

# Inzulinu podobné a jiné růstové faktory a nádory

Insulin like and other growth factors and tumors

## Disertační práce

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### Summary

The interaction between growth factors and cancer incidence and development has been discussed recently. First works suggesting possible connection between increased production of insulin like growth factors with an increased incidence of tumors came already from early 80s of the last century.

The aim of my work was focused on evaluation of possible relation between insulin like growth factors or their binding proteins and tumors from different perspectives, to assess their significance and try to determine what role the IGFs and IGFBPs may play in the current tumor diagnostics.

The work itself is divided into two parts, the theoretical and practical ones. In the theoretical part, I summarized the action of IGF in human body and also focused on previous findings on the role of IGF system in cancer diagnoses. In the practical part, divided into three subsections, I focused on investigation of relations in a large set of patients with different cancer diagnoses, in a group of women with breast cancer and, finally, I focused on changes of IGF1 levels during follow-up.

### Theoretical part

Insulin-like growth factors (IGF) are peptides, that participate on growth regulation, metabolism regulation, cell survival and differentiation. They are regulated by growth hormone (GH). IGFs are synthesized in liver and they also occur in various body fluids. Their extrahepatic production, as well as their autocrine and paracrine mechanism has been already described.

IGFBPs occur in different body fluids like serum, amniotic fluid and cerebrospinal fluid. IGFBPs are synthesized in liver but can be also synthesized by cancer cells. IGFBPs increase the half-life of IGFs in serum and inhibit or stimulate IGFs action by binding to the target cells receptors. These binding proteins serve to create a storage pool of IGFs in intercellular space.

Effect of IGF1 on cell is mediated by receptors. Signal transduction follows the successful binding to the receptor via signal intracellular pathway – i.e. cascade of enzymes and its substrates.

### Experimental part

#### IGF1 and colorectal, lung, breast and prostate carcinoma

There were 681 patients in the group. Evaluation was done on patient serum samples processed in Immunodiagnostic Laboratory of the University Hospital in Pilsen. Samples were obtained between years 2000 and 2008. Patients were divided into five groups according to the histological findings. Obtained values were compared with normal laboratory values and then compared with data in literature.

#### Tumor markers, growth factors and breast tumors

Two groups of patients were compared. The first group consisted of 89 women with malignant breast cancer. The second group covered 21 women with benign breast tumor, mostly fibroadenoma. Patient serum samples were processed in immunodiagnostic laboratory of the University Hospital in Pilsen in the period 2008-2010. In particular, I focused on the differences between the groups with malignant and benign tumors, but I also evaluated the changes in levels of all analytes in the group of women with malignant breast cancer and in subgroups divided by the stage of disease.

### **Conclusion**

- 1) was investigated IGF1 in a group of 681 patients with the following tumor types: colorectal cancer, lung, breast and prostate.
- 2) was further examined 100 women with benign and malignant breast tumors.
- 3) HGF is the only growth factor that is statistically significantly higher serum levels in malignant tumors than in benign diagnoses.
- 4) The growth factor HGF positively correlated with the severity of cancer.
- 5) In evaluating IGF1 is necessary to take into account the age aspect and in different age groups, the results obtained adjustovot of age. If age does not take into account the aspect may be an incorrect interpretation of results.
- 6) IGF1 in tumors colorectal cancer has increased approximately the same percentage as the reduced results, which correlates with the findings from the literature.
- 7) For prostate cancer, I have found a significant preponderance of elevated IGF1. This finding agrees with the conclusions from the literature.
- 8) In the case of lung tumors predominated significantly higher values of IGF1 which does not correspond with the findings in the literature.
- 9) In the case of breast cancer slightly higher values prevailed over the lower IGF1. The available literature was the ascendancy of high levels considerably higher.
- 10) Serum levels of IGF1 variability is significant for each type of tumor develops in another way.
- 11) Tumor markers can not be used for differential diagnosis of benign and malignant tumors.
- 12) Serum growth factors and IGFBP3 after surgery does not change significantly.
- 13) Tumour markers correlate with the severity of the disease.
- 14) together with IGF1 IGFBP3 reach higher levels in earlier stages of breast cancer and higher stage disease, their level decreases.
- 15) growth factor EGF positively correlated with the severity of cancer, addiction is not as linear as HGF.
- 16) Serum TGF $\alpha$  negatively correlated with the severity of cancer.
- 17) Serum levels of VEGF in no way correlate with the severity of cancer.
- 18) Luminex xMAP multiplex analysis proves to be very helpful in tracking etiopatologie cancer. Allows you to track particular mutual vrtahy between markers of biological activity. Reduces biological material is quick and convenient.

### **Conclusion for clinical practice**

- 1) Monitoring of growth factors is not suitable for routine diagnostics.
- 2) Only HGF appears to be promising diagnostic and prognostic marker.
- 3) absolutely important and irreplaceable role, however, are growth factors and IGFBP3 in the investigation of processes in the human body at the cellular level. Because we already know the functioning of entire signaling pathways can be used also as growth factors suitable indicators to verify the theory formulated on the performance of various substances on cell (physiological growth and metabolic processes, their disorders, drug exposure and other

chemical substances, etc.). It is also possible that despite the large amount of accumulated results from many studies, we still escape a connection that can be discovered in the future and growth factors aid is in the higher meaning in everyday clinical practice.