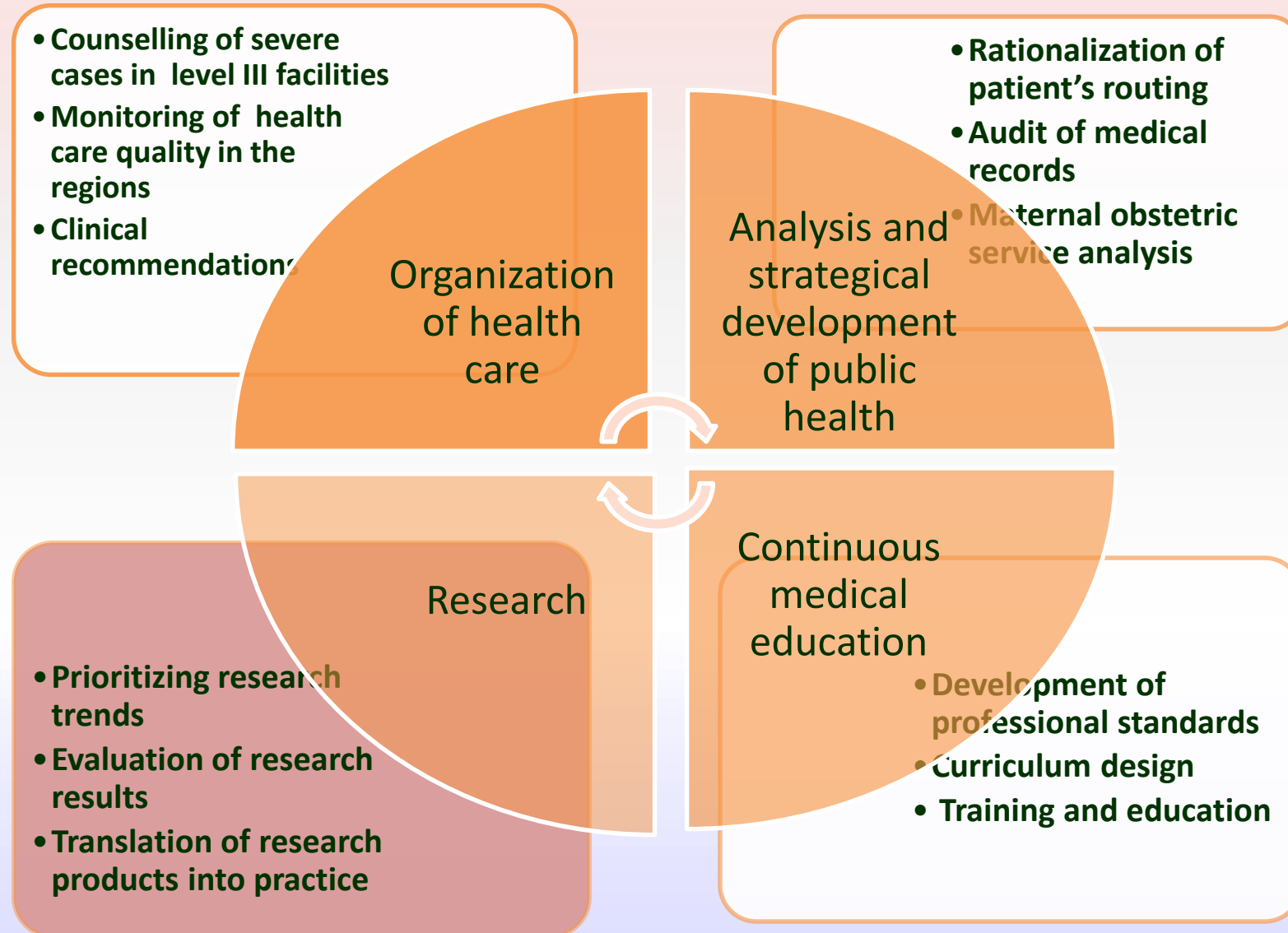
Clinical and Diagnostical Center

2, 500 employees
8 490 births
23 000 surgical procedures
20 operating rooms
18 labor wards
583 beds
22 laboratories
25 departments of different profiles
180 000 consultations per year
> 1 000 000 tests

