ERASMUS UNIVERSITEIT ROTTERDAM

Erasmus University Rotterdam, the Netherlands
CSC PhD 2015 Project Description

School/Department:	Department of Internal Medicine, Division of Endocrinology, Erasmus MC, Rotterdam, The Netherlands Clinical and Experimental Neuroendocrinology PhD program is part of the post-graduate school Molecular Medicine (www.molmed.nl)
Project Title:	**Characterization of molecular determinants of effectiveness of medical treatment of patients with neuroendocrine tumors: the road to personalized medicine**
Abstract:	Neuroendocrine tumors (NET) originate from enterochromaffin cells that are part of the neuroendocrine system of the bronchial and gastrointestinal tracts. NET located in the gastrointestinal tract and pancreas are also referred as gastroenteropancreatic neuroendocrine tumors (GEP-NET). NET are considered as rare tumors, but recent studies indicate that the incidence of NET is increasing, in part due to the increased use of advanced diagnostic procedures. NET can be divided into functional and non-functional tumors. Functional tumors are able to produce, store and secrete bioactive peptides with related clinical signs and symptoms. The clinical course of NET can be highly variable and includes a spectrum ranging from well-differentiated, indolent growing tumors to aggressive, highly proliferative tumors. Surgery is the primary treatment option for GEP-NET patients with localized disease in order to achieve curation. However, at presentation many patients already have metastasized disease. Medical therapy with somatostatin (SS) analogs (SSA) plays an important role in the management of NET. This is due to the expression of a high density of SS receptors (SSR) on the NET cells. In addition to SSA, also other medical therapies, such as Interferon-alpha, chemotherapy and inhibitors of growth factor action (e.g. bevacizumab, and VEGF-inhibitor; Everolimus, an mTOR inhibitor and Sunitinib, a tyrosine-kinase inhibitor) are applied or currently tested in the treatment of patients with NET. However, a main concern with most medical therapies is that their effect is either transient (e.g. tachyphylaxis in case e.g. SSA) or that only a small proportion of patients show a significant tumor response. **Currently, it is not clear which factors cause this tachyphylaxis to treatment with SSA, nor which mechanisms are responsible for the variable response of NET patients to newly developed biotherapies.** A better understanding of these factors and mechanisms will help to select those patients that will benefit best from a particular medical treatment.

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	The Division of Endocrinology of the Department of Internal Internal Medicine of the Erasmus MC has a longstanding track record in translational research on the medical treatment of patients with (neuro-)endocrine tumors, including the role of SSA. In the laboratory of Clinical and Experimental Neuroendocrinology there is ample experience with techniques as cell culture (cell lines and primary cultures), mRNA and protein detection by real-time PCR, Western blot and immunohistochemistry, and with the measurement of cell growth and apoptosis. **The anticipated PhD candidate will be involved in studies to identify the molecular determinants of sensitivity or resistance to the various currently available medical treatment modalities. The work will include studies on NET tissues, as well as functional studies and molecular biological studies on primary NET cultures and well-defined NET cell lines**.
Requirements of candidate:	Background: Physician with laboratory experience or Medical Biologist. A strong affinity with translational research is required. Master degree: Yes IELTS Grade: 7.0 *(minimal 6.0 per component)* *or* TOEFL: *100 (minimal 20 per component)*
Supervisor information:	Prof. dr. Leo J. Hofland E-mail: l.hofland@erasmusmc.nl Website: http://www.erasmusmc.nl/inwendige_geneeskunde/endocrinologie/research/neuroendocrinology/3605838/ ***Selected publications 2010-2014*** **Gatto F, Feelders R, van der Pas R, Kros JM, Dogan F, van Koetsveld PM, van der Lelij AJ, Neggers SJ, Minuto F, de Herder W, Lamberts SW, Ferone D, and Hofland LJ.** beta-Arrestin 1 and 2 and G Protein-Coupled Receptor Kinase 2 Expression in Pituitary Adenomas: Role in the Regulation of Response to Somatostatin Analogue Treatment in Patients With Acromegaly. *Endocrinology 2013; 154:4715-25* **Gatto F, Feelders RA, van der Pas R, Kros JM, Waaijers M, Sprij-Mooij D, Neggers SJ, van der Lelij AJ, Minuto F, Lamberts SW, de Herder WW, Ferone D, and Hofland LJ.** Immunoreactivity score using an anti-sst2A

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