

(A-i) Summary

This habilitation thesis represents a summary of my scientific, professional and academic activities which I developed from 2003 to 2016, after defending my doctorate dissertation "Evolutive Dynamics of Chronic Hepatitis", defended at "IULIU Hatieganu UMF –Cluj Napoca"

The habilitation thesis is conceived and edited according to the CNATDCU recommendations, being divided into three sections, beginning with the scientific, academic and professional development, focusing on my personal contributions in several research areas, followed by the plans for future professional and scientific development, bibliography and references.

The first section contains the main personal results in the academic, scientific, professional areas. I perfected my entire preparation in the medical field at the University of Medicine and Pharmacy of Cluj-Napoca, as a student, registrar, Master and PhD student. Moral and professional models offered by this higher education institution have guided my further evolution. Thus, graduating the Department of General medicine, I followed specialization in internal medicine, a doctorate in digestive pathology and I hold a master's degree in the field of Clinical Pharmacology.

The foundation of the Faculty of Medicine in 1992 at Transylvania University of Brasov allowed me as a part of a group of young specialists, to start the university career: (1996), Assistant Lecturer (1996) , Assistant Professor (1999) and Associate Professor (2004). At the institutional level, I have gone through different stages of different administrative positions: head of discipline, head of Department, Vice-Dean, member of the Faculty Board, and member of the University Senate. At present I am the head of the Medical Semiology course and coordinator of the registrars` training in internal medicine.

Since the beginning of my university career I have been attracted by research, which has been highlighted by the publication of 10 articles in ISI Thomson's Reuters -indexed journals and 49 articles in extenso in journals and volumes of ISI or BDI indexed scientific manifestations. In 2016, I published two books in the field of Internal Medicine and Medical Semiology as a main author, at a national publishing house recognised by CNCSIS. I have 133 citations, h-index 4 and i10-index 4.

I was the project manager of the grant "Researches on the pleiotropic effects of Lovastatin, Simvastatin, Pentoxifilin and Verapamil on the evolution of malignant

homeopathies and chronic hepatitis", research excellence grant (CEEX 179/2006) contracted with the Romanian Academy of Medical Sciences, by VIASAN, won through national competition, which allowed me to collaborate with other universities. As a project manager, I coordinated another educational project -CEEPUS in 2005-2015: "The multidisciplinary approach of psychosomatic diseases in Central and East Europe" project CEEPUS EN 128/2005 CII-EN-0016-04-0809. This project made possible collaboration with universities from Central and Eastern Europe and provided a greater visibility to our University.

I have had the opportunity to participate as a principal investigator to a lot of multi-centre clinical trials, five multinationals and over 25 other clinical trials as a monitor, national coordinator, and director of the research organization under contract or medical review.

I am a member of the Board of Internal Medicine of the Ministry of Health, of the Board of Romanian Society of Internal Medicine and the Vice President of the Romanian Society of Bio-psycho-social Medicine. Medical events requested not only organizational efforts, but also scientific and networking efforts: the first Congress of Neuro-gastroenterology, Medicine based on evidences, Psychosomatic National Symposia of Psychosomatic Medicine, etc.

In the wide field of Internal Medicine, I was focused on some fields of research: functional digestive disorders, hepatology, and neuro-gastroenterology. I have also published works and delivered conferences in the field of Psychosomatic Medicine, trying a modern approach to the concept of Somatisation.

In this habilitation thesis, I am referring to a group of works that bring up aspects of chronicization of digestive pathology with emphasis on chronic liver disease. The thematic interest exceeds the scientific framework, involving medical and social issues related to new diagnostic methods and actual therapeutic perspectives.

The first multicentre epidemiological study tried to establish the prevalence, clinical and biological characteristics of the liver chronic diseases in Transylvania. In the studied group, the prevalence of HCV infection was greater than the estimated global prevalence of about 3%. It is known that HCV can affect the nervous system and can induce neurological and mental disorders. Excepting the symptoms occurring during interferon therapy, neuropsychiatric manifestations of the patients without interferon therapy are the least known. Our prospective study included all patients infected with HCV who had not been treated with interferon, hospitalized for 8 month period in the Emergency Hospitals from Braşov and

Sibiu. The patients were examined neurologically and psychiatrically, EEG and biological tests specific for liver diseases were carried out. In our study, 36.36% of patients presented neurological disorders, possibly due to HCV infection (sensitive or sensory-motor polyneuropathy, unstable walk, cerebellum syndrome, grand-mal crises, dizziness, insomnia) and EEG highlighted changes in 18.2% of cases.

Some experimental studies mentioned the existence of the beneficial effects of statins, Pentoxifilin and Verapamil on chronic hepatitis, but their clinic effects are little known. We intended to make clinical trials on patients diagnosed with non- alcoholic steatohepatitis and chronic hepatitis C, to study the effect of the above mentioned drugs.

I developed a multicenter prospective study, to evaluate the efficacy of Lovastatin administered to patients with SHNA and Dyslipidemia and that of Pentoxifilin administrated to patients with SHNA, but without Dyslipidemia. Our study pleads for individualizing treatment for patients with SHNA, taking into consideration the presence of elements of the metabolic syndrome. Beneficial results recommend the use of drugs, Lovastatin and Pentoxifilin, whose side effects were rare and transient.

I continued my studies to evaluate if Lovastatin and Fluvastatin reduce viremy and Pro-Inflammatory Cytokines in patients with Chronic Hepatitis. I evaluated the effect of the both Statins on HCV RNA and on the modification of biological tests. We planned to study the possible correlations between the response to this treatment and anti-inflammatory pro Cytokine level. Patients were treated for 4 weeks and were randomized into two groups: Group F, treated with Fluvastatin, 40 mg/day, in the evening and Group L, treated with Lovastatin 20 mg/day in the evening. Our findings show that 63.64% of patients with detectable viremy at the first determination, decreased the viremy after 4 weeks of treatment with Statins, and in 3.03% of them, viremy was undetectable. The decrease of viremy after the treatment with Statins in the whole group was significant ($p = 0, 000987$). Administration of Lovastatin for 4 weeks resulted in a decrease of the serum level of IL-6 and TNF-alpha pro-inflammatory cytokines, and administration of Fluvastatin for 4 weeks resulted in a decrease of serum level of IL-6, IL-8 and TNF-alpha pro- inflammatory cytokines.

Effects of Simvastatin in the patients with chronic viral hepatitis C was studied in patients who did not register a significant virological response after antiviral therapy.

Nearly 60% of patients with liver viremy and hepatic cytolysis at the beginning of the study also registered a significant decrease of viremy after treatment. During 3 months of

study there were not recorded significant changes in patients without cytolysis at the beginning of the trial, regardless they were treated or not with simvastatin.

In the second part of the thesis, I have presented proposals for the evolution and development of my own academic, scientific and professional career. To ensure a proper academic environment is necessary for all students, registrars, and PhD students. It is mandatory for me to maintain those values which have guided me throughout my entire career: honour, honesty, common sense and respect. Some attributes must be consolidated in the relationship between the PhD coordinator and PhD student: communication, teamwork, interest in research and information dissemination. I will support the organization of PhD`s together with colleagues from other universities, as well as I will promote interdisciplinary PhD themes.