frequent in the TS group compared with TR group \( (p = 0.043) \). A significant association between IVS7+24G>A SNP and high TGF-
\( \beta R1 \) protein expression was observed \( (p = 0.044) \). Nonetheless,
among all studied polymorphisms only ESR12014G>A SNP was correlated with a heterogeneous distribution of \( ERx \) expression
\( (r = 0.353, p = 0.016) \).

**Conclusion:** These data suggest that the distribution pattern of
\( ERx \) expression, EGFR expression and ESR1 2014G>A genetic variation could be useful additional prognostic markers for
hormone receptor-positive breast cancer patients treated with adjuvant tamoxifen.

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T125

**Effect of carcinoembryonic antigen production by colorectal cancer cells on tumor microenvironment and cancer progression**

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Tumor markers play an important role in the identification of human malignancies. It has been shown that the carcinoembry-
onic antigen (CEA, CEACAMS) is a promoter of metastasis in epithelial cancers that is widely used as a clinical marker. The
aim of this study is to elucidate the network of genes that are involved in the CEA-induced liver metastasis. Previously, we have
shown that CEA is accumulated in the livers and livers of rats by interacting with their macrophages. We identified and cloned a
new gene (CEAR) for the CEA-binding protein, which is located on the surface of fixed liver macrophages, Kupffer cells (Bajenova
et al, 2001). It has been shown that the interaction of CEA and CEAR proteins increases the production of IL-1, IL-10, IL-6,
TNF-\( \alpha \) cytokines (Thomas et al, 2011). This interaction changes the expression of liver adhesion molecules that enhances the
survival of cancer cells to the liver. We also suggested that CEA synthesis by cancer cells may influence the E-cadherin adhesion
junction complexes and have shown that CEA production violates the functional relationship between Ecadherin and its partners \( \gamma \)-,
\( \beta \)- and \( \alpha \)120 catenin. A new type of interaction was discovered between the CEA and \( \beta \)-catenin and the increased amount of
\( \beta \)-catenin in the nuclei of CEA producing cells. The data show that
CEA production can cause the dissociation of cancer cells and trigger cancer progression. The CEA synthesis also alters splicing
of p120 catenin protein and causes the release of soluble E-cadherin. Previously, CEA and epithelial E-cadherin were
considered as independent tumor markers. Our data explain the correlation between the elevated levels of CEA and the increase in soluble E-cadherin in the progression of colorectal cancer (Bajenova et al, 2014).

We carried out a comparative transcriptome analysis of CEA-
producing cell lines. The RNA transcriptome libraries were obtained and sequenced. By pairwise comparisons of CEA pro-
ducing and non-producing cell lines using Cummerband pro-
gram, we selected the set of genes (90 total genes) whose expression have been changed in the CEA-producing cell lines
(overexpressed or downregulated). The biological processes that
are linked to this differential gene expression were identified by
Gene Set Enrichment Analysis (GSEA). In total, 8 significantly
enriched GO terms related to the cellular components and biological processes were identified. Using KEGG and GO databases, we also identified the signaling pathways involved in the response to
CEA. These findings have direct medical application, since they
allow not only to establish the relationships between the existing biomarkers but also to discover the new ones. These biomarkers
are used for diagnosis and monitoring of metastatic carcinomas
and for the drug development.

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T86

**New approaches to the rational design of anticancer drugs**

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Discovery of new pharmacologically active small molecules is an important and rapidly expanding area of modern molecular pharmacology. Given a limited number of proteins that are drug-
gable, it is important to identify as many chemical effectors as possible to define the best regimen of anti-cancer therapy in each particular case. An E3 ubiquitin ligase, Mdm2, which mediates ubiquitin-dependent degradation of the critical tumor suppressor
p53, is a promising target for small molecule inhibitors. Using a hybrid approach which combines the rational design of small molecules selected from the virtual library and the high-content screening using cancer cell lines we discovered several new inhibi-
itors of the p53-Mdm2 interaction. These compounds were able to activate and stabilize the p53 protein causing massive apoptosis preferably in p53-positive cells at rates higher than the well-known inhibitor of Mdm2, Nutlin-3. The molecular mechanisms of their action will be discussed.

As another example of rational design of potential anti-cancer
drugs, we will talk about artificial nano-Matrix-Imprinted -
Polymers (MIPs) that recognize the structure of peptides and other biological molecules and thus dubbed as “plastic antibodi-
es”. We have generated such nanoparticles against the surface region of the oncogenic receptor, EGFR, which is overexpressed in many forms of solid tumors. Selection of the linear epitope
for creating “plastic antibodies” against the receptor was performed by analysis of a three-dimensional structure of the pro-
tein. The obtained “plastic antibodies” were specific against the epitope of EGFR. These plastic antibodies when loaded with a
genotoxic drug, doxorubicin, were able to specifically induce cell
death of breast cancer cell lines that overexpress the EGFR recep-
tor. Experiments in vivo using xenografts of breast cancer cell lines pre-incubated with these plastic antibodies in nude mice showed that they have a pronounced therapeutic effect. Further-
more, since the commercial drug, Cetuximab, recognizes an epi-
tope of EGFR, different from the one recognized by our plastic
antibodies, it is likely that the latter may increase the efficacy of
the commercial monoclonal antibody. Collectively, we demonstrate that the rationally designed small molecules can be potent and specific drugs for anti-cancer therapy.

