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The hypothesis of the possible evolutionary role of tumors suggests that hereditary tumors may supply evolving multicellular organisms with extra cell masses for the expression of newly evolving genes (Kozlov, 2014). After expression of novel genes in tumor cells, tumors may differentiate in new directions and give rise to new cell types, tissues and organs.

In the presentation, the bulk of data supporting the positive evolutionary role of tumors will be reviewed, obtained both in the lab of the author and from the literature sources.

The following issues will be addressed: the widespread occurrence of tumors in multicellular organisms; features of tumors that could be used in evolution; the relationship of tumors to evo-devo; examples of recapitulation of some tumor features in recently evolved organs; the types of tumors that might play the role in evolution; examples of tumors that already have played the role in evolution.

The discussion of experimental confirmation of nontrivial predictions of the hypothesis will include the analysis of evolutionary novelty of tumor-specifically expressed EST sequences; ELFNI – AS1, a human gene with possible microRNA function expressed predominantly in tumors and originated in primates; PBOV1, a human gene of the recent de novo origin with predicted highly tumor-specific expression profile; and the evolutionary novelty of human cancer/testis antigen genes; the data obtained on transgenic fish tumors regression model; and other data.

It can be concluded that expression of protogenes, evolutionarily young and/or novel genes in tumors might be a new biological phenomenon, a phenomenon of carcino-evo-devo genes, predicted by the hypothesis of evolution by tumor neofunctionalization.

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T143

Integrated genomic analyses of breast cancer, relevance for better prognosis and treatment evaluation

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Combined analyses of molecular data, such as DNA copy-number alteration, mRNA and protein expression, point to biological functions and molecular pathways being deregulated in multiple cancers. Genomic, metabolomic and clinical data from a variety of solid cancers and model systems are emerging and can be used to identify novel patient subgroups for tailored therapy and monitoring. The first solid tumor to be profiled by expression arrays was carcinoma of the breast. The most reproducible classification by mRNA expression is based on the biological entities referred to as the intrinsic subtypes; Luminal A, Luminal B, Basal-like, HER2 enriched, and the Normal-like groups. In the past decade a number of molecular studies to classify breast cancer have added one or two additional molecular levels, most frequently DNA copy number, and gene sequencing. However, few of the studies have integrated more than two levels of information from the same patients. We have in our lab collected several layers of high throughput molecular data, TP53 mutation status and high throughput paired end sequencing on a dataset of 110 patients. This dataset was clustered according to each molecular level studied using an unbiased, unsupervised clustering, and survival KM plots for each patient subgroup was created. While some samples always cluster together at any molecular level, others cluster in different groups according to each particular molecular endpoint. Therefore, we used an integrated approach to understand breast cancer heterogeneity by modeling mRNA, copy number alterations, microRNAs, and methylation in a pathway context utilizing the pathway recognition algorithm using data integration on genomic models (PARADIGM). We show that massive interleukin signaling profiles are observed in invasive cancers and are absent or weakly expressed in healthy tissue but already prominent in ductal carcinoma in situ, together with ECM and cell-cell adhesion regulating pathways. A good correlation was observed between methylation and mRNA expression based classification ($p = 2.29 \times 10^{-6}$). Using PARADIGM based on mRNA and miRNA expression, CNAs, and methylation five new clusters with survival differences were revealed. Given the increasing importance of immune constitution for the success of chemotherapy and targeted treatment, this additional information may prove useful in the clinic in the future.

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P41

Role of the optical methods for blood study in staging of colorectal cancer

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Background: The aim of this work was to assess the potential of the optical methods for studying erythrocytes (Er) and blood serum (BS) of patients with colorectal cancer (CC).
Methods: A total of 26 persons (52 + 8 years old) with CC (histologically – adenocarcinoma) in the T1–2 stage (the 1st group consisting of 10 patients) and in the terminal stage T3–4 (the 2nd group involving 16 patients) were examined. The metastases (in the liver area) were detected in 6 patients; the remaining patients had no metastases. The degree of lymph node involvement in most patients was not determined, the ten corresponding N1. The control group consisted of 16 healthy people (50 + 6 years old). Electric and viscoelastic Er parameters were investigated by dielectrophoresis, their membrane structure – by TLC and gas chromatography. The optical properties of BS were studied by the methods of ellipsometry. The reaction of the monoclonal

antibody CD 24 with BS antigens of CC patients was studied by spectroscopic ellipsometry close to the conditions of surface plasmon resonance (SPR) (ProteOn XPR36 (BioRad).

