UNIVERSITATEA DE MEDICINĂ ȘI FARMACIE
”CAROL DAVILA” BUCUREȘTI
ȘCOALA DOCTORALĂ
DOMENIUL MEDICINĂ

Conexiuni endocrine: acromegalia și diabetul zaharat; hormonii și funcția renală

REZUMATUL TEZEI DE ABILITARE

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ABSTRACT OF THE HABILITATION THESIS

The habilitation thesis "Endocrine connections: acromegaly and diabetes mellitus, hormones and kidney function" presents my scientific, academic and professional activity. Most of this activity took place after defending my PhD thesis "The role of GH/IGF-1 and sleep apnea in insulin resistance and diabetes mellitus prognosis in acromegaly" in 2011. The last part of the habilitation thesis tackles the future plans for my career based on the results accomplished so far.

I fulfill all scientific criteria necessary for defending the habilitation thesis. I published 20 ISI indexed scientific papers as the main author and 7 as co-author which granted a Hirsch index of 7. The cumulative impact factor of scientific journals where I published my papers as the main author is 22.2 (based on the IF for the year of publication) or 31 (based on the current IF).

My scientific activity followed two main subjects: the glucose metabolism in patients with acromegaly and the relation of hormones with kidney function. There are also other published papers, mainly in the field of thyroid disorders.

The dysregulation of glucose metabolism in acromegaly was my first research subject. From the first published paper, in 2007, I tried to discover the pathogenic mechanisms behind glucose intolerance, a well-known complication of acromegaly. To accomplish my goal, I've done intensive clinical research and looked at different aspects of the problem: insulin sensitivity, insulin secretion, relation with disease activity. I won three scientific grants (2007, 2013, 2020) that provided some of the funding needed for research. The most important papers published in this field were "Insulin-like growth factor-I correlates more closely than growth hormone with insulin resistance and glucose intolerance in patients with acromegaly" (*Pituitary*, 2013) and "Disposition index in active acromegaly" (*Frontiers in Endocrinology*, 2019).

My work contributed to the progress in this field and suggested that diabetes mellitus secondary to acromegaly and type 2 diabetes mellitus share a common pathogenesis, contrary to current theory. My research showed that growth hormone excess causes insulin resistance, a status similar to insulin resistance induced by obesity. However, only those with deficiencies of insulin secretion will develop diabetes mellitus. This allows, when GH excess cannot be controlled, to focus more on increasing/substituting insulin secretion than on reducing insulin resistance by conventional means.

The relation between hormones and kidney function is the other important direction of my research work. Most of my papers covered bone quality in patients on chronic dialysis but or the physiological variation of hormones strongly dependent on kidney function like vitamin D or parathyroid hormone.

I was able to demonstrate that plasma metanephrine and normetanephrine, metabolites of adrenaline and noradrenaline widely used in the diagnosis of pheochromocytoma, are significantly elevated in patients with chronic kidney disease, particularly in those on dialysis. This paper, "Plasma free metanephrine and normetanephrine levels are increased in patients with chronic kidney disease" (*Endocrine Practice*, 2014) suggested that these metabolites are false-positive in chronic kidney disease and can lead to unnecessary laboratory and imaging work-up for a presumed pheochromocytoma.

Other papers, "Chronic hemodialysis is associated with lower trabecular bone score, independent of bone mineral density: a case-control study" (*Archives of Osteoporosis*, 2018) and „Bone turnover correlates with bone quantity but not bone microarchitecture in chronic hemodialysis" (*Journal of Bone and Mineral Metabolism*, 2020) demonstrated that bone quality, measured using Trabecular Bone Score, in significantly lower in patients on hemodialysis, independent of bone mineral density and this contributes to the increased risk of low trauma fracture in this population. Moreover, this low bone quality is dependent on currently unknown factors, other than increased bone turnover.

Using the large body of laboratory data available at the C. I. Parhon National Institute of Endocrinology our group was able to publish a couple of papers („Seasonal variation of serum vitamin D levels in Romania" and „Seasonal periodicity of serum parathyroid hormone and its relation with vitamin D in Romania", both in *Archives of Osteoporosis* in 2017 and 2020) on the physiological and seasonal variation of vitamin D and parathyroid hormone in Romania. Both papers demonstrated that population variation of these hormones are linked to the seasons of temperate climate and age. Taken together these findings suggest that thresholds for intervention should be adjusted for age and time of the year.

My academic career started in 2005 when I joined the Department of Endocrinology at the School of Medicine, Carol Davila University of Medicine and Pharmacy, as a Junior University Assistant. Currently I am Lecturer at the same department.

Throughout these years I work with numerous 5th grade students for both the practical and theoretical part of their endocrine course and 2nd grade students on their Human Behavior Course. Also, I guided several students for their graduation thesis.

One of the most important achievements of my academic career was publication of a guide on how to write a PhD thesis ("Teza de doctorat? Cam a asa…", Smashwords, 2017). At that time our university did not have an official guide for PhD Students. My work was based on my personal experience with PhD thesis and on technical characteristics of other PhD theses from Carol Davila University, Bucharest Polytechnic University and Bucharest Technical University of Civil Engineering. The work had general view on PhD thesis writing and guidance on any chapter that can be part of it, from "Methods" or "Results" to "Acknowledgments" or "Funding". Moreover, there were interesting advices on figures, graphs, tables or references. Recommended number of pages, figures, tables, etc., was based on mean/median values of comparison theses.

Regarding my professional activity, I became resident in endocrinology in 2003 at the C. I. Parhon National Institute of Endocrinology. Currently I am Consultant in Endocrinology at the Department of Pituitary and Neuroendocrine Disorders of the same institution. I have daily activities in both in-patients and out-patients clinic, with focus on pituitary, thyroid and bone diseases. I regularly perform cervical ultrasound and fine-needle aspiration biopsies for thyroid and parathyroid disorders. Also, I attend regularly the meetings of a pituitary multidisciplinary team.

Since 2017 I am the Head of the Department of Pituitary and Neuroendocrine Disorders, the largest of the C. I. Parhon Institute of Endocrinology. Since 2018 I am the Secretary of the Romanian Society of Endocrinology.

I have definite, measurable objectives for the next five years of my research, academic and professional career. Most important of these are: (i) publication of at least 2 ISI indexed papers per year in journals with an IF over 2; (ii) a Hirsch index over 8 at the end of 2021; (iii) at least 1 international clinical trial as principal investigator; (iv) publication of the results of a graduation thesis in a scientific journal; (v) involvement of in-training medical doctors in high risk medical procedures; (vi) continuation of multidisciplinary team meetings; (vii) a closer cooperation between Carol Davila University of Medicine and Pharmacy and C. I. Parhon National Institute of Endocrinology.

I demonstrated solid achievements in my research, academic and professional career. I published sound scientific papers, conducted research projects and ensured a proper funding. I gathered a rich teaching experience, from undergraduate students to high-end courses. I work in a top medical institution that provides the settings required for clinical research. I consider that all these grant the success of my future PhD Supervisor activity.