



**OLV Hospital
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To
Prof. MUDr. Peter Labas, CSc.
Dekan Lekarskej fakulty UK
Spitalska 24
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Re: Review of the habilitation thesis Dr. Juraj Madaric

Aalst, October 14, 2014

Dear Professor Labas,

I am pleased to support the promotion of Dr. Juraj Madaric M.D., Ph.D. to Associate Professor at the Medical Faculty of the Comenius University, Bratislava

Dr. Madaric submits the habilitation thesis addressing the role of novel regenerative therapies in patients with advanced peripheral vascular disease. The thesis consists of 10 chapters totalling 47 pages, 94 references and appendix of 3 original contributions published in peer-reviewed journals and as a book chapter.

The thesis is presented in a highly structured manner demonstrating the professional maturity of a clinician and scientist. In the first chapter, Dr. Madaric underscores the unmet clinical needs in patients with critical limb ischemia requiring the introduction of novel therapeutic approaches. He has introduced the concept of cell therapy providing the overview of various cell types, mechanisms and strategies for regenerative interventions in critical limb ischemia. With great didactic clarity he demonstrates in-depth knowledge of biological properties and potential advantages of individual progenitors in regenerative vascular medicine. Together with his collaborators, he investigated the biological properties and paracrine function of bone marrow progenitors. Their findings indicate that mesenchymal stem cells retain the paracrine functional properties also in hypoxic conditions and thus validating their use in the hypoxic setting of the chronic critical limb ischemia. He further succeeds in synthesizing the knowledge about individual cell progenitors in providing a succinct and clear review of their involvement in mechanisms underlying postnatal revascularization and healing, as critical mechanisms underlying the repair in critical limb ischemia.

In the next chapters on source of cell progenitors, their selection and delivery, he highlights the current state-of-the art technologies and methods available in clinical translation of regenerative vascular medicine. He provides his and his team's own original experience regarding the intra-arterial and intramuscular modes of delivery in patients with critical limb ischemia and establishing the optimal delivery platform for the future clinical trials with the currently available delivery techniques. In the

chapter on the stimulation of impaired cell function, he examines strategies that could be considered for the enhancement of the cell-based regenerative interventions.

Ensuing chapters are focusing the current clinical state-of-the-art of regenerative therapies in critical limb ischemia. With great details and clinical proficiency, he reviews the clinical trials in the field. His analysis is didactic and balanced aiming at identification of the optimally eligible patients with the most optimal chance for the recovery of the ischemic limb. He and his team contributed to this topic by the study describing the biological profiles of autologous cell source in clinical responders to cell therapy. This has been highly accepted in the regenerative field of critical limb ischemia.

In the final chapters, Dr. Madaric summarizes unanswered question and future directions in the clinical translation of cell-based regenerative interventions in critical limb ischemia. Here, he demonstrates his forward-looking and creative thinking of an investigator closing the loop with the clinical reality and expectations. He presents several progressive proposals for the future directions of the clinical and translational research in the field of his expertise aiming at effectiveness and durability of the interventional therapy.

I have known Dr. Madaric for several years and had a chance to work with him during his clinical and research fellowship at Cardiovascular Center, Aalst, Belgium. From the early days of his professional career, he demonstrated eagerness being intellectually intrigued to bridge in-depth scientific knowledge with the high quality clinical care. I personally perceive the current thesis as the culminating point of his current professional career. He provides here with the evidence of an established clinician and investigator advancing to the next cycle of the academical and professional career. He has an ideal profile of the mature, and yet young, clinical professional with great promise to the field of his expertise. His work is internationally competitive, he is recognized by his international peers.

Dr. Madaric is a model clinician-scientist with excellent communication didactic skills belonging to the class of opinion leaders in cardiovascular regenerative medicine. His determination in pursuing high quality clinical science, easiness in providing high quality opinions on variety of related issue with clarity and balance are key features in his communication. His praiseworthy perseverance in pursuing clinical research goals coupled with both drive and organization would be a guarantee for successful clinical and research academical career at any world-class institution.

I have no doubt that Dr. Madaric will further enrich Slovak and international cardiovascular science. His presence in any division is a major asset for the translational cardiovascular science and development of the original research. I wholeheartedly support his current promotion to Associate Professor at the Comenius University. I am always willing to provide further information on him. I look forward to his further international contributions to the cardiovascular research. It will remain a privilege to interact with him or develop common clinical research protocols with him and his group.

Sincerely Yours



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