- **Institute of Obstetrics**
- **Institute of Neonatology and Pediatrics**
- **Institute of Oncogynecology and Mammology**
- **Institute of Reproductive Genetics**
- **Institute of Reproductive Medicine**
- Simulation and Training Center
- F. Paulsen Sr. ART Academic Center
- Telemedicine Center
- R&D Department
- Regional Integration Department
- RSOG Headquarters
- National Journal *Obstetrics and Gynecology* Editorial Board

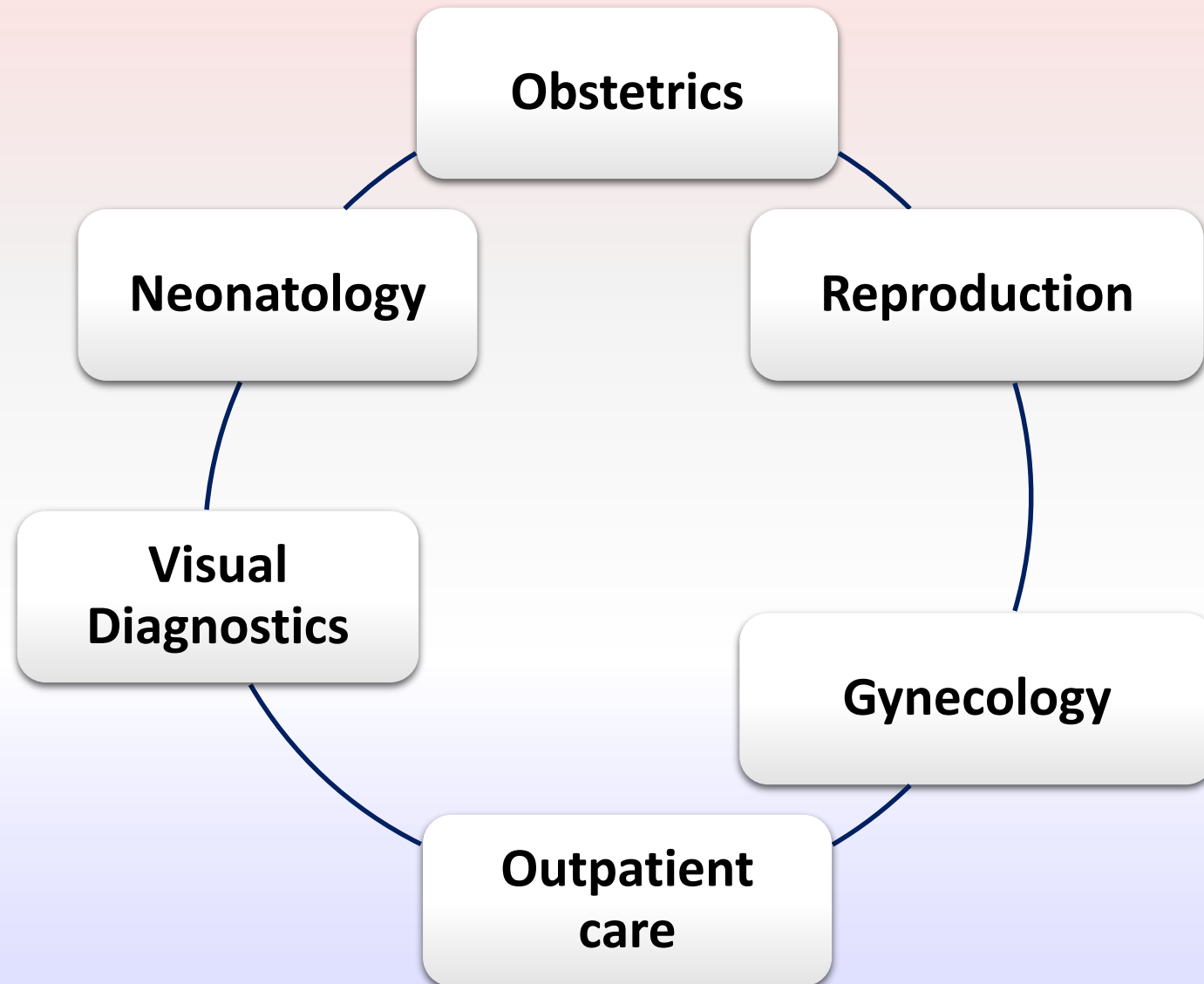


FUNCTIONS OF THE NATIONAL CENTER





MEDICAL CARE





LABORATORY UNIT: **24** laboratories and Biobank

- Diagnostic
- Clinical immunology
- Molecular genetics
- Reproductive genetics
- Microbiology
- Clinical pharmacology
- Clinical epidemiology
- Pathology
- Mitochondrial medicine
- Neurocybernetics
- Molecular adaptation
- Cell technologies
- Regenerative medicine
- Cytology
- System biology in reproduction
- Proteomics and metabolomics
- Cells pathophysiology (micro RNAs)
- Bioinformatics
- Genome editing
- Genetic mechanisms of development
- Biobank



Laboratory for collection and storage of biomaterial samples (Biobank)



Storage space

15 refrigerators with **32 400** storage units = **565 000**
storage units



Storage conditions and monitoring comply with international standards
(International Society for Biological and Environmental Repositories)



Laboratory for collection and storage of biomaterial samples (**Biobank**)

Samples

- More than **400,000** samples from patients with different obstetrical, gynecological and neonatal pathologies, including cervical cancer, ovarian cancer, breast cancer, preeclampsia, gestational diabetes, habitual miscarriage, fetal growth retardation syndrome, chromosomal aberrations. Material: placenta, umbilical cord, amniotic fluid, fetal and embryonic tissues, biologic liquids, pathologic tissue samples, etc.
