FROM BASIC GENETICS TO BIOMEDICAL APPLICATIONS

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Academgorodok

Institute of Cytology and Genetics (IC&G)
Siberian Branch of the Russian Academy of Sciences

Permanent staff: 687
Post-graduate students: 85
Graduate students: 70
http://www.bionet.nsc.ru

Director:
Professor Nikolay A. KOLCHANOV
Full Member of the Russian Academy of Sciences

IC&G research directions

Underlying the development of the IC&G was the idea to integrate molecular, cellular, developmental and population studies aiming at a better understanding of the genetic mechanisms of variability and evolution. Research emphasis was on the development of plant and animal models for investigating the genetic structure of complex, in functional terms, characters of behavior, stress reactivity, reproductive systems, hereditary human and animal diseases, symbiotic nitrogen fixation in plants, among others.

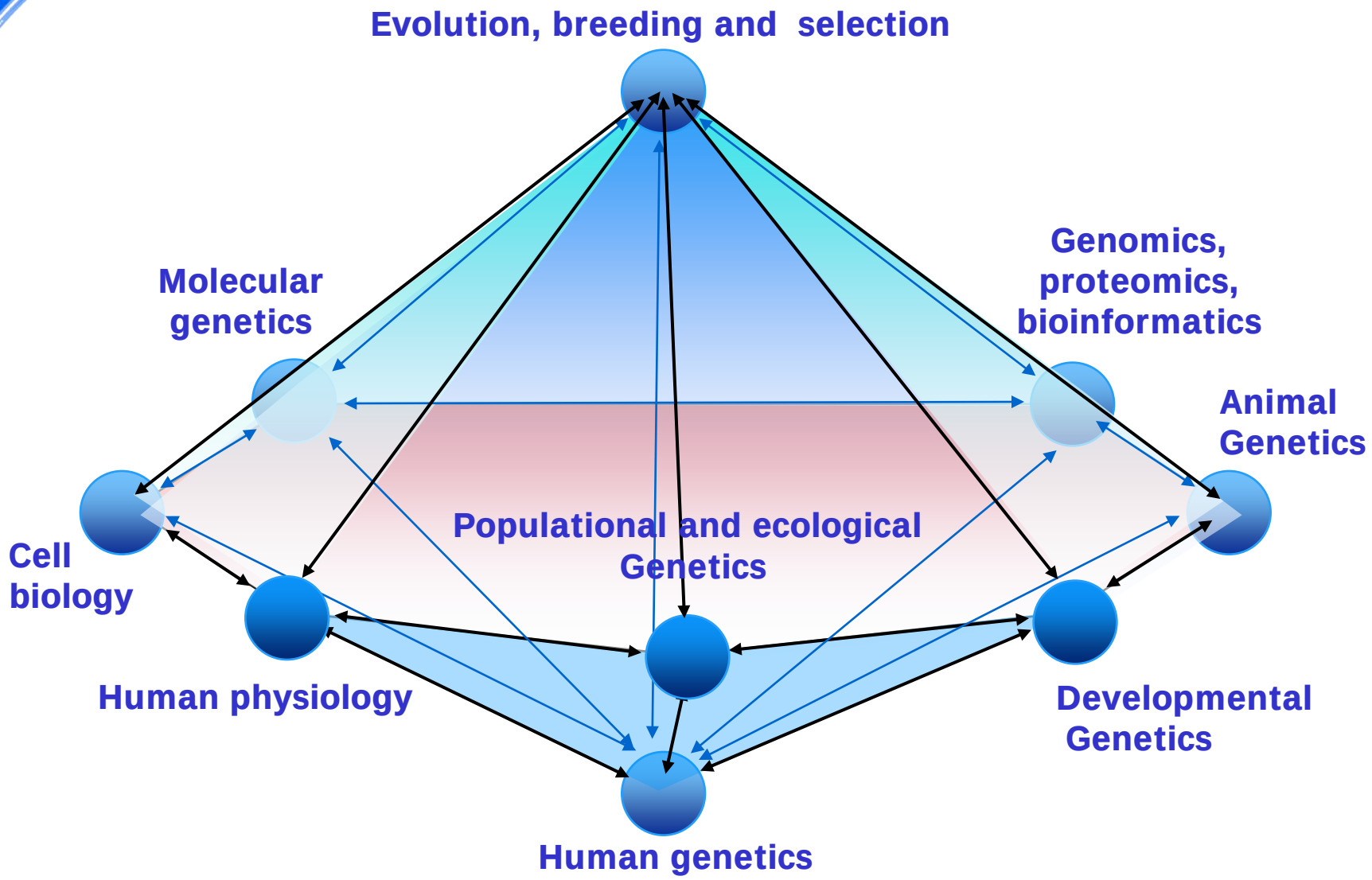
Accordingly, the research of the IC&G is summmarized under three headings.

- The structural and functional organization of genetic material at the levels of the genome, chromosome, and gene. Reconstruction of the genome, transgenesis in plants and animals.

- The molecular-genetic and genetic-evolutionary bases of the functioning of physiological systems providing vital processes. Chromosome and gene diagnostics of inherited and multifactorial diseases.

- The genetic-evolutionary aspects of population biology and biodiversity, development of new methods of animal and plant genetics and breeding for efficient use of gene pools.

Main fields of IC&G research: an integrated approach



The integrated molecular-genetic approach in the research of the Opisthorchiidae liver flukes

The influence of the Opisthorchiidae liver flukes invasion on Russian Federation population health

