263. BIOMARKERS IN OVARIAN CANCER

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Introduction: Elucidation of the most frequent biomarkers in ovarian cancer.

Materials and methods: The study was based on the analysis of biographical sources from 2007-2014.

Discussion results: One of the major challenges in cancer research is the identification of stable biomarkers, which can be routinely measured noninvasively in easily accessible samples. Ovarian cancer is one such disease that would benefit from improved diagnostic markers. Ovarian cancer is the leading cause of death from gynecological malignancy in the western world. One way to facilitate early detection of ovarian cancer is through screening, but currently available diagnostic tools, including ovarian cancer biomarkers and clinical imaging, lack sufficient specificity and sensitivity for implementation in a population-based screening program.

Conclusions: The ability to sensitively and specifically predict the presence of early disease and its status, stage and Associated therapeutic efficacy has the potential to revolutionize ovarian cancer detection and treatment and to greatly improve the quality of life and survival rates of ovarian cancer patients.

Key words: ovarian cancer, diagnosis, biomarker, early detection.

264. THE ROLE OF GLUTATHIONE IN CANCER DEVELOPMENT AND CHEMORESISTANCE

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Introduction: Glutathione (GSH) is a tripeptide produced by the liver and has the ability (among others) to remove a wide range of toxins, including those produced by heavy metals, alcohol, smoking, radiation and cancer chemotherapy. Elevated GSH levels were detected in various types of tumors, along with high levels of GSH-related enzymes, such as γ-glutamylcysteine ligase (GCL) and γ-glutamyl-transpeptidase (GGT), GSH-transporting export pumps. This makes the neoplastic tissues more resistant to chemotherapy. Therefore, the GSH system attracted the attention of scientists as a possible target for medical intervention against cancer progression and chemoresistance.

Materials and methods: The presentation represents an extensive literature review and is based on relevant scientific articles regarding the subject from medical databases.

Discussion results: The main research in the field aimed at depleting GSH by a specific inhibition of GCL, a key enzyme of GSH biosynthesis. But GSH depletion appears to be therapeutically effective when very low levels (<10% of their control values) can be achieved within the cancer cells. Thus, achievement of selective tumor GSH depletion under in vivo circumstances is a pharmacological challenge. Also, GSH synthesis and GSH synthesis-linked genes are up-regulated during oxidative stress and inflammation. Furthermore, Nrf-2 deficient cells were more susceptible to doxorubicin and BSO treatment-induced cell death than wild cells. Moreover, propyl gallate activated caspases 3, 8, and 9, and induced an increase in p53, Bax, Fas, and Fas Ligand; whereas MAPKs inhibited nuclear translocation of Nrf-2 and induced intracellular GSH depletion in human leukemia. This indicates that Nrf-2 is one of the first factors that induce cell survival under GSH depletion, which points out to this transcription factor as an attractive target in leukemia but also in other cancers sharing similar molecular mechanisms. The increase in GSH is a major contributing factor to drug resistance by binding to or reacting with, drugs, interacting with ROS, preventing damage to proteins or DNA, or by participating in DNA repair processes.

Conclusion: The modulation of cellular GSH is a double-edged sword. On one hand, enhancing the capacity of GSH and its Associated enzymes represents an aim in the search for cytoprotective strategies against cancer. On the other hand, the strategy of depleting GSH and GSH-related detoxification pathways is aimed at sensitizing cancer cells to chemotherapy. **Keywords:** Glutathione, cancer development, chemoresistance.

265. TUFTSIN-BIOLOGICAL ROLE AND PHARMACEUTICAL VALUE

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Introduction: Despite the high level the human civilization achieved, we still constantly face dangers as viral infections, bacteria, traumas, chronic disease, cancer etc. Thanks to the development of medicine and pharmaceutics, antibiotics, anti-inflammatory and immunomodulatory drugs as well as cytostatic and cancer killing drugs were developed. Still, many of them have many adverse reactions, or are expensive, or both. That is why the discovery of Tuftsin in 1970 is considered one of a high value for the modern medicine, by offering new ways of treatment of the diseases, which endanger health and life.

Objectives and Purposes of this work was to identify the immunomodulatory, anti-inflammatory, antibacterial and cancer killing properties of Tuftsin.

Materials and Methods: A bibliographic review of the scientific articles published over the studies of Tuftsin and its properties, during 1980-2012, was performed.

Results: In 1970s, Victor A. Najjar and Kenji Nishioka found a new natural tetrapeptide (Thr-Lys-Pro-Arg) derived from the proteolytic degradation of the 289–292 amino acid residues of the IgG heavy chain Fc domain that was named tuftsin. Tuftsin is produced by the action of two proteolytic enzymes – splenic tuftsin edocarboxypeptidase and leukokininase.