- All samples are characterized in detail with patients' demographic and clinical features, anonymized and bear a QR –code
- Biobank is integrated into the Center's internal patients database Medialogue and therefore easily accessible for clinicians and researchers



Laboratory for collection and storage of biomaterial samples (**Biobank**)

Activities

✓ Research

- The samples and collections are currently used for more than 20 research projects carried out by the Center and supported by several national foundations;
- In the international collaborative projects with:
 - Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden;
 - Center for Research in Cancerology and Immunology Nantes-Angers, France;
 - Oxford Maternal & Perinatal Health Institute, Oxford, UK;
 - The Westerdijk Fungal Biodiversity Institute, Utrecht, Netherlands;
 - International Network on Cancer, Infertility and Pregnancy (INCIP)
 - European Surveillance of Congenital Anomalies (EUROCAT)

✓ **Validation of tests (on request on manufacturers)** – e.g. kits for antibodies to COVID

✓ **Development and validation of samples collection and storage protocols**



Institute of Reproductive Genetics

- Non-invasive **prenatal DNA screening** of fetal aneuploidies based on maternal blood
- Molecular **karyotyping** (micro-matrix DNA analysis)
- Preimplantation genetic screening (PGS)
- Study of › 60 000 single nucleotide polymorphism in the genome and › 55 000 mRNA measured levels
- Sequencing of › 100 **bacterial genomes**
- BRCA **genes mutations** tests
- Implementation of preimplantation genetic testing using aCGH and NGS methods
- The use of NGS technologies for **exome sequencing** in prenatal and neonatal diagnosis
- COVID-19 test development and validation