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P81

Recovery of distinct T cell subsets under severe lymphopenic conditions in hemoblastosis patients


Numerous studies have shown that high-dose chemotherapy and autologous hematopoietic stem cell transplantation (AH SCT) led to a profound and long-lasting state of immunodeficiency characterized by persisting low levels of T cells in hemoblastosis patients. Well-timed T-cell reconstitution is crucial for early restoration of anti-infectious and anti-tumor immune response. Lymphocyte recovery is mediated through the two main mechanisms – a homeostatic proliferation of T cells and generation of new naive T cells via thymopoiesis. It is known, that homeostatic proliferation is important for the restoration of T cell count in immune competent host during the 1st year following AH SCT. Thymus begins to fill up T cell repertoire approximately from the 6th month following AH SCT.

We have investigated dynamics of CD4+FOXP3+ Treg recovery following AH SCT and possible relationship between Tregs and clinical outcomes since the suppressive activity of Tregs under lymphopenic conditions may influence on peripheral expansion of T cells. Thymic activity following AH SCT has been evaluated by measuring amounts of CD4+ CD45RA+CD31+ naive T cells, i.e. “recent thymic emigrants” (RTEs). 109 patients with non-Hodgkin’s lymphomas, Hodgkin’s lymphoma and multiple myeloma underwent AH SCT in 2009–2014. The content of circulating CD4+FOXP3+ Tregs and CD4+CD45RA+CD31+ T cells was evaluated using flow cytometry before AH SCT, at the day of engraftment, and following 6 and 12 months.

Pre-transplant count of CD4+FOXP3+ Tregs was significantly higher compared to healthy controls (5.4 ± 2.9 vs 3.8 ± 1.9%; pU = 0.011; here and below data presented as Mean ± SD). Percentage of Tregs restored rapidly and reached initially high level at the time of engraftment, and then subsequently decreased within a year until it lowered to healthy donors’ values. CD4+FOXP3+ Tregs at the time of engraftment were increased in patients with relapse or progression of disease within 6 and 12 months following AH SCT compared to non-relapsed patients (11.0 ± 6.1 vs 6.2 ± 3.0%; pU = 0.016, and 10.1 ± 5.2 vs 6.1 ± 3.8%; pU = 0.008). Pre-transplant count of CD4+CD45RA+CD31+ T cells was significantly lower compared to healthy controls (17.1 ± 11.4 vs 30.3 ± 11.2%; pU = 0.0005) and did not reach donors’ values following 12 month (23.1 ± 13.5%, pU = 0.032). Relapsed patients had the same quantity of RTEs as the patients with remission within the 1st year following AH SCT. There was no any significant association between RTEs and Tregs counts.

Surprisingly, we have found high levels of circulating CD4+CD45RA+ T cells co-expressing CD31 molecule in patients before AH SCT, since this molecule is infrequent on memory subsets in healthy controls (20.7 ± 12.0 vs 8.2 ± 2.1%, p < 0.0001). Relative amount of CD4+CD45RA-CD31+ T cells highly correlated with CD4+CD45RO+CD31+ population (rS=0.72; p < 0.0001). The count of CD4+CD45RA-CD31+ T cells recovered intensively and reached the pre-transplant level within the 1st month following AH SCT, and remained at the same level throughout the follow-up. There were no any differences in relative count of CD4+CD45RA-CD31+ T cells between patients with early relapse and remission during the 1st post-transplant year.

Our data of Tregs reconstitution may confirm the earlier assumption that the presence of Tregs during the period of immune recovery preserves optimal T cell receptors diversity. However, the excess of these cells leads to the inhibition of proliferative activity and immune response and is associated with early relapse. Conversely, relatively slow recovery of RTEs determines their lack of influence on survival within the 1st post-transplant year.

The biological role and the way of appearance of CD31 molecule on T cell memory subset (CD4+CD45RA- and/or CD4+CD45RO+) still remain unclear. Further studies are required to enlighten the role of CD31+ memory T cells on lymphoproliferative disorders pathogenesis.

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P57

The first Siberian experience of gastric cancer riskometry: Prospective “case-control” study


Background: Gastric cancer (GC) remains one of the most important gastrointestinal cancers worldwide. The incidence and mortality rate from GC in Russia is higher in comparison with other European countries and USA. It should be noted that riskometry for the GC doesn’t exist. Parallel assessment of pepsinogen I (PG I), pepsinogen II (PG II), PG I/PG II ratio and gastrin-17 (G-17), as well as antibodies to Helicobacter pylori is an exact and validated set of stomach-specific biomarkers that reflect the extent and grade of gastric atrophy as a main pre-malignant condition for GC.

Aim: To study the diagnostic and predicting value of biomarkers of atrophic gastritis (AG) in retro-prospective cohort case-control study in Siberian population.

Object and methods: General population sample was surveyed in Novosibirsk in 2003–2005 (10.000 subjects aged 45–69 years). Each serum sample was deep-frozen and stored. In 2008 and