The samples were subjected to mass spectrometric analysis after pre-separation by UHLC Ultimate 3000 RS ( Dionex, USA) in a column Dionex Acclaim RSLC 120 C18 (2.1 × 50 mm 120 Å, 0.2 μm) flow rate of 0.5 ml/min using as eluents 0.1% solution of formic acid in water (A) and 0.1% solution of formic acid in asetonitrile (B). Elution was carried out in gradient mode: (%B): 0–3 min (5%), 3–28 min (5–95%), 28–30 min (95%), 30–31 min (95–5%), 31–35 min (5%). Mass spectrometry was carried out on ESI-qTOF ultrahigh resolution Maxis 4G (Bruker, Germany) in the positive ion detection mode range 50–1000 m/z, 2 Hz with the following settings electrospray ion source: CV 3800 V, Nebulizer gas 1 bar, Dry Gas 8 l/min, Dry Temp: 200 °C.

**Results:** It was found that the DNA which was cleaved with acid hydrolysis in the result contained single DNA bases. The number of DNA adducts was evaluated by the integrated value of the mass spectrometric response detector. It was shown that most amount of adducts 4-hydroxy-1-(3-pyridyl)-1- butanone and N3-(2-carbamoyl-2-hydroxyethyl)adene was found in DNA samples derived from tumor tissue. The adduct N7-(2-carbamoyl-2-hydroxyethyl)guanine was found in tumor tissue samples and DNA derived from plasma, as well as in all samples of healthy tissue.

**Conclusion:** The established protocol of DNA sample preparation followed by analysis using a mass spectrometer high resolution allows to detect the content of the DNA adducts in small DNA probes (100 ng). We found, that acid hydrolysis is cheaper and more practical in comparison to enzymatic digestion in order to generated samples containing single DNA bases without damaging the structure of adducts.

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**P107**

**Two-years long genetic screening of breast cancer patients in Novosibirsk (Russia) – first practical results**

S. Kovalenkoab, G. Paulb, N. Matyashb, A. Kozyakovc. a Institute of Molecular Biology and Biophysics, Novosibirsk, Russian Federation, ab Biolink Ltd., Novosibirsk, Russian Federation, b Novosibirsk Regional Oncology Hospital, Novosibirsk, Russian Federation c Corresponding author.

Mutations in BRCA1 and CHEK2 genes associated with hereditary breast cancer were tested in 7920 randomly selected individuals of Novosibirsk (Russia). Mutations BRCA1 5382insC and CHEK2 1100delC were the most frequent, they were found in 0.25% and 0.4% of the general population respectively. We suggested to find mutations carrier by the screening of all breast/ovary cancer patients for the most frequent mutations (BRCA1 5382insC and CHEK2 1100delC) with subsequent analysis of the first-line relatives of cancer patients if one of the mutations was found.

From June 2013 till January 2015, all patients from Novosibirsk regional oncology hospital with the diagnosis of breast cancer and some patients with the diagnosis of ovary cancer were tested for mutations BRCA1 5382insC and CHEK2 1100delC. A total of 2655 cancer patients were analyzed independently of their family history. We found 122 mutations carriers, among them 99 patients with mutations in BRCA1 gene and 23 patients with mutation CHEK2 1100delC. Among mutation carriers, 105 patients agreed to have a medical genetic counseling and after pedigree analysis 193 first-line relatives aged above 25 years were elucidated. One hundred ten first-line relatives of mutation carriers were analyzed for the mutations presence and 40 mutations carriers were found among relatives.

From September 2013 till December 2013, 32 relatives of BRCA mutation carriers underwent breast MRI. In 5 cases, breast cancer was detected by MRI and all cancers except one were confirmed histologically with biopsy analysis. Importantly, all tumors were 5 mm and less in size, stage I cancer was detected in all cases.

At a follow-up of 1.5 years, all 105 mutation carrier probands were interviewed by phone regarding possible relapse and/or possible primary cancer in their relatives. Five of 105 probands lost to follow-up may have died. Among responding 100 patients, 2 died as reported by relatives, relapse was reported in 7 probands – mutation carrier probands, primary tumors were reported in 8 relatives of probands.

Mutation carrier probands reported one bilateral breast cancer, four ovary cancers, one bladder cancer and one non-specified oncogynecological tumor.

There were five cases of primary breast cancer, one ovary cancer, one colon cancer, one lung cancer among relatives of breast cancer patients with mutations. The frequency of tumors found in mutation carriers exceeded the average frequencies of cancer for this population.

The economic value of the regional genetic screening can be easily estimated according to the data obtained in this study and data on treatment cost for stage I and stage IV breast cancer. To summarize brieﬂy, the screening of hot-spot mutations provides not only increase of lifespan expectancy and life quality for mutation carriers, but can be also a tool for saving of medical system due to the increase of early stage breast cancer detection.

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**A118**

**New data in support of the possible evolutionary role of tumors**

A. Kozlov. The Biomedical Center Peter the Great St. Petersburg Polytechnic University, St. Petersburg, Russian Federation
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 neo-functionalization.

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T143

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

V. Kristensen. University of Oslo, Oslo, Norway

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 ($p = 2.29 \times 10^{-5}$). 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

M. Kruchinina a,*, A. Starikov b, S. Kurilovich a, V. Kruchinin c, V. Volodin a, S. Rykhlietskii a, A. Gromov a, S. Peltec d, S. Shehovtsov e, V. Generalov a. a. Institute of Internal and Preventive Medicine, Novosibirsk, Russian Federation, b Regional Oncology Center, Novosibirsk, Russian Federation, c Institute of Cytology and Genetics of the Siberian Branch of Russian Academy of Sciences, Novosibirsk, Russian Federation, d Institute of Physics Siberian Branch of Russian Academy of Sciences, Novosibirsk, Russian Federation, e State Research Center of Virology and Biotechnology (Vector), Koltsovo, Novosibirsk Region, Russian Federation * Corresponding author.

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