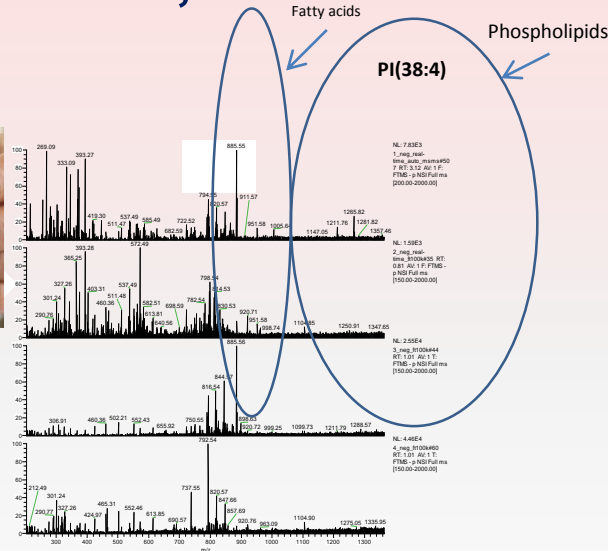
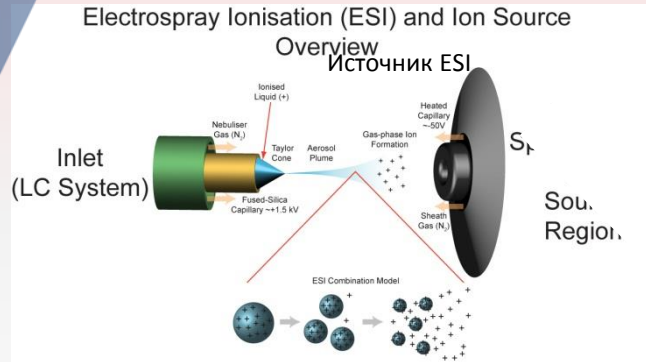


Laboratory of microbiology and epidemiology

- The study of the reproductive tract microbiocenosis and of microbiota of newborns
- Development of new test systems
- medications based on lactobacilli and bacteriophages alternative to antibiotics
- Study of the distribution and intensity of circulation of strains of infectious pathogens
- Study of new molecular mechanisms of drug resistance
- Decoding the bacterial genome



System Biology Department: Proteomics and metabolomics research; Bioinformatics; MicroRNA





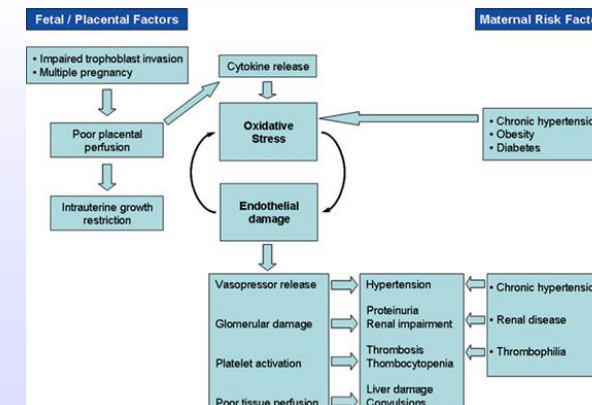
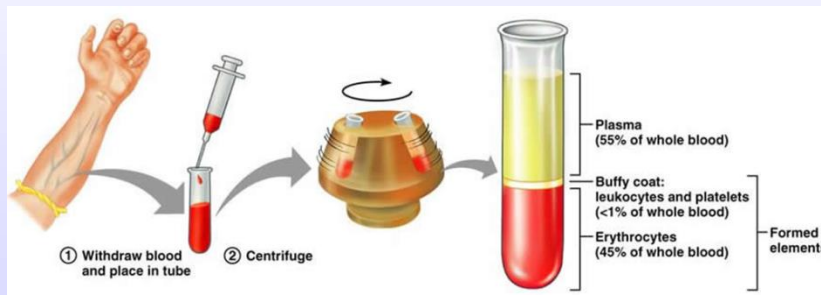
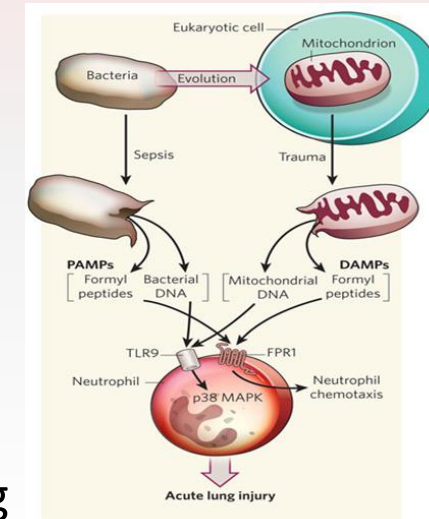
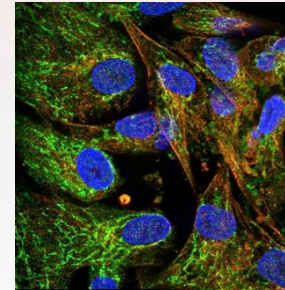
Laboratory of mitochondrial medicine

