P15-110
Polylectrolyte oil-core nanocarriers of up-converting $NaYF_4$:Tm^{3+},Yb^{3+} nanocrystals for enhanced delivery and bioimaging in human ovarian carcinoma (SKOV3) cells

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There is increasing attention in development of theranostic nanocarriers that are intended to deliver separately hydrophobic drugs (mainly cytostatics for the anticancer therapy) as well as imaging agents (organic dyes, quantum dots or up-converting nanocrystals) to the target cells.

Thus, the present contribution deals with encapsulation of Tm^{3+} and Yb^{3+} co-doped $NaYF_4$ NCs in three types of multilayer nanocapsules obtained by layer-by-layer coating of silicone-core polymeric nanoparticles stabilized by cationic dicephalic-type surfactant, i.e., N,N-bis[3,3-(dimethylamine)propyl] dodecanamide dichloride, $C_{12}(DAPACl)_2$, via different, i.e, standard (PSS/PDADMAC), sugar-based (DEX/CHIT) and pegylated (PGA-*g*-PEG) polyelectrolyte shells. The biological potential of the obtained nanosystems was evaluated in cytotoxicity studies as well as in imaging of their intracellular distribution upon well characterized human cancer cell line – ovarian carcinoma (SKOV3) – and normal human vaginal fibroblasts (HVFs). DLS measurements confirmed the nanoparticle diameter below 200 nm, while AFM and TEM – its shape, morphology and the NCs encapsulation. Doppler electrophoresis provided a highly positive ζ-potential and colloidal stability. The fabricated long-lasting nanosystems exhibited good luminescence properties – under the 980 nm excitation, infrared and blue up-conversion emissions centered at 800 and 480 nm were observed. The performed studies point out to a opportunity for the development of complex theranostic modalities – a platform by co-encapsulating hydrophobic cytostatic agents and labeling $NaYF_4$:Tm^{3+},Yb^{3+} NCs within the oil-core compartment of the nanocapsules – that would allow investigation of penetration and localization of the multifunctional nanocarriers in various cancer cells.

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P15-111
Targeting the breast tumor in mouse model using undifferentiated mesenchymal stem cells and VEGFR-expressing endothelial-like cells

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Stem cell therapy of breast cancer is promising in controlling micro-metastasis and tumor progression. Stem cells with proliferation and differentiation potential such as mesenchymal stem cells (MSCs) are implicated in tumor control. However there are controversies in targeting tumors with either differentiated cells or undifferentiated progenitor MSCs. It is assumed that expression of vascular endothelial growth factor receptor (VEGFR) in cells at early stage of differentiation induction can help directing cells to the tumor site with abnormal capillary network. In the present study a mouse model of breast cancer were used to investigation of the efficiency of MSCs and endothelial cells derived from them to control angiogenesis-mediated tumor growth. The results of tumor size monitored for 4 weeks after tumor induction, suggesting that both MSCs and endothelial-like cells are involved in breast tumor regeneration and suppression. This was consistent with pathological characters in experimental groups of mice treated with either MSCs or endothelial-like cells in comparison with untreated group. In conclusion, using of VEGFR-expressing cells in the host tissue is an approach to target solid tumors with abnormal angiogenesis.

P15-112
A novel immunotherapeutic and anti-cancer drug GA-40

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Search nontoxic naturally-occurring substances that can cause selective destruction of cancer cells directly or by activating antitumour immunity are the two major strategies for development anti-cancer drug discovery. As a result of such works novel immunotherapeutic and anticancer drug GA-40 was created. Drug is a standardized complex of multiple peptides obtained from plant, widely used for medical cancer treatment since old times in Georgia. *In vivo* and *in vitro* preclinical studies and clinical trials of GA-40 shows, that it is not toxic and has no contra-indications, and is completely safe for the patients. It was shown that GA-40 has a direct apoptotic effect in malignant tumor cells and unlike chemical preparations has no negative effect on the normal cells. GA-40 direct action induces differentiation of human myeloid leukemia cells (HL-60) into non-growing mature granulocytes. GA-40 by its direct action on mononuclear cells causes the activation of anti-tumor cellular immunity. GA-40 activates cytotoxic-T cells, macrophages, production of Tumor Necrosis Factor and Interferon-γ, which play important role in the destruction and selectively remove cancer cells by the way apoptosis. GA-40 inhibits the release of vascular epithelial cell growth factor (VEGF) by cancer cells and the development of new blood vessels the process of revascularization in malignant neoplasm's preventing tumor growth and spread of metastases. GA-40 shows high antioxidant activity.

P15-113
Antioxidant activitis of *Salvia fruticosa* and its effects on HT-29 cell line

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Many epidemiological studies have revealed that there is a strong correlation between consumption of polyphenol-rich foods or beverages and the prevention of certain diseases such as cancers, cardiovascular diseases and aging. Phenolic compounds are abundant in all plants, therefore they form an integral part of the human diet. Salvia species, commonly known as sage, have been used since ancient times for more than 60 different ailments ranging from aches to epilepsy. There are around 900 species of Salvia, 95 of which are represented in Turkey including *Salvia fruticosa*.

