

ABSTRACT

The habilitation thesis untitled " Ion channels as sensors for toxic substances and targets in cancer therapy" presented here, focuses on the work carried out since 2005, consecutive to the Ph. D program carried out in Belgium at the Catholic University of Leuven (KU Leuven) between 2000 and 2004. The work is structured in two main chapters. The first chapter (B) called "Scientific, professional and academic achievements" describes the results obtained as researcher and are related to the research topic of the institutions where I was hired: the International Centre for Biodynamics (I.C.B) and the Department of Anatomy, Physiology and Biophysics (DAFAB) from the Faculty of Biology, University of Bucharest. The second chapter (C) contains the plans for the development of the professional career in which I briefly described the ongoing projects and the new directions in the scientific career.

The first chapter is in turn structured in three main sections. Section B1 contains a detailed description of the relevant scientific activity supported by publications in scientific articles and research projects, in which I have been involved. Section B2 describes the administrative activity of developing a new research infrastructure in ICB, which also included a cell biology laboratory and the research projects I coordinated, and section B3 presents the academic results of the courses and practical laboratories for students developed and supported during this period in DAFAB.

The scientific activity is structured according to the research fields in which I have been active in these 15 years called: I) "Cellular toxicology studies on cell lines from renal epithelium" containing results obtained in research projects conducted in ICB, where I was employed between 2005 and 2010 and II) Ionic channels in pancreatic tumours -markers or therapeutic targets- which brings together the results of the last 10 years and are the basis of future research projects. During this period when I was employed in DAFAB as a researcher or teacher:

Cellular toxicology studies on renal cell lines were supported by national (two projects in which I was director and two in which I was responsible for ICB) and international (a bilateral project and a NATO Reintegration project). The results have been presented in numerous international and national congresses and seminars and have materialized by publishing the results in different ISI journals (Cucu, D'Haese, De Beuf, & Verhulst, 2011; Gaspar, Niculite, Cucu, & Marcu, 2010; Mernea et al., 2016).

These studies started from analysis regarding the effect of cadmium on the epithelial channel of Na⁺ (ENaC) expressed in renal cells from the distal nephron presented in subchapter I.1. In this context, the structural models of ENaC related to the specific antagonist (amiloride) and Cd²⁺ are presented. The conclusion of this project was obvious: cadmium produces cellular and molecular changes in the distal tubes, less studied until then and that these changes are related, among other things, to the production of reactive oxygen species (ROS). This oxidative response was quantified in a subsequent project, presented in subchapter I.3, by the development of a biosensor by the group coordinated by Dr. Szilveszter Gáspár from ICB and which has been successfully used in determining oxidative responses in renal cells following treatment with calcium oxalate (Gaspar et al., 2010).

The second part of the scientific activity presented in section II) is dedicated to recent studies that began with investigations of the expression and function of channels with transient receptor potential (TRP) expressed in tumour cells, in particular cells isolated from patients with pancreatic adenocarcinoma (PANC). These studies have been and are the subject of ongoing projects in the group I coordinate within DAFAB. They are dedicated to the overexpressed TRPM8 and TRPA1 channels in tumor cells, whose role in tumorigenesis processes are about to be deciphered by the scientific community.

In the second part of the paper I gathered under chapter B2-Other professional and administrative activities - those results that did not materialize through scientific articles, but by creating the infrastructure and research environment in which I worked in these years. The subchapter briefly presents the participation in ICB infrastructure development projects, in proposals for applications of research results or in other projects that led to the creation of a small research group in DAFAB:

The third subchapter (B3) presents the academic achievements of the Faculty of Biology, University of Bucharest, which describe in detail the manner and results obtained, including the latest assessments of students of the courses taken at the Master of Medical Biology and Master of Neurobiology as methods with the best results, especially online methods practiced and diversified in the unfortunate period in which this thesis was written, March-May 2020