Goal:

Study of mitochondrial physiology role in pathogenesis of human reproductive system diseases and in developmental disorders

Focus on:

- Preeclampsia
- Fetal growth restriction
- Premature delivery
- Endometriosis
- Metabolic reprogramming at neoplastic and tumor transformation
- Bioenergetics of gametes and reproductive tissues during lifecourse
- Premature ovarian failure
- Polycystic ovaries





Laboratory of cells molecular pathophysiology

Main trends: endometriosis, preeclampsia, fetal hypoxia

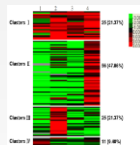
Workflow

miRNA isolation
cDNA libraries
synthesis



Endometriosis

In endometriosis lesions 13 differentially expressed miRNA were found compared to endometrium and blood plasma



Preeclampsia

Simultaneous expression changes of miRNA in blood plasma and placentas on 25 and 39 gestation days: 6 up regulated and 1 down regulated.



Hypoxic-ischemic encephalopathy

miRNA analysis of blood plasma revealed 2 fold changes of 38 miRNA on 1st and 3d days after birth



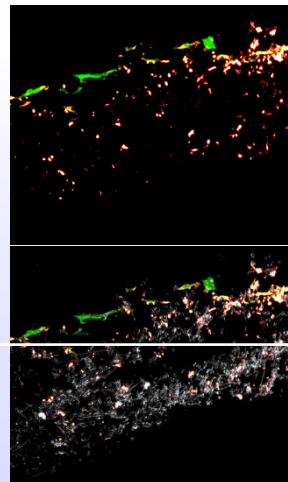
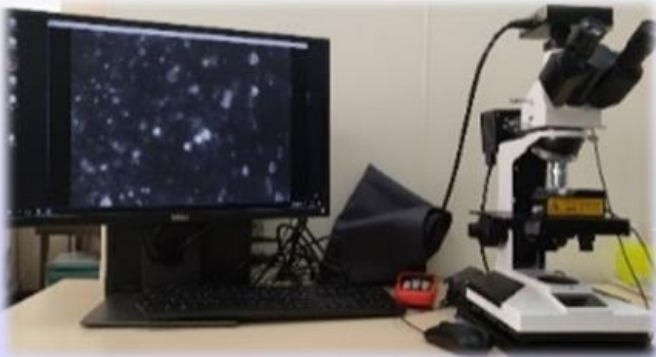
Signalling pathways
analysis
Omics,
bioinformatics

The identified miRNAs have regulatory role in cell proliferation, differentiation, angiogenesis, inflammation, mitochondrial function, synaptic plasticity



Laboratory of regenerative medicine

- Development and introduction of methods of cell therapy and
- tissue engineering and other tools of regenerative medicine in the field of reproduction
- (pelvic floor, endometrium, vagina reconstruction)



Laboratory of cell technologies

- Isolation and characterization of Multipotent Mesenchymal Stromal Cells (MMSCs) of perinatal tissues
- Isolation and characterization of extracellular vesicles (EVs) MMSCs
- Isolation and characterization of extracellular vesicles (EVs) MMSCs