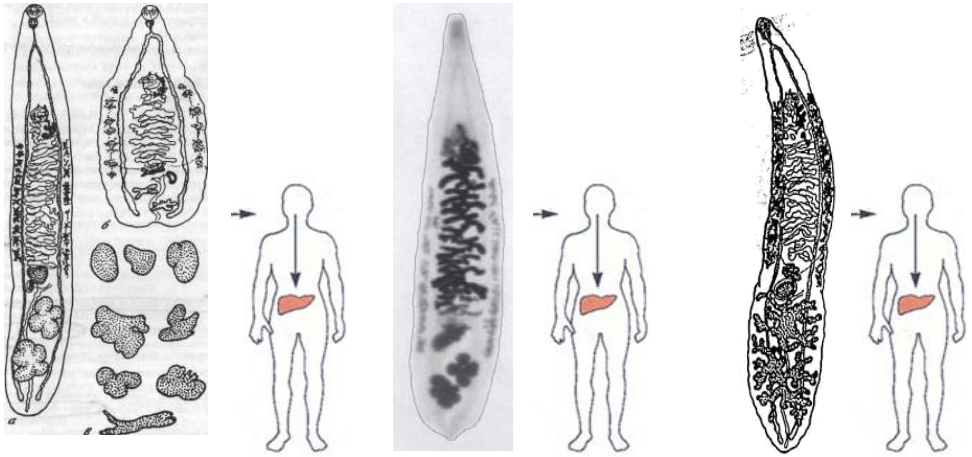
Opisthorchis viverrini

Opisthorchis felineus

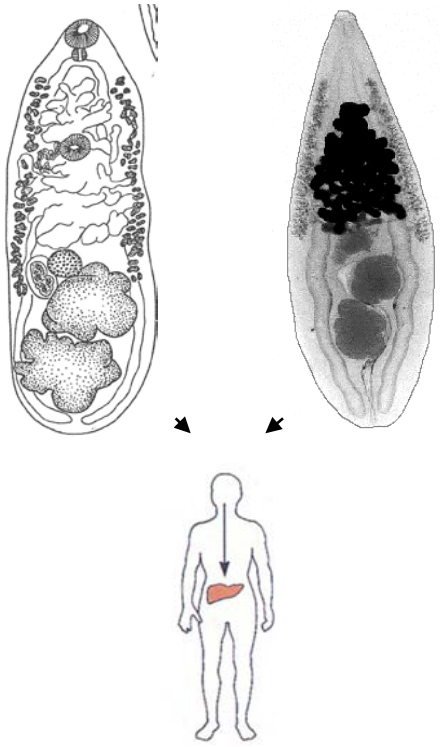
Clonorchis sinensis

Opisthorchiidae liver flukes

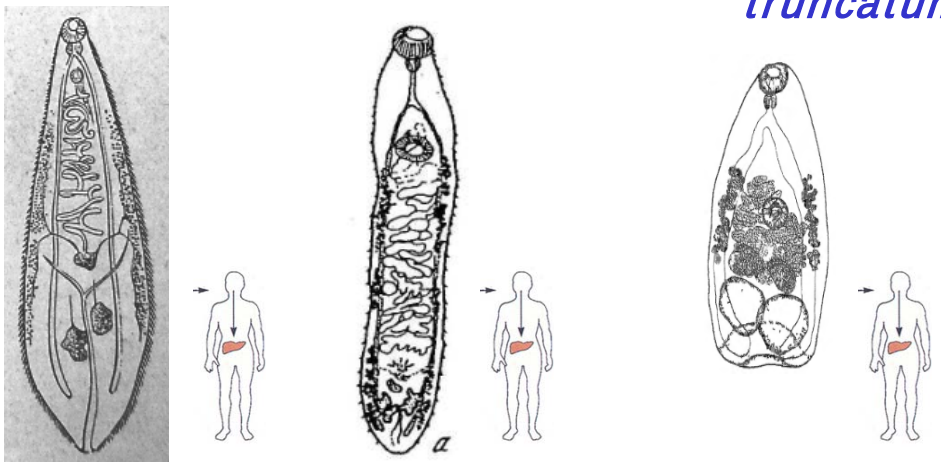
O. felineus *O. viverrini* *Clonorchis sinensis*



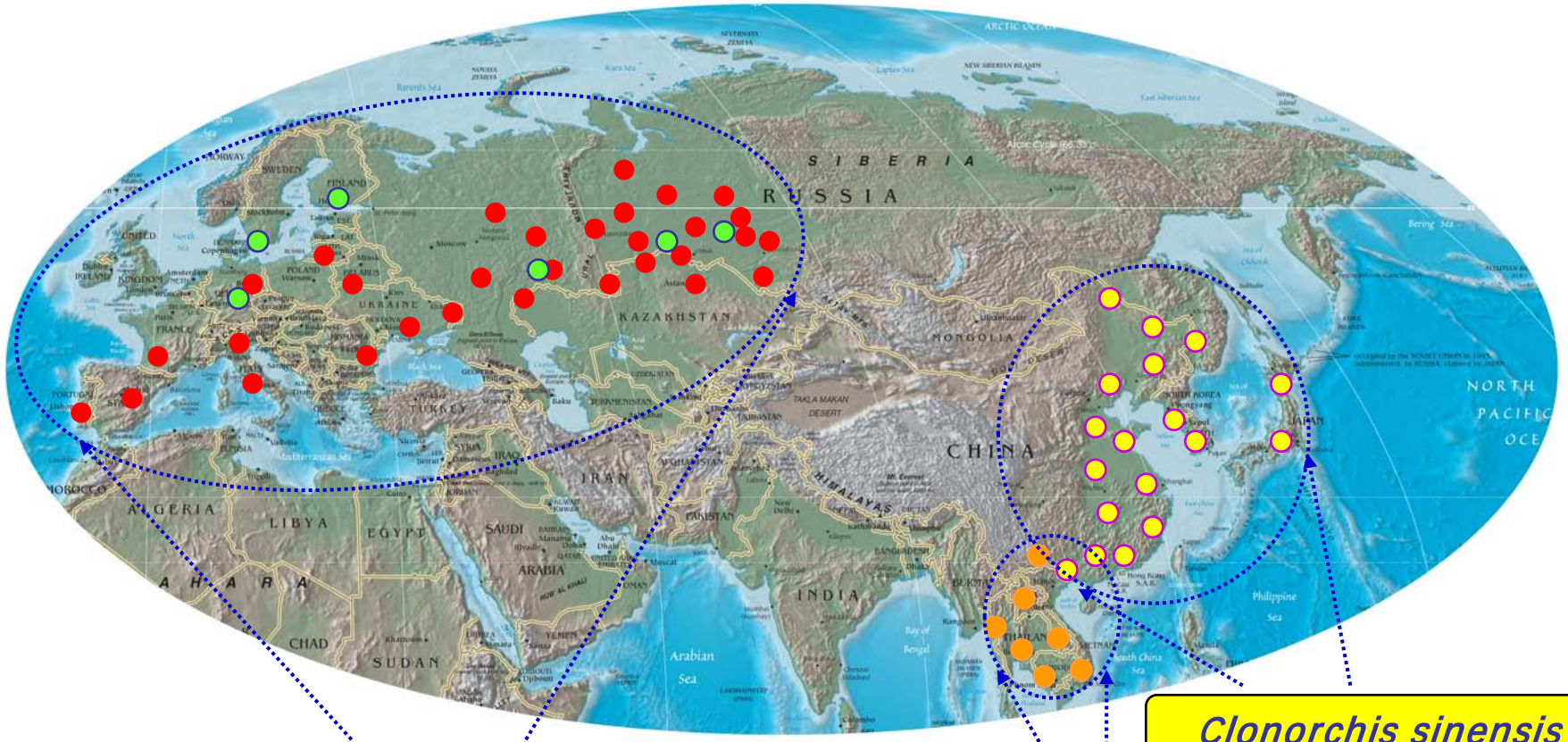
Metorchis bilis(albidus), M. conjuctus



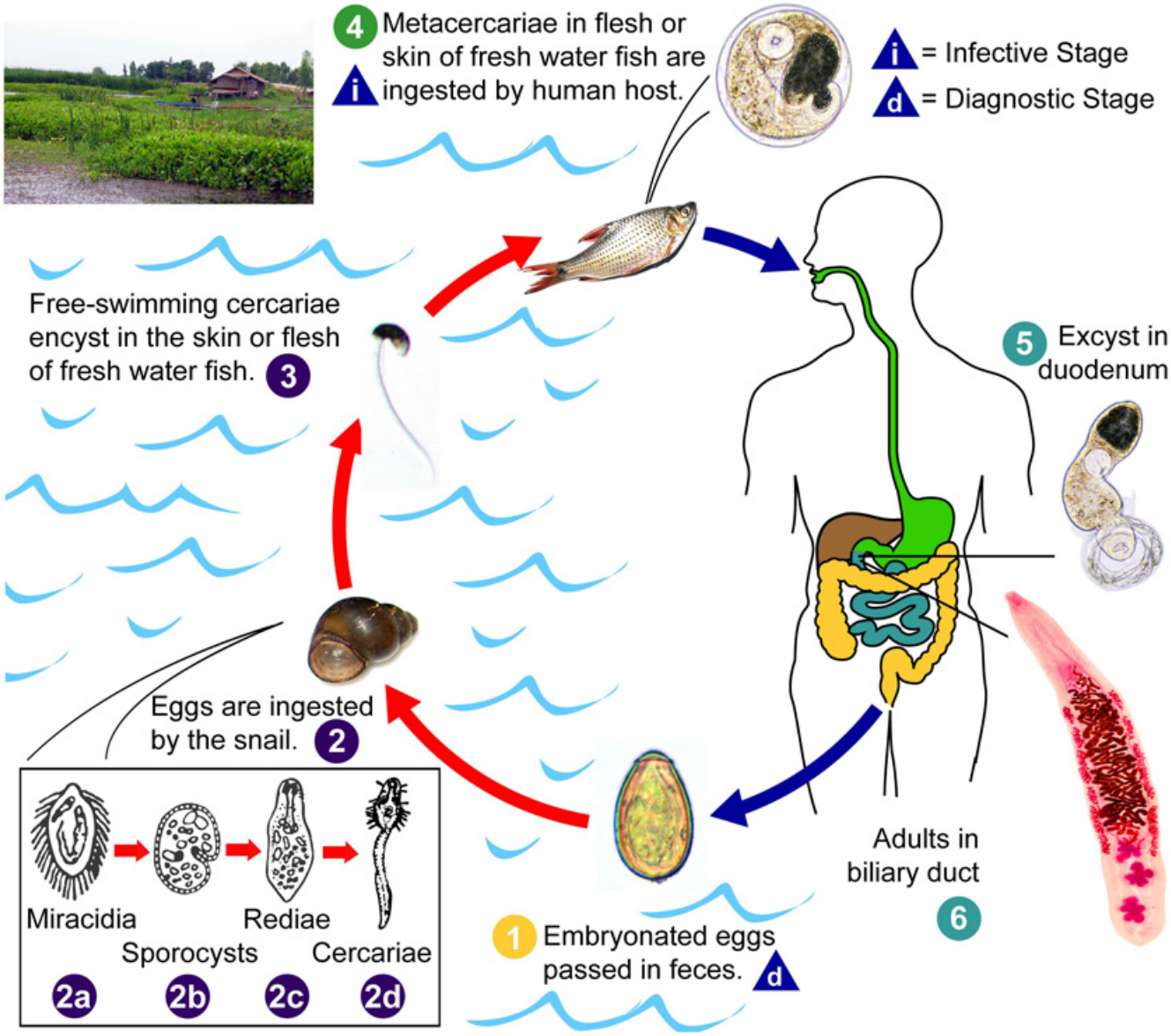
O. noverca *Amphimerus sp.,* *Pseudamphistomum truncatum*



