ABSTRACT

The habilitation thesis entitled "Implications of genetic testing in obstetrics and gynecology – towards an individualized medicine" brings together scientific, didactic, and professional achievements following the completion of doctoral studies as well as perspectives on academic career development.

The thesis is structured in three parts, which successively present the main stages of my professional and academic development, the main results of my postdoctoral research and finally the main directions of academic career development. At the end the list of bibliographic references is presented.

The first part includes two chapters. The first chapter provides a concise retrospective of my teaching, clinical and scientific work. These previous achievements are prerequisites for my ability to lead research projects in the future but also to coordinate teams of researchers. I believe that teaching and research must be doubled by a thorough practical training; professional activity being presented in Chapter 1.1 . I am currently a Senior Physician in Obstetrics and Gynecology with numerous certifications in Romania and abroad. My academic career took place mostly at University of Medicine and Pharmacy "Iuliu Haţieganu", 1st Department of Obstetrics and Gynecology, starting from 2008 as teaching assistant, currently being an associate professor. Research has been a priority in the development of my academic career. Throughout this period, I was involved in 5 national and international academic development projects, two research grants at UMF Cluj, and in 2014 I obtained a research scholarship within the POSDRU Transcent program. A period that marked all my further evolution as a researcher was the scholarship obtained at Claflin University in Orangeburg, USA. Another important project carried out together with Babeş Bolyai University in Cluj Napoca, the Department of Public Health in collaboration with UNICEF aimed at analyzing the situation of prenatal care in Romania, a project completed with the development of a guide for pregnant women.

The research activity resulted in the publication of 40 articles (of which 58% main author) in ISI journals, two of these articles being awarded by CNCSIS. As coordinator, I wrote two specialized monographs dedicated to preinvasive cervical pathology, two courses for students of the French line and a volume of case presentations in Obstetrics and Gynecology, I also contributed as author to many books.

In the second chapter is included the postdoctoral research part there are five major themes: cervical dysplasia, a continuation of my doctoral research, breast cancer, postsurgical wound healing, neonatal hemochromatosis and HELLP syndrome.

The first studies within the cervical dysplasia section were dedicated to diagnostic methods the concordance between cytology, colposcopy, histopathological result, respectively the second role of testing L1 protein, the major capsid protein encoded by the L1 gene compared to other genetic HPV DNA testing techniques (hybridization, PCR techniques with different primers).

Most of the dysplasia subchapter analyzed the possibility of a genetic predisposition explaining the possibility of elimination/persistence of HPV virus due to a genetic predisposition of molecules involved in maintaining HPV in the epithelium, respectively antiviral or antitumor factors. For this purpose, four case-control studies were conducted, including HPV-positive patient (cases) with cytological changes, respectively HPV-negative controls with normal cytology in which TNF-α 308 G/A, -160 A/C E-cadherin genotyping, Glutathione-S transferase variants GSTM1 and GSTT1 and VEGF +936 C/T were performed. RFLP PCR techniques were used for genotyping. A separate study looked at the impact of reproductive factors in patients diagnosed with breast cancer with/without BRCA or non-BRCA gene mutations. The study demonstrated the protective impact of breastfeeding in patients without genetic risk, but not in BRCA-positive patients. Four studies have been dedicated to analyzing genetic predisposition as a possible predictor that would explain the possibility that using the same surgical technique, the same postoperative care may occur normal and abnormal scarring (hypertrophic or atrophic). In the fourth part case-control studies were designed that included three groups with normal, hypertrophic and atrophic scarring, respectively. The enrolled patients were followed for 6 months, for each of them a genotyping was performed by PCR method RFLP COL5A2

(rs369072636), TGF-β1 (rs201700967 and rs200230083), GSTT/GSTM, hTERT rs2736100 and vitamin D receptor polymorphism rs2228570, respectively).

In HELLP syndrome, a severe complication of preeclampsia, were incriminated glucocorticoid receptor gene (SNP Bell), TLR gene (polymorphisms D299G, T3991), VEGF gene (C-460 T, G+405C), Fas gene (A-670G), respectively factor V Leiden.

In neonatal hemochromatosis, an extremely rarely diagnosed antenatal condition, genetic testing plays an important role, the karyotype entering the basic investigations, respectively the testing of gene panels to exclude / confirm rare metabolic causes.

In **the second part**, the directions of didactic, academic and professional development are detailed: continuing studies on genetic implications in obstetrics and gynecology, submitting grant projects to ensure their funding, promoting multidisciplinary, continuing the process of educating students, residents and young specialists with their involvement in research projects.

Part three is devoted to bibliographic references.