Results: We observed significant differences in Er parameters, associated with the CC stage. Given in the 2nd group (T3–4) summarized rigidity, viscosity, electrical conductivity, the relative polarizability, indexes of aggregation and destruction were significantly higher than those in the 1st (T1–2) and in the control group ($p < 0.001$–0.05). At the same time the patients of the 2nd group had marked disturbances of Er deformability, leading to the development of microcirculatory disorders and tissue hypoxia with the expressed deficit of intracellular macroergs. We observed high levels of cholesterol fraction, oleic, stearic acids, high index of cholesterol/phospholipids (PHL) and low levels of total lipids, easily oxidable PHL, arachidonic acid, omega-3 index in Er membranes in the 2nd group in comparison with those in the 1st group of patients ($p < 0.0001$–0.03). Scanning ellipsometry showed marked heterogeneity in thickness and composition, the abundance of discontinuities in thin films of BS of patients in the 2nd group compared to the 1st one ($p < 0.001$). Increasing the refractive index in combination with the reduction in film thickness as CC stage was weighting has been observed ($p < 0.01$–$0,\.05$). The concentration of the antigens to the CD24 in the BS of patients (obtained by SPR) in the terminal stages of CC was higher than that in the T1–2 ($p < 0.001$). We revealed correlations between Er parameters, BS ellipsometry characteristics and biochemical parameters, which reflected the interaction between these components depending on the CC stage.

Conclusion: Identified microcirculatory disturbances probably aggravate the course of CC and, therefore, require additional therapeutic effects. Differences in Er and BS parameters associated with the stage of CC, give hope for the development of new diagnostic methods at the early stages of the disease.

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P64

Cytokine production by malignant and benign breast tumors

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Growing tumor and its microenvironment are capable to produce a number of cytokines that alter the nature of the antitumor surveillance by host immune system.

Objective: Comparative evaluation of cytokine-producing function of the invasive ductal carcinoma and fibroadenoma of the breast in vitro.

Materials and methods: Similar biopsies ($V = 8\ mm^3$) of the breast tumors were obtained using a special device, cultivated in DMEM F-12 at 37 °C for 72 h. Concentrations of the following cytokines: IL-1β, IL-1Ra, TNFα, IL-2, IL-6, IL-8, IL-10, IL-17, IL-18, VEGF and IFNγ in the supernatant of the tumor were measured with enzyme-linked immunosorbent assay (ELISA).

Results: The investigation of cytokines level in the supernatant of malignant and benign breast tumors revealed significant differences only in concentrations of IL-10, IL-17, IL-18 and IFNγ which had a contrary tendency. For example, the concentration of IL-10 was lower at invasive ductal carcinoma in comparison with fibroadenomas. The concentrations of IL-17, IL-18 and IFNγ at invasive ductal carcinoma were significantly higher than those of breast fibroadenomas. IL-17 and IL-18 are known to be pro-oncogenic cytokines, and the higher the level, the higher the severity of tumor progression. Reduction in the IL-10 concentration might be explained by the already formed neoplasm, which depends on angiogenesis. In this case, IL-10 no longer exerts antiangiogenic action, which contributes to tumor progression. Reduction in the IL-10 concentration, which inhibits the production of IFNγ leads to an increase in the IFNγ level. In early stages of tumor development, IFNγ provides an antitumor effect and at the same time facilitates the selection of a more malignant clones but its pro-tumoral action predominates at advanced stages of tumorigenesis. Moreover, higher concentration of IFNγ is supposed to be associated with biological effects of IL-18, which is its immediate inductor. In addition, malignant tumor cells are capable to produce their own IL-18, which stimulates tumor progression and facilitates the migration of endothelial cells involved in angiogenesis, which leads to intensified invasion and metastasis.

Conclusion: Cytokine production in supernatants of invasive ductal carcinoma compared with fibroadenoma of the breast is characterized by increase in IL-17, IL-18 and IFNγ concentrations and decrease in IL-10 concentration. Findings suggest the ability of malignant tumor and its microenvironment to secrete the pro-oncogenic cytokines. Fibroadenoma is also able to produce cytokines due to fibroblasts, fibrocytes and some leukocytes in its content.

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P53

Long-term monitoring of the digestive cancer in Novosibirsk

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This study used data from population-based cancer registries and total mortality over the past quarter of a century in NIITPM, Novosibirsk. The follow-up period was from 1985 to 2014. Both registers operated in the two regions, the most typical for the city. The results can be extrapolated to the entire population of Novosibirsk. For long-term analysis we used data from two registers concerning gastric cancer, colorectal cancer and liver cancer. Morbidity and mortality from stomach cancer over the past 25 years have declined, however, the proportion of GC 3–4 (end-stage) remains constant with a tendency to increase. In general, the incidence of colorectal cancer in the Novosibirsk