Distribution of Opisthorchiidae liver flukes

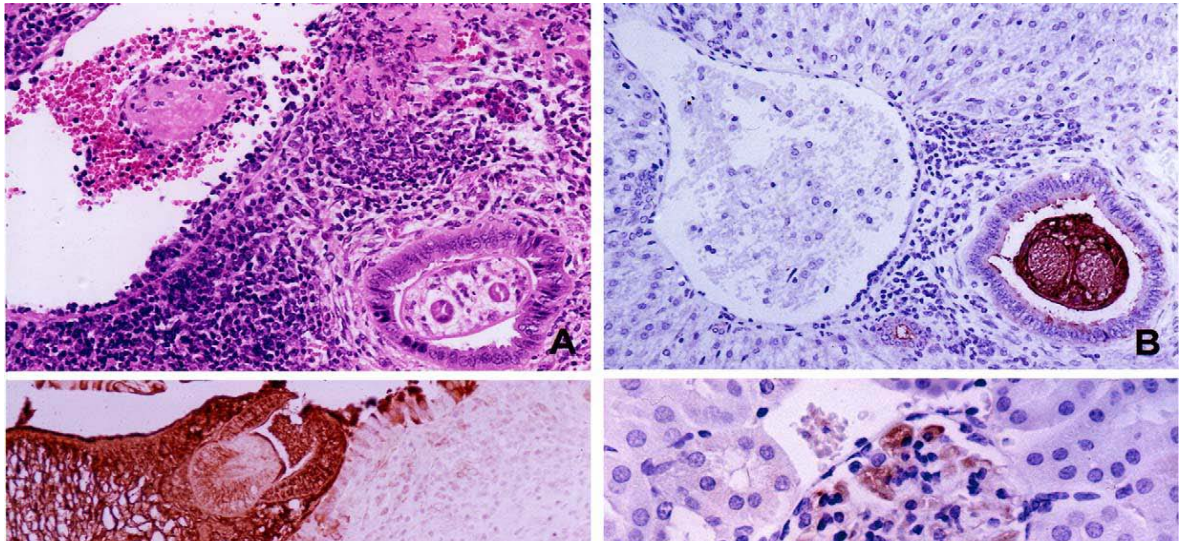


Life cycle of Opisthorchiidae liver flukes



Pathology of opisthorchiasis

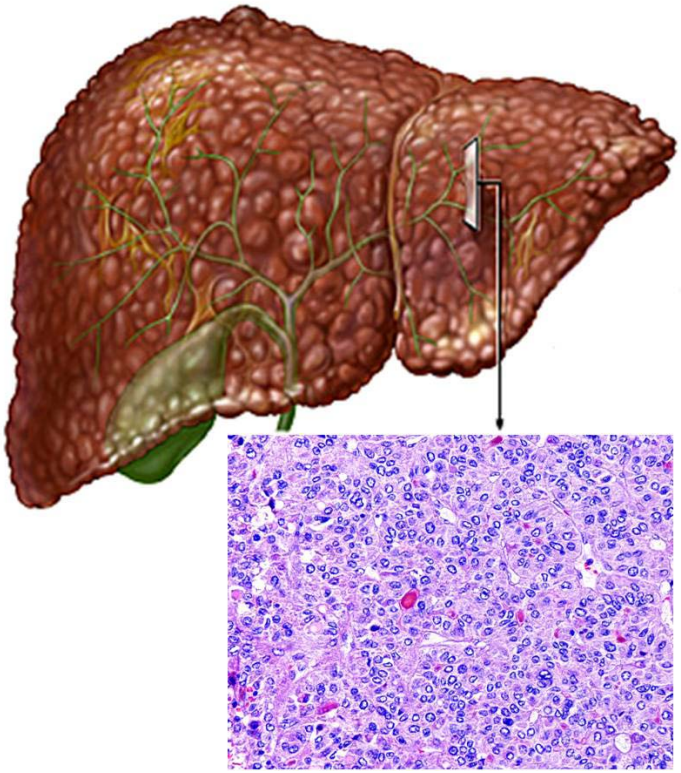
- Inflammation
- Epithelial desquamation
- Epithelial hyperplasia
- Goblet cell metaplasia
- Periductal fibrosis / cholangiofibrosis
- Granulomatous inflammation
- Adenomatous hyperplasia



(Sripa, 2003)

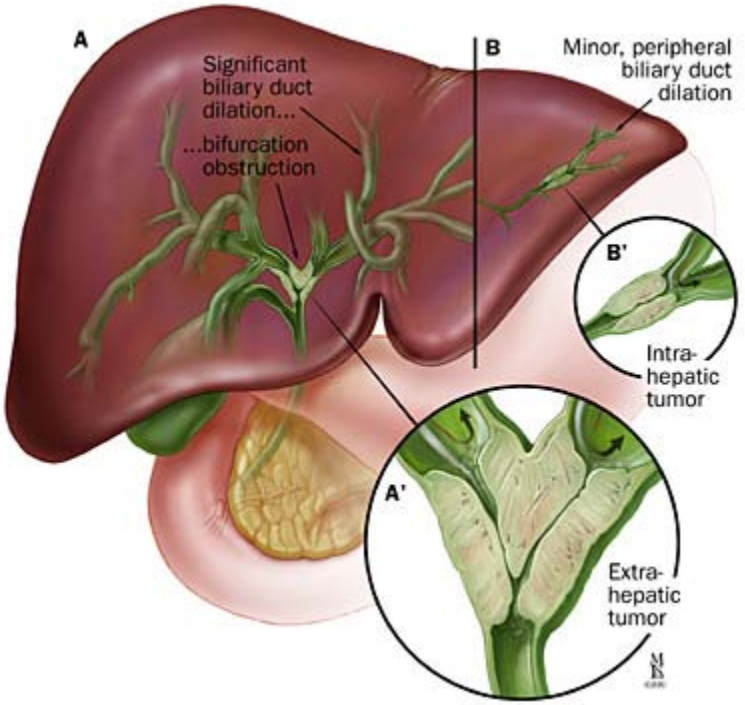
Cholangiocarcinoma

Hepatocellular carcinoma (HCC)



Hepatitis virus

Cholangiocarcinoma (CCA)



Liver fluke

Liver Fluke

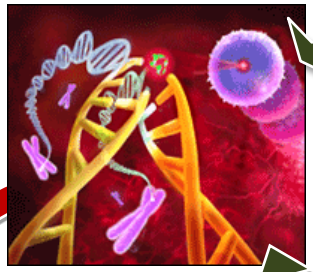
Physica
l

Immunopathology

Epith. desquamation
Parasite molecules

ROI
NO

Inflammation



DNA damage

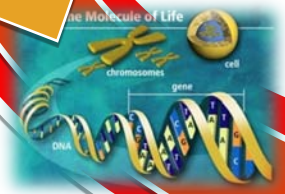
Endogenous
nitrosation

Periductal
fibrosis

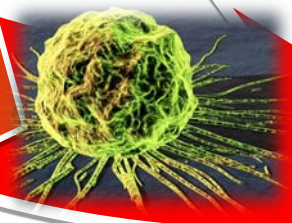
Epithelial hyperplasia
Goblet cell metaplasia
Adenomatous hyperplasia

