**JOB OPENING**

1. Description

**PhD student**

It is increasingly recognized that modulation of the immune system and inflammatory responses by immune checkpoint regulators, such as co-stimulatory molecules, control cellular functioning in health and disease. Our laboratory has a long history in the investigation of the role of co-stimulatory molecules in cardiovascular disease, including atherosclerosis and obesity. A recently obtained grant will further focus on the cell type specific regulation of immune checkpoint inhibitors, including CD40-CD40L interactions, and the signaling intermediates involved, in order to design and test novel therapeutics. TRAF signaling is an essential step in the co-stimulatory signaling process through the TNF-receptor in response to the presence of several known ligands. Functional CD40-TRAF signaling is known to have important contributions to development of a number of pathologies, including atherosclerosis and diabetes. You will use structural bioinformatics methods including virtual ligand screening to develop and optimize novel small-compound based therapeutic strategies. You will use rational methods to select potential ligands that target TRAF isoforms which may eventually be developed into novel orally available drugs to treat atherosclerosis. Based on the information collected in a previous project and based on functional studies of the same biological pathways also small compounds interfering with other targets in the same signaling pathway may be addressed. The compounds will be tested for their efficacy in *in vitro* assays as well as several relevant mouse models.

**Relevant papers**

* Zarzycka B, Seijkens T, Nabuurs SB, Ritschel T, Grommes J, Soehnlein O, Schrijver R, van Tiel CM, Hackeng TM, Weber C, Giehler F, Kieser A, Lutgens E, Vriend G, Nicolaes GA. [Discovery of small molecule CD40-TRAF6 inhibitors.](http://www.ncbi.nlm.nih.gov/pubmed/25622654) J Chem Inf Model. 2015 23;55:294-307.
* Chatzigeorgiou A, Seijkens T, Zarzycka B, ……Nicolaes G, Chavakis T, Lutgens E. [Blocking CD40-TRAF6 signaling is a therapeutic target in obesity-associated insulin resistance.](http://www.ncbi.nlm.nih.gov/pubmed/24492375) Proc Natl Acad Sci U S A. 2014; 111:2686-91.

2. We ask

For this four-year project (ERC Consolidator grant) we are searching for a PhD-student with a master degree in biomedical sciences, life sciences or biochemistry. Especially candidates with experience in structural bioinformatics, drug design and programming in a LINUX environment are requested to apply. We search a PhD-student who is fascinated by scientific research and innovation, motivated and eager to learn, who can work methodically and accurately and who is a great team player and has great communication and presentation skills in English. The ideal candidate will combine in silico and in vitro experimentation. Considering a potential small teaching opportunity, the ability to speak Dutch would be considered an advantage.

3. Where…

You will work in a multidisciplinary international team that focuses on the interplay between the vessel wall, plasma proteins and immune cells. This team is embedded in the Department of Medical Biochemistry of the Academic Medical