Assisted reproductive technologies and embryology labs

Growing of euploid blastocysts from immature oocytes of patients with cancer *ex vivo*

FLIM
(fluorescence-lifetime imaging microscopy) of mature sperm in real time

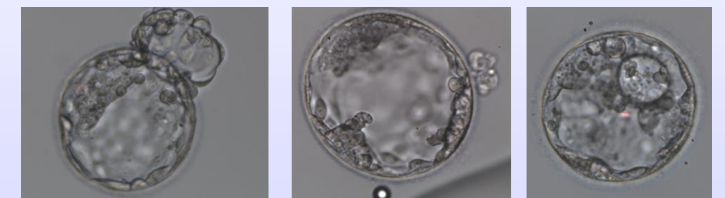
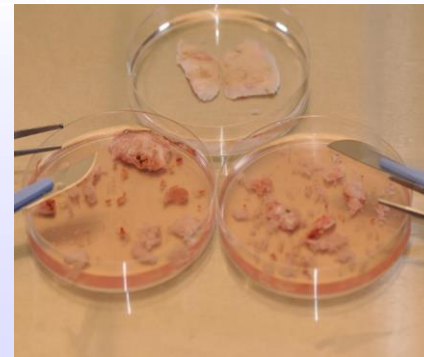
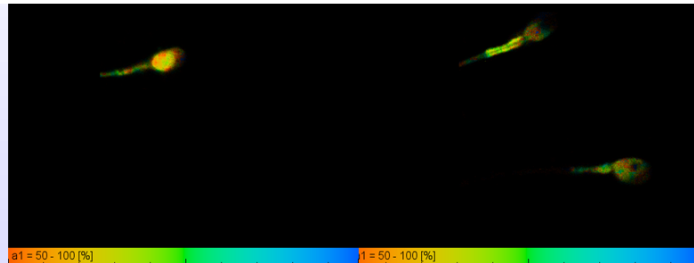
3D bioprinted ovarian construct

Embryo co-culturing with various cells

Microvibration



Патология: головка ярко светится (гликолиз) NADH
Норма: шейка ярко светится (окислительное фосфорилирование NADH), головка не светится