Exogenous
nitrosamines

Cholestasis
Cholangitis



Fixed genetic
alterations



Malignant
transformation

Cholangiocarcinoma

Sripa & Pairojkul (2008)

The integrated molecular-genetic approach

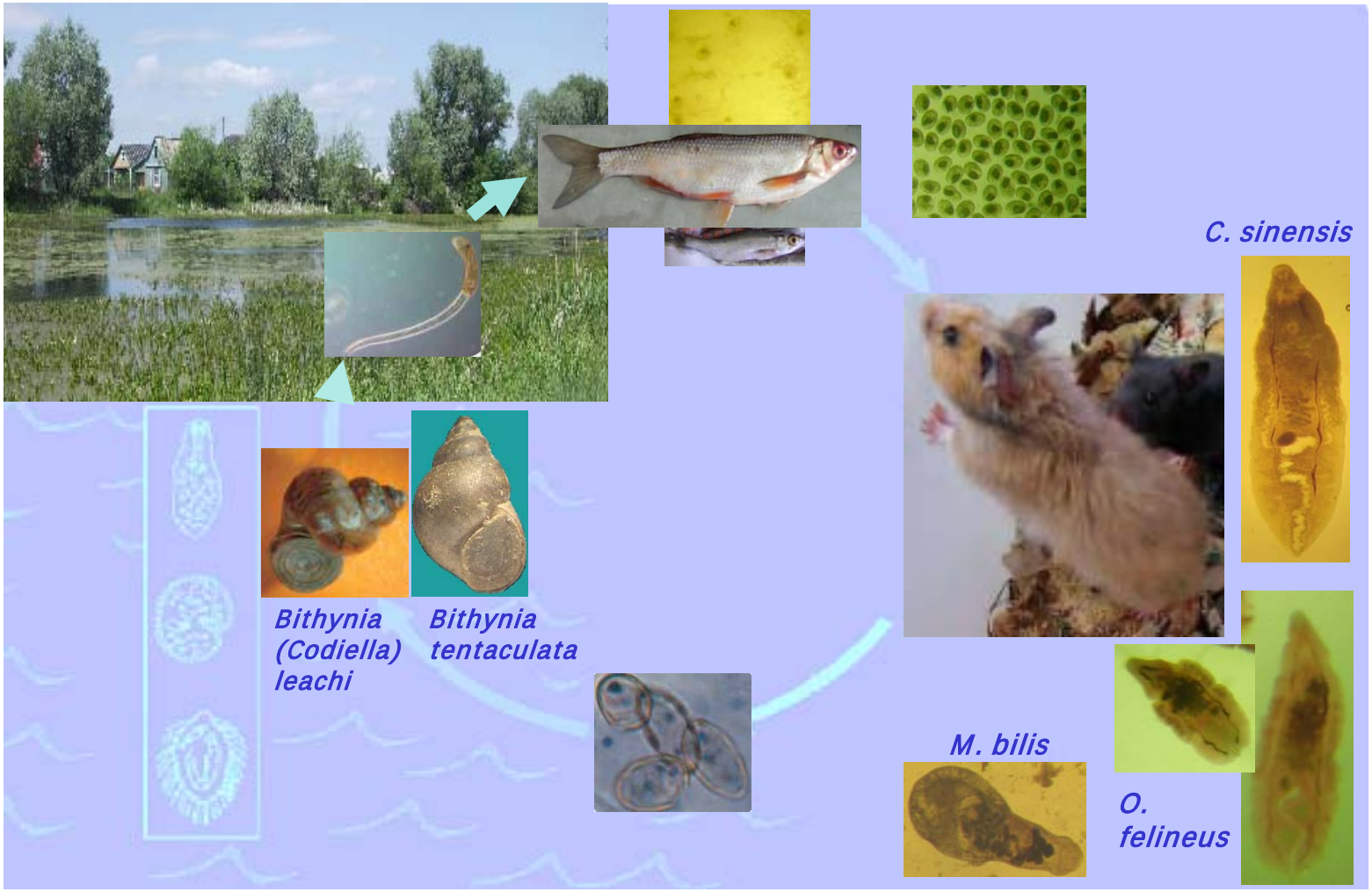
To use of modern methods of genomics, proteomics, molecular biology and microscopy for improvement of species identification of parasites, enrichment of our knowledge of their biology, investigation of parasite adaptation mechanisms to various ecological factors and mechanisms of interaction of parasites with hosts.

Research directions

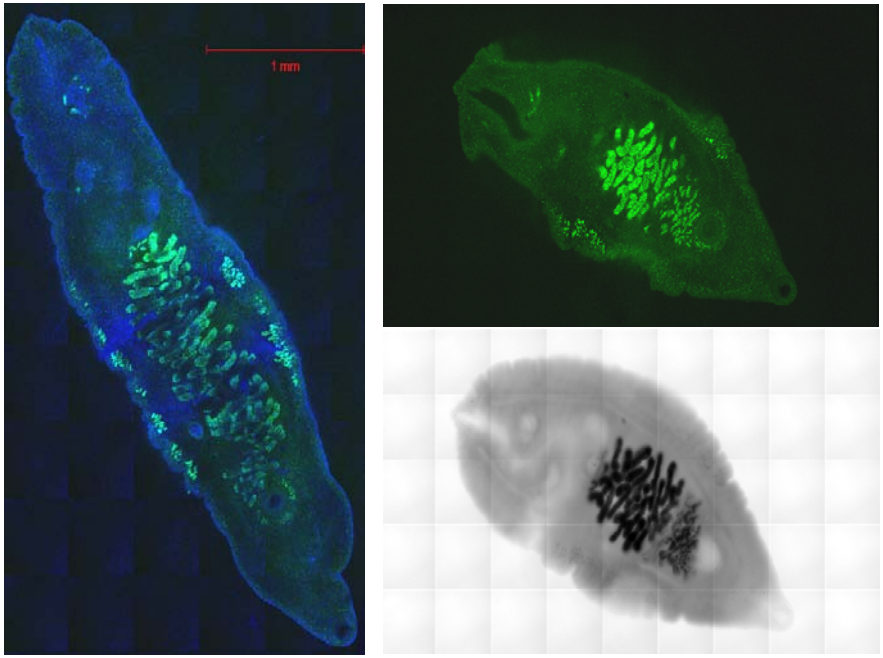
- **Molecular systematics and population genetics of opisthorchiids**
- **The analysis of karyotypes in different opisthorchiid species**
- **Construction of chromosome specific DNA-libraries and analysis of opisthorchiid chromosomes structure**
- ***Opisthorchis felineu*s genome and transcriptome sequencing**
- **Reconstruction and functional annotation of *Opisthorchis felineus* genome and transcriptome**
- **Morphology and histology of opisthorchiids on all life cycle phases**
- **Comparative studies of transcriptome and proteome of opisthorchiid different vital forms**
- **Research of host-parasite interrelations molecular mechanisms**
- **Development of species specific opisthorchiid DNA-diagnostics**

Life cycle modeling

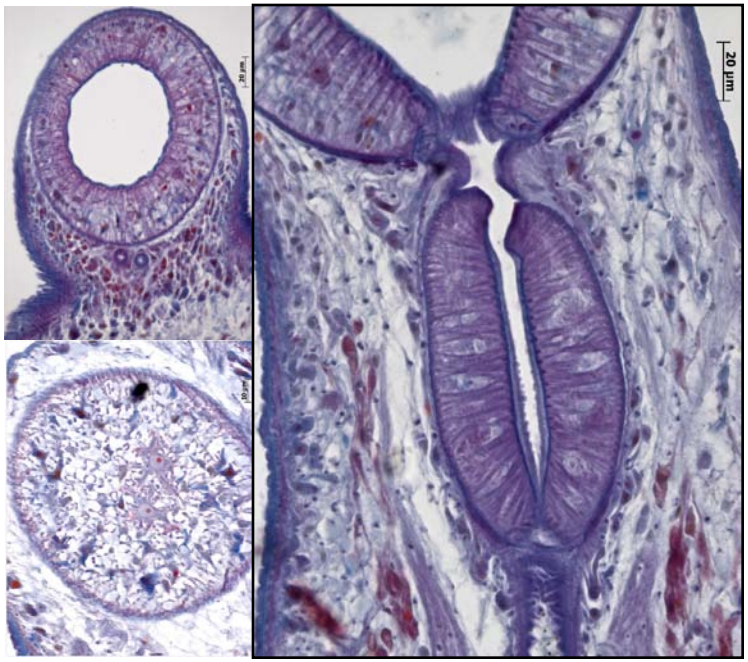
Life cycle phases of *O. felineus*, *C. Sinensis*, *M. bilis* in laboratory



