Screening of biologically active natural products in PIBOC.

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The Pacific Institute of Bioorganic Chemistry (PIBOC) is a research institute belonging to the Far Eastern Branch of the Russian Academy of Sciences (FEBRAS). The institute was founded with the aim of implementation of chemical and biochemical studies on unique Far-Eastern higher plants and marine organisms of the World Ocean. The latter trend has become the main direction of the studies at present. The institute conducts scientific investigations in bioorganic chemistry, molecular immunology, molecular biology, biotechnology and related fields. The institute's current research in the chemistry of secondary metabolites of marine invertebrates and marine microorganisms as well as in enzymology and molecular immunology are of special scientific value.

The search for biologically active compounds in the Laboratory of Bioassay of PIBOC consists mainly of cell based screening, image technology and ion channels as cellular targets as well as several in vivo models. This work includes application of the technique of radioisotopes, ion-selective electrodes, fluorescent spectroscopy, cytotoxicity, BLM technique and cell image analysis which afford evaluation of interaction of substances with various types of cells, biological and model lipid membranes. We perform our investigations using some cell cultures, embryos of marine invertebrates (Echinodermata), different microorganisms including two-hybrid transgenic yeasts with human estrogen receptors, and lipid liposomes. We screen natural products for antimicrobial, antiviral and anticancer activity, immunomodulatory effects, as inhibitors of cell adhesion and antioxidants. High resolution MRI-tomography with 7T magnet (PharmaScan 70/16US, Bruker) allows us to search in situ for compounds with anticancer, anti stroke and anti ischemia activity, inhibitors of angiogenesis and hepatoprotective substances. Structures of complexes of some testing compounds with viral and cellular proteins and ion channels are theoretically predicted in experiments in silico by the methods of molecular modeling and the docking approach using Linux cluster of interdepartmental supercomputer center of FEBRAS.

Detection of lyosomal activity in mouse peritoneal macrophages
Pseudocolor fluorescence image of mouse BALB/C line peritoneal macrophage monolayer stained with Acridine orange
A - cells isolated from control mouse; B - macrophages isolated on 4th day after mouse injection with cucumarioside A$_2$.

Cytotoxic and cytostatic activities using sea urchin embryos
A - control embryos
Development stage of 8-blastomeres
B - stop of development and blastomere lysis

Detection of intracellular concentration of Ca$^{2+}$ using fluorescent probe Calcium green-1/AM
A - non activated human lymphocytes
B - activated cells

Two-hybrid transgenic yeast system
to detect natural pro- and anti-estrogenic compounds

Use of BLM for screening and investigation of channel-forming activity of proteins, low molecular compounds and other membranotropic substances

Structure of HIV-1 protease complexed with betulinic acid predicted by computer modeling