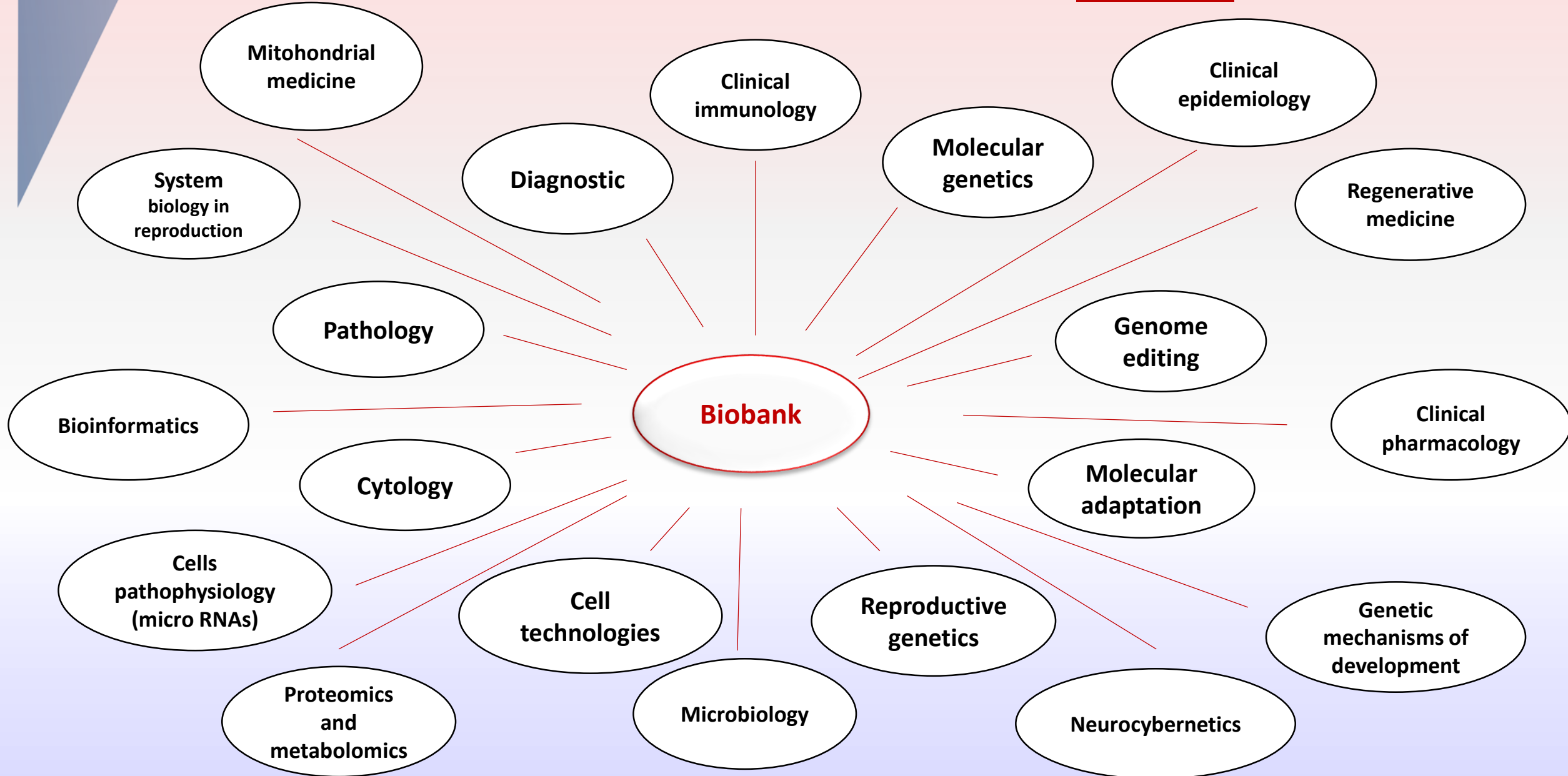


Bioinformatics laboratory

- software package for omix data analysis and evaluation of laboratory studies
- methods for joint analysis of pathomorphological images and data of genetic tests
- Models for cancer metastases prediction



INFRASTRUCTURE: 24 laboratories and Biobank





The Center is a **unique** integrity of clinical practice and scientific research

Open for collaboration with the research teams in Europe in the burning areas of medicine:

- high-risk pregnancy;
- adverse perinatal outcomes;
- infertility;
- gynecologic cancers and oncofertility

Keen to exchange with **European research infrastructures**, including:

- biobanks;
- disease registries;
- databases of laboratory and instrumental research



Current users of the facility /infrastructure

The main users are the Center staff: 204 researchers, 381 doctors.

The total **h-index** of employees (according to RSCI) at the end of 2019 was 1 593. The total **impact factor** of publications at the end of 2019 was 72.705 (including RSCI 5-year impact factor) and 65.540 (including RSCI 2-year impact factor without self-citation).

The total **impact factor of all publications** (with impact factor of 0.3 and higher) was 306.263 (including RSCI 2-year impact factor without self-citation) and 329.561 (including RSCI 5-year impact factor).



Access to the facility

Remote: televideoconferencing, access to databases (to be discussed)

Personal: upon administration permission and within a joint research project confirmed by a signed cooperation agreement. The Center provides visa support.

Access to **biologic material** may be a challenge (across the border transportation)

European colleagues (up to 70 per year) regularly visit the Center to share experience and knowledge and to participate in scientific and educational events.



Website: <https://www.ncagp.ru/>

Short English version of the website: <http://en.ncagp.ru/>

(an extended version is under development).

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