Opisthorchiids morphology

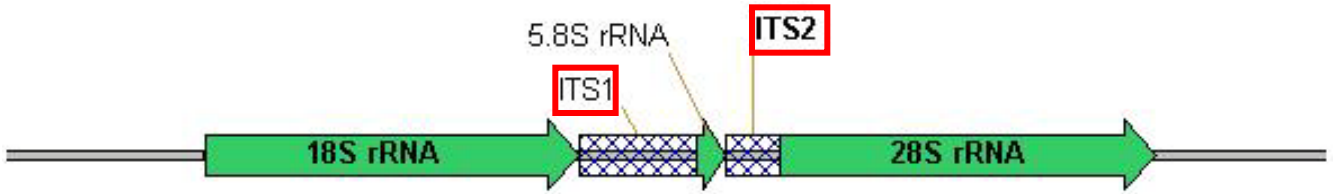


Opisthorchiids histology

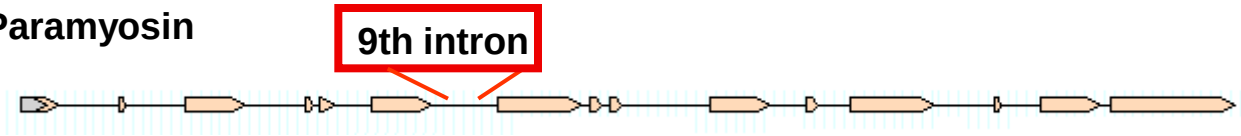


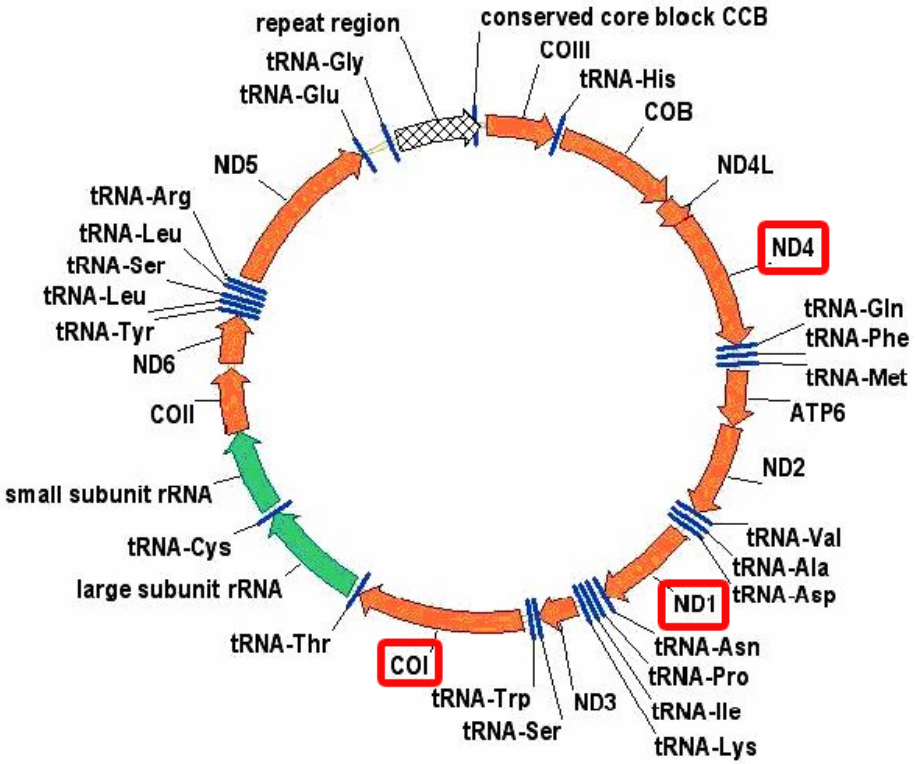
Studies of tegument and other organs structure of *O. felineus* maritae by laser scanning and conventional light microscopy

Nuclear and mitochondrial markers for opisthorchiid species genotyping



Paramyosin





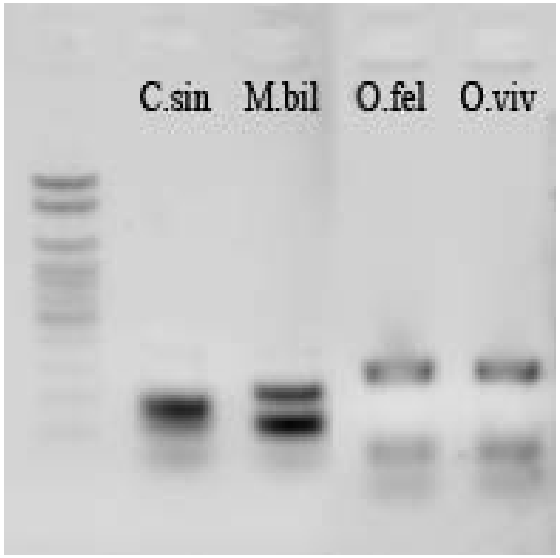
Nuclear markers:

- ITS2;
- ITS2;
- 9th paramyosin gene intron

Mitochondrial markers:

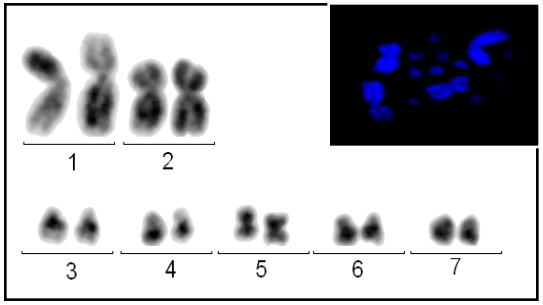
- cox1 (cytochrome oxidase 1);
- cox2 (cytochrome oxidase 2);
- cox3 (cytochrome oxidase 3);
- ND1 (NADH dehydrogenase 1);
- ND4 (NADH dehydrogenase 4).

Opisthorchiid species identification methods

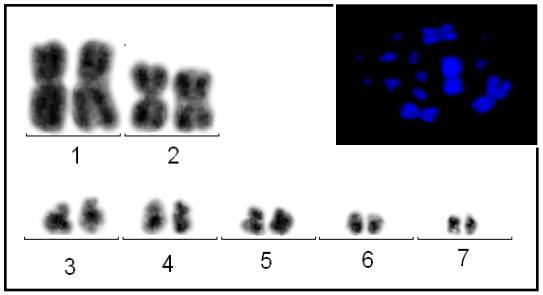


The interspecies genetic variation revealed for ITS2 marker is used for development of methods for opisthorchiid species identification

Opisthorchiids karyology and cytogenetics



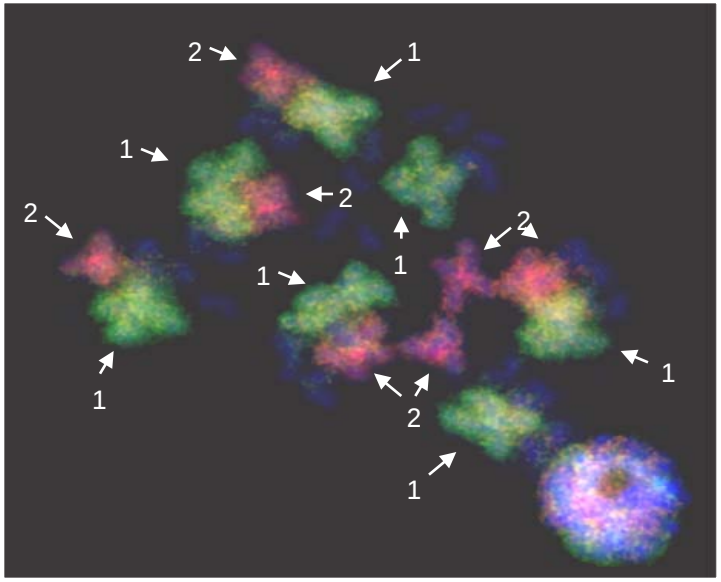
Opisthorchis felineus
mitotic chromosomes