In this study, $DPPH^{\bullet}$ and $ABTS^{\bullet}$ radicals scavenging activities, total phenolic and flavanoid contents of water extract of *S. fruticosa* was determined by spectrophotometrically. Rosmaniric acid, caffeic acid, gallic acid, syringic acid, quercetin and t-resveratrol contents of water extract of *S. fruticosa* were determined by using RP-HPLC. Cytotoxic effect of the extract on HT-29 adenocarcinoma cell lines was examined via XTT colorimetric and Trypan Dye Exclusion cell viability assay. Effects of the extract on the expression of phase I and phase II detoxcification enzymes in HT-29 cell line were investigated with q-RT-PCR technique.

Turkish endemic sage, *S. fruticosa*, is reported to be a promising medicinal plant, it has the potential to be used as adjuvant with chemoterapeutic agents to overcome the drug resistance occuring during chemotherapy. Further investigations are ungoing to reveal its bioactive components and their beneficial activities in biological systems.

P15-114
Demonstration of apoptosis via TUNEL assay and Codon 72 Polymorphism of p53 gene of MCF-7 and MDA-MB-231 cell lines upon treatment of Doxorubicin

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Apoptosis is programmed cell death which is characterized by morphological alterations such as shrinkage of cell and nucleus, roundation of cells, chromatin condensation and nuclear fragmentation as well as biochemical alterations which includes caspase activation, protein cleavage, DNA breakdown and cell outer membrane modification that results in phagocytic recognition. DOX is a potent chemotherapeutic drug approved by FDA which is clinically applied to treat various types of cancer including breast cancer. In the present study, drug-sensitive and drug-resistant breast cancer cell lines MCF-7 and MDA-MB-231 respectively were treated with 2 doses of DOX (200 nM and 800 nM) or not treated with the drug at all as control. After 48 h of incubation, TUNEL assay was performed with the aim of examining apoptosis via DNA fragmentation. It was demonstrated that both of the doses of DOX induced apoptosis in MCF-7 cells *in situ*. When compared to the control, effect of the drug was more significant with the dose of 0,8 μM. As for MDA-MB-231 cells, apoptosis was not triggered significantly with the dose of 0,2 μM and triggered slighty with the dose of 0,8 μM of DOX. Finally, in order to investigate codon 72 polymorphism profile of p53 gene, standard PCR was performed to amlify the p53 gene with DNA samples of both cells. FnuDI restriction enzyme was established to recognize and cut CGC but not CCC. It was demonstrated that these cell lines have different poymorphism profiles.

P15-115
Approaches to Multiple Sclerosis therapy by selective autoreactive B-cells depletion

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Multiple Sclerosis (MS) is a dreadful disease associated with inflammation in the central nervous system white matter and is thought to be mediated by autoimmune processes. Clonal expansion of B-cells, their antibody products, and T-cells, hallmarks of inflammation in the central nervous system are found in MS. Today, MS is usually treated with glatiramer acetate (Copaxone), injections of cytokines (IFNγ) and various monoclonal Abs (Natalizumab, Rituximab, etc.), and orally administered low-molecular-weight chemical drugs. Despite the variety of therapeutics available against MS mostly of them affect overall balance in patient's immune system. Development of novel more specific approaches to MS treatment is of high importance in modern pharmaceutics. We tried to create more selective and effective way to eliminate pathogenic B-Cells. We have designed therapeutic molecules based on immunodominant peptides of the myelin basic protein (MBP) fused with Fc domain of antibody.

We demonstrated functional activity of designed Fc-MBP chimeric molecules *in vitro* and showed that obtained fusion molecules were recognized by antibodies produced by autoreactive lymphocytes.

Further, on animal model of MS – experimental autoimmune encephalomyelitis induced in SJL/J mice, we provide selective elimination of autoreactive B-cells *in vivo*, by injection of the recombinant Fc-MBP molecules. Moreover, we found that injection of Fc-$MBP_{82–103}$ fusion molecule lead to depletion of $MBP_{82–103}$ specific B-cells and suppress formation of autoreactive B-cells population toward C-terminal part of MBP.

Our data suggest that Fc-MBP molecules are best choice for pathological B-cells depletion due to the excellent balance between their legibility and cytotoxic properties.

P15-116
Identification and characterization of small molecule inhibitors targeting DNA polymerase gamma for the treatment of cancers deficient in mismatch repair

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Synthetic lethal interactions between mutated oncogenes or tumor suppressor genes with molecules involved in the DNA repair pathways can be therapeutically exploited to preferentially kill cancer cells. Recently it was demonstrated that DNA polymerase gamma (POLG) inhibition in MLH1-deficient cells or tumors, which are defective in mismatch repair (MMR) displays synthetic lethality. Germline mutations in the MLH1 gene predispose to hereditary nonpolyposis colorectal cancer. MLH1 acts as tumor suppressor protein where tumor cells can have complete loss of MLH1 function, whereas normal cells retain at least one functional allele. Although MMR is involved in repair of base mispairs arising during replication, it also plays a role in the repair of oxidative damage induced DNA lesions. These lesions are repaired mainly by base excision repair (BER) pathway. POLG is involved in the mitochondrial BER and in mtDNA replication. Synthetic lethality of MLH1/POLG led to the accumulation of 8-oxoguanine in mtDNA. Thus, the inhibition of POLG may have a role for the selective treatment of cancer arising from MMR deficiency with MLH1 mutation. Therefore, to identify and characterize inhibitory molecules specific to POLG, we performed *in silico* screening of in-house and commercial small mol-