UNIVERSITATEA TITU MAIORESCU DIN BUCUREŞTI
ŞCOALA DOCTORALĂ - DOMENIUL MEDICINĂ

BIOCHEMISTRY OF HEAVY METAL, MOLECULAR MECHANISMS OF INDUCTION OF CARCINOGENESIS AND THERAPEUTIC RELEVANCE

HABILITATION THESIS
SUMMARY

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The habilitation thesis entitled **"Biochemistry of heavy metals, molecular mechanisms of carcinogenesis induction and therapeutic relevance"**, brings together the directions of scientific, professional and academic research, carried out after the completion of doctoral studies, based on interdisciplinary biochemical and molecular studies of carcinogenesis induction as a result of heavy metal bioaccumulation and therapeutic relevance.

The topic addressed is important because traces of heavy metals can concentrate along the food chain, and the human body does not possess efficient excretion mechanisms, they accumulate in vital organs (liver, kidneys, bones), generating chronic toxicity even at very low doses. Controlling bioaccumulation is a fundamental strategy for cancer prevention and improving the quality of life.

The habilitation thesis is structured according to the recommendations of CNATDCU and includes three main sections, in which the scientific, professional and academic achievements since obtaining the of the PhD in Chemistry to date, as well as future directions of professional and academic development.

1. Scientific, academic and professional activity

Graduate (1997) of the University of Bucharest, Faculty of Chemistry, with a degree in Chemistry and Physics. Master's studies (2009-2011) at the Babeș Bolyai University of Cluj-Napoca, Faculty of Biology and Geology, in the field of Biology-Nutritional Sciences. Doctoral studies (2000-2004) dedicated to the topic "Control of active principles in exciting food products", coordinated by Prof. dr. Pătroescu Constantin, at the Doctoral School of Chemistry, University of Bucharest.

I am an associate professor at the Faculty of Medical and Behavioral Sciences, Constantin Brâncuși University of Târgu-Jiu, I have teaching activities in the disciplines of Biochemistry, Nutrition and Dietetics, Biophysics for the study programs General Medical Assistance and Pharmacy Assistance. I have been involved in interdisciplinary research projects, collaborating with specialists from various biomedical fields.

The scientific activity following the defense of the doctoral thesis was materialized by publishing **28 papers in ISI Web of Science indexed journals** as main author or co-author; **42 articles indexed BDI** and **Hirsch Index 6.**

2. Research directions

2.1. Toxicology of heavy metal bioaccumulation: from environmental contamination to human pathology

This direction highlights the level of bioaccumulation and the implications of exposure on health, reflected by the level of concentrations of traces of toxic or potentially toxic heavy metals in soil and plants, reported to the norms and literature of the field on food safety.

The assessment of the risks caused by exposure to toxic heavy metals, carried out through the individual risk for Ni, Cd, Pb, Hg, is based on the limit level of 10-6 of the individual carcinogenic risk index, established by the WHO, confirmed by other reports. A study published in 2014, evaluates the correlation of respiratory pathologies of the population with the level of traces of toxic or potentially toxic heavy metals in the atmosphere in the Roșiuța area, Gorj.

2.2. Studies on the mechanism of genotoxicity/carcinogenicity of heavy metals

According to the results of the studies, heavy metals can generate free radicals inside the cell that selectively activate transcription factors, it can be stated that cell proliferation or cell death can be linked to the exposure and activation of redox-sensitive transcription factors such as AP-1, NF-κB and p-53. Exposure to carcinogenic metals, genotoxic mechanisms and induction of carcinogenesis are significant for five toxic metals: Cd, Ni, Cr, Pb, Hg being presented in the synthesis and which determine changes in the metal balance. Demonstrative studies have highlighted the link between toxic metals and hematological malignant tumors, but also the fact that there is still a gap in knowledge about the degree of association.

2.3. Contributions on molecular mechanisms and antitumor therapeutic relevance

It presents molecular mechanisms of carcinogenesis induction and antitumor therapeutic relevance in the following research directions: heavy metals, risk factor in hematological malignancies; significance of p-53 protein isoforms in immune therapy in chronic lymphocytic leukemia (anti PD therapy) and in failed cases of chronic lymphocytic leukemia; association of autophagic dysfunction with cancer cells and their therapeutic implications; relevance of vitamin D supplementation in anticancer activity through different signaling pathways, as well as suppression of metastasis and angiogenesis in different types of cancer.

The role of the p-53 isoform protein in molecular mechanisms and hematological antitumor therapeutics has been experimentally demonstrated in the context of cases of chronic lymphocytic leukemia, is that in the context of a heterogeneous malignant disease such as Chronic Lymphocytic Leukemia, the ELISA method is useful for identifying patients who

should be considered candidates for personalized therapeutic strategies based on the TP-53 gene mutation and the presence of the p-53 isoform protein.

3. Scientific, professional and academic development plans

The vision of scientific research includes the publication of specialized books, articles in prestigious journals and involvement in interdisciplinary research activities, continuing professional development in the field of Medical Biochemistry.

The professional and academic priority will be through participation in advanced training courses and a permanent adaptation to the latest developments in the field. The objective of the department is to promote student-centered education, through interactive teaching methods and interdisciplinary research. I will coordinate students, master's students, in carrying out activities for bachelor's/dissertation papers, for interdisciplinary scientific circles and other activities in the field of research.