Metorchis xanthosomus
mitotic chromosomes

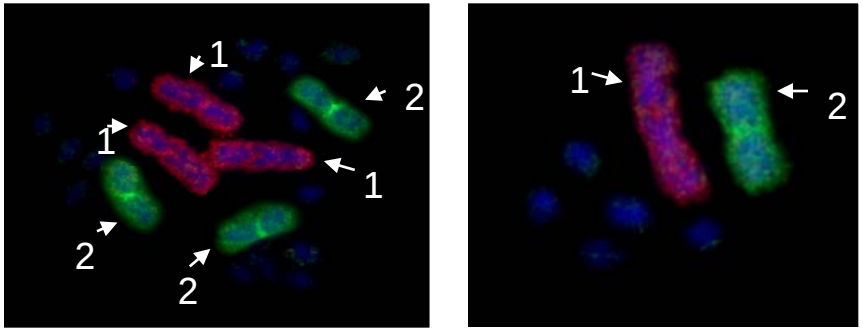
Opisthorchiids Karyology and Cytogenetics

Opisthorchis felineus

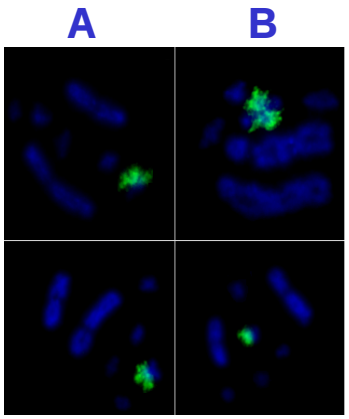


FISH of DNA probes specific to *O. felineus* chromosomes 1 and 2 on *O. felineus* chromosomes. Arrows indicate chromosomes 1 (*FITC*) and 2 (*Cy3*).

Metorchis xanthosomus



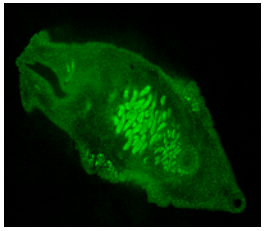
FISH of DNA probes specific to *M. xanthosomus* 1 and 2 chromosomes on *M. xanthosomus* chromosomes. Arrows indicate chromosomes 1 (*Cy3*) and 2 (*FITC*).

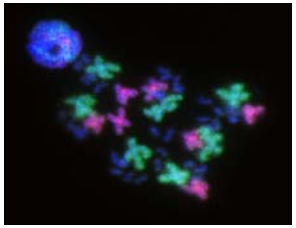


FISH of *18S rDNA* probe on *O. felineus* (A) and *M. xanthosomus* (B) chromosomes

Opisthorchis felineus Genome Project: basic research and applied aspects

- *Opisthorchis felineus* genome and transcriptome sequencing
- Reconstruction and functional annotation of *Opisthorchis felineus* genome and transcriptome
- Comparative studies of transcriptome and proteome of opisthorchiid different vital forms
- Research of host-parasite interrelations molecular mechanisms
- Development of species specific opisthorchiid DNA-diagnostics, immunodiagnostics and vaccine





Applied aspects of plant transgenesis and genetic engineering

Transgenic plants as bioreactors for production of proteins of medical importance

Traditional medicine from the Altay ecoregion

Ecologically clean region
Ecologically conscious factory
Biologically active substance

*Ganoderma lucidum (Reishi , Ling Zhi) h*as been widely used as a medicine to promote health and longevity in China for thousands of years. *Ganoderma lucidum* is effective in the treatment of chronic hepatopathy, hypertension, hyperglycemia and neoplasia under modern pharmacological research in recent 30 years.

The Altay ecoregion covers vast 845,000 square kilometer area at the junction of four countries: Russia, Kazakhstan, Mongolia and China. Forests cover about 25% of the republic's territory. The Altay is the gateway to mystical *Shambhala*.

MYCOMEDICINALS

Fungi Perfecti's
MYCOMEDICINALS®
BULK MEDICINAL MUSHROOM POWDERS
FOR THE NUTRACEUTICAL INDUSTRY

Cross-Index of Mushrooms and Targeted Therapeutic Effects

Species Abbreviations (for full species names, see Key Guide below)

	Ab	Cs	Ff	Fv	Ga	Gf	Gl	Go	He	Io	Le	Ls	Pl	Po	Pu	Sc	Tv
anti-bacterial		●	●		●	●	○	●	●	●	●	●	●	●	●		●
anti-candida						●					●					●	
anti-inflammatory					●		○		●	●			●		●		
antioxidant		●															●
anti-tumor	●	●		●	●	●	○	●	●	●	●		●		●	●	●
anti-viral	●		●			●	○			●	●		●	●	●	●	●
blood pressure		●				●	○				●			●			
blood sugar moderating	●	●				●	○				●						
cardio-vascular		●					○	●						●			
cholesterol reducing	●	●		●		●	○				●			●			
immune enhancer	●	●		●		●	○	●		●	●				●		●
kidney tonic		●					○				●						●
liver tonic		●					○			●	●				●		●
lungs/respiratory		●			●	●	○	●							●		
nerve tonic		●					○	●	●					●			
sexual potentiator		●									●						
stress reducing		●				●	○				●						

Key Codes to Medicinal Mushroom Species

Ab	*Agaricus blazei* (Royal Sun Agaricus)	Go	*Ganoderma oregonense* (Oregon ganoderma)	Pl	*Phellinus linteus* (Meshimakobu)
Cs	*Cordyceps sinensis* (Cordyceps)	He	*Hericium erinaceus* (Yamabushitake)	Po	*Pleurotus ostreatus* (Oyster)
Ff	*Fomes fomentarius* (Tinder fungus)	Io	*Inonotus obliquus* (Chaga)	Pu	*Polyporus umbellatus* (Zhu ling)
Fv	*Flammulina velutipes* (Enoki)	Le	*Lentinula edodes* (Shiitake)	Sc	*Schizophyllum commune* (Split-gill Polypore or Suehirotake)
Ga	*Ganoderma applanatum* (Artist Conk)	Ls	*Laetiporus sulphureus* (Chicken-of-the-Woods or Sulphur Tuft)	Tv	*Trametes versicolor* (Turkey Tail or Yun Zhi)
Gf	*Grifola frondosa* (Maitake)				
Gl	*Ganoderma lucidum* (Reishi)				

Source: Supporting reference information at <http://www.fungi.com/mycomed.html> (Below Table of Contents, select "Information about medicinal mushrooms")

The IC&G's SPF animal facility

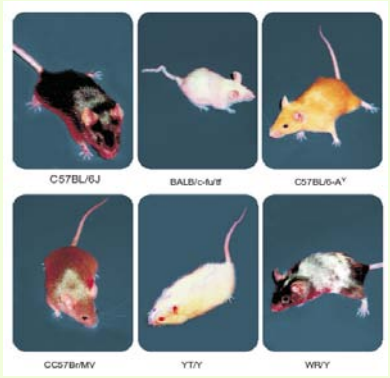
Phenotyping

Ethological and morphophysiological phenotyping

Cryo-archiving

Reproductive technologies

Selection, transgenesis, panels of recombinant lines



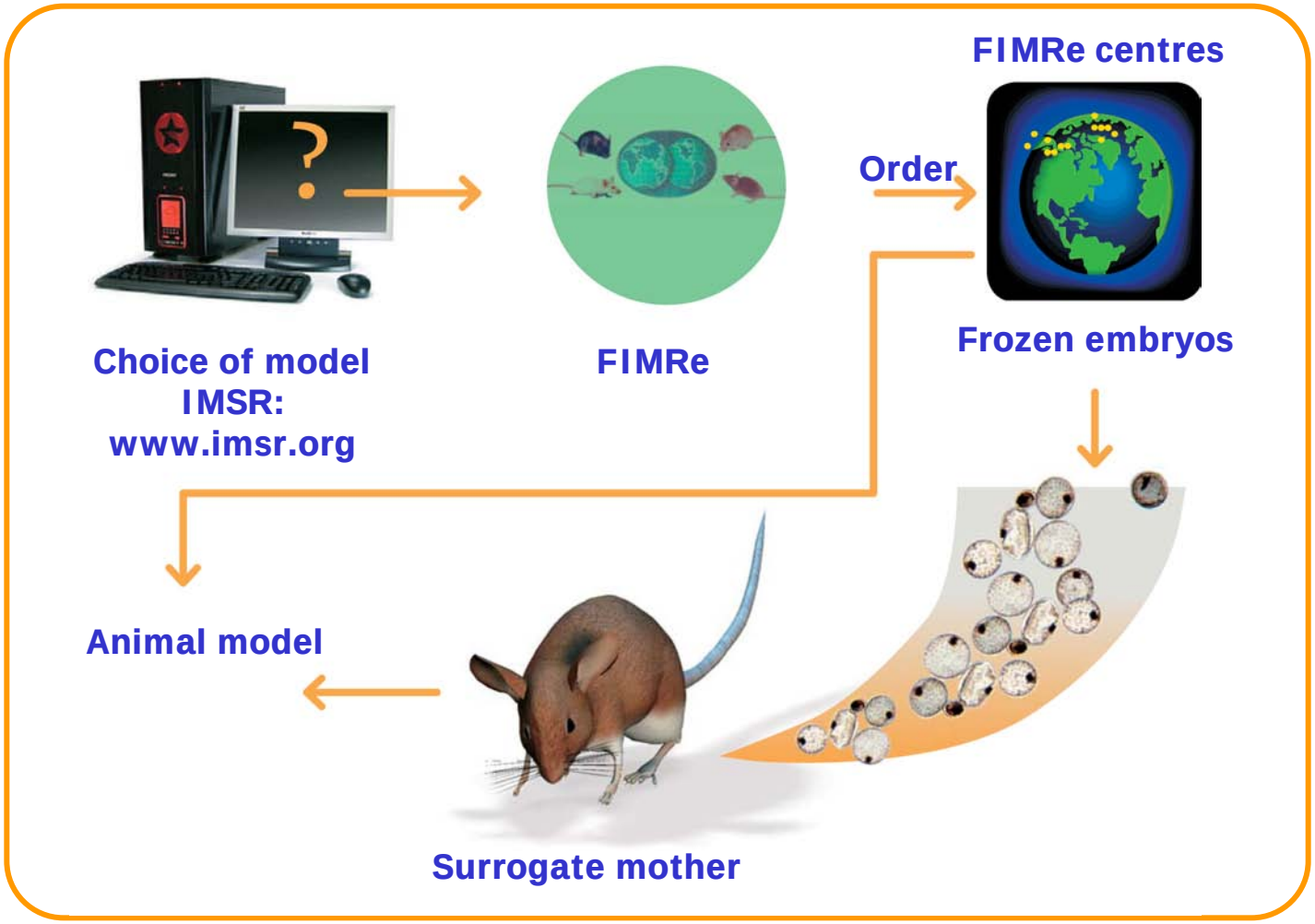
Genetic, virologic and microbiological control, pathomorphology, hematology, and biochemistry of the blood

Functional tomography

IC&G's Animal Facility for SPF mice and rats

- Total area — 4500 m2
- 2 barrier zones (on the 2 and 3 floors) > 1300 m2
- Positive air pressure
- High-effciancy 3 stepped cleaning-up of incoming air (15-20th air exchange per hour);
  1 stepped cleaning-up of de-air
- Maintenance of 25 000 mice and 10 000 rats according to SPF standard

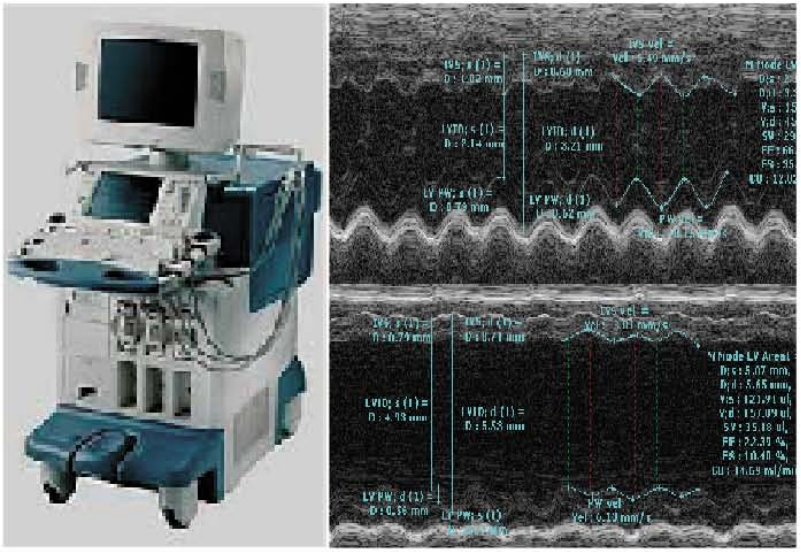
Animal models from FIMRe and AMMRA



Animal Facility's equipment: cages, racks and washing machine

Research equipment

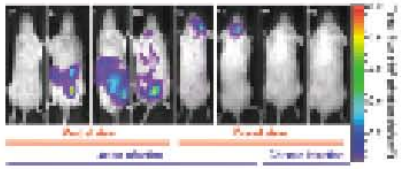
Functional morphology (imaging)



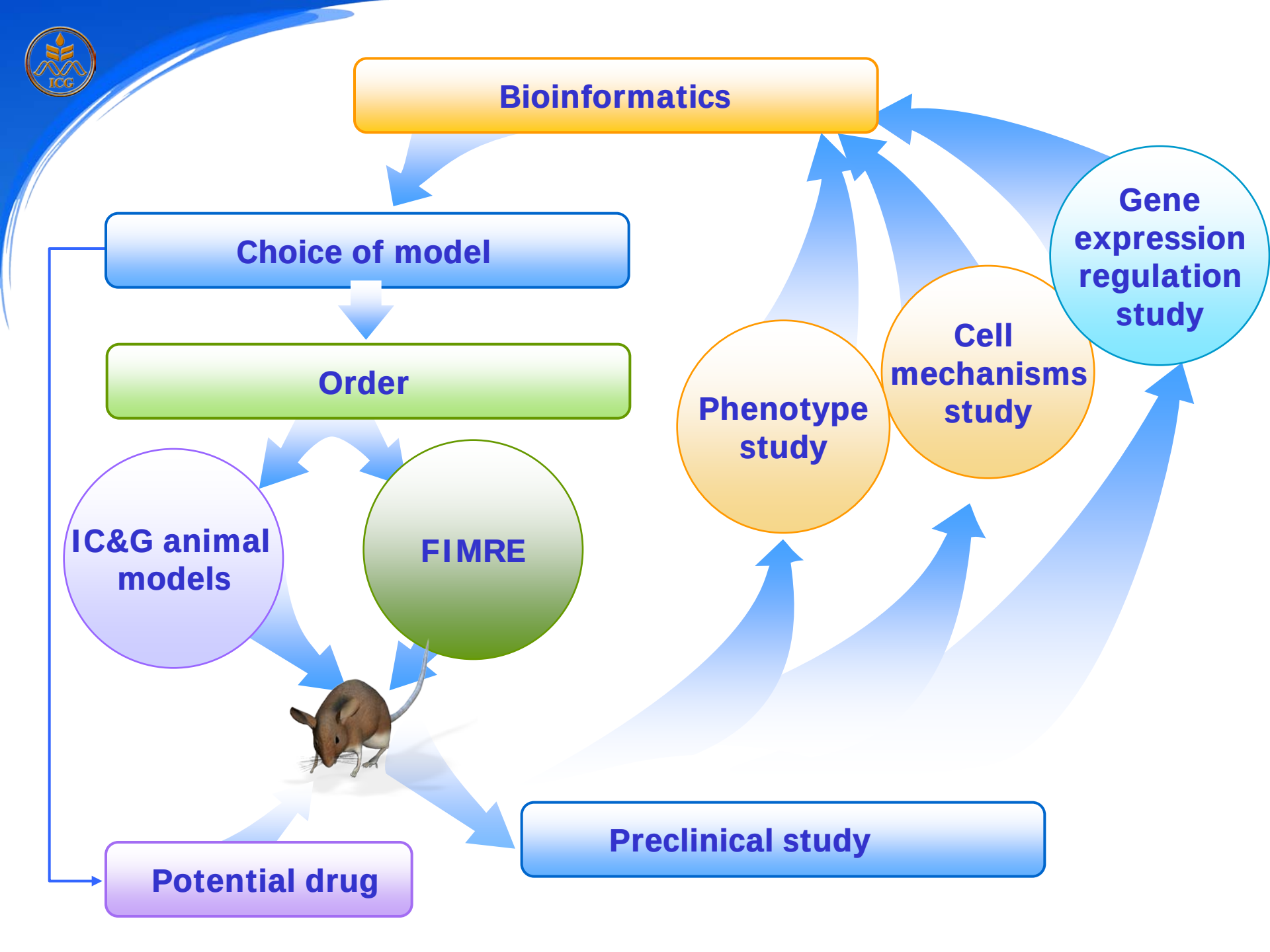
Aplio Toshiba SSA-700A (770A)

Lunar PIXImus I

fMRI for mice and hamsters
BioSpec Avance II (Bruker)
11.7 Tesla

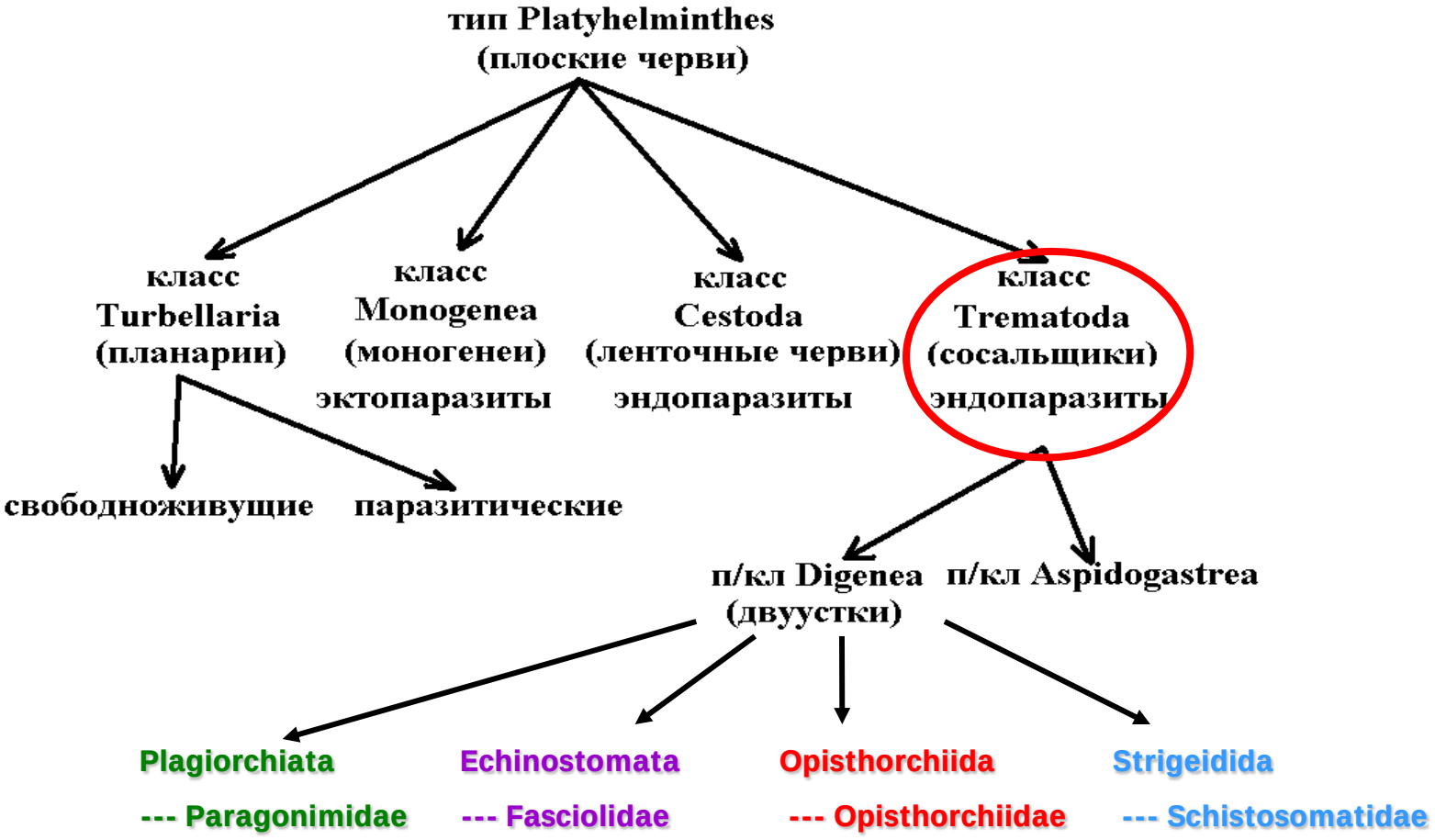


Pearl-imaging system LiCor


Bioinformatics
Choice of model
Order
IC&G animal models
FIMRE
Potential drug
Preclinical study
Phenotype study
Cell mechanisms study
Gene expression regulation study

Thank you for your attention!

Classes and orders of Platyhelminthes

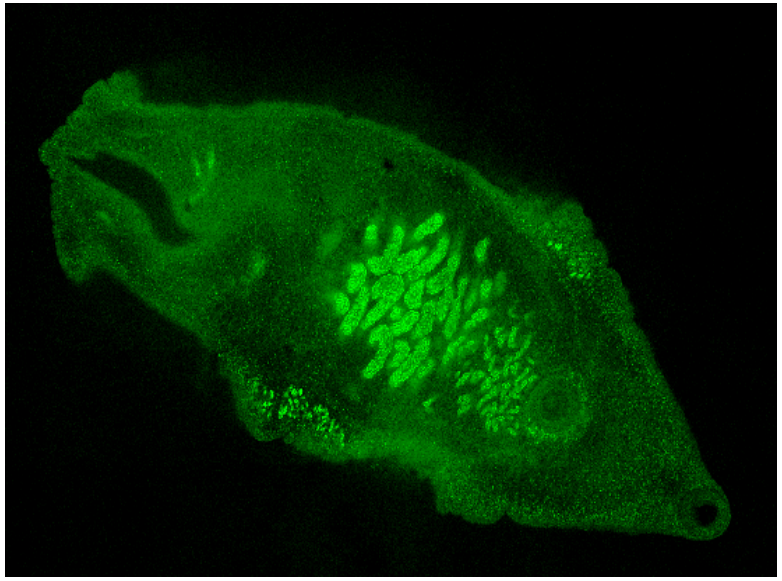


Molecular systematics and population genetics of Opisthorchiidae family trematodes

Research problems:

- **Collection of DNA samples of *Opisthorchis felineus* and other Opisthorchiidae species from different natural populations;**
- **Development of molecular markers for studying heterogeneity of opisthorchiids populations;**
- **Development of methods for identification and differentiation of Opisthorchiidae species;**
- **Development of methods for Opisthorchiidae parasites detection in various organisms (snails, fish, mammals) and in water bodies.**

GENOMICS, PROTEOMICS, BIOINFORMATICS AND EPIDEMIOLOGY OF OPISTHORCHIS FELINEUS



This organism has a very complex life cycle with six life forms, which can infest three different hosts. These amusing properties are supported by a complex organization of its genome,which supports several developmental genetic programs and various molecular mechanisms to enable interaction with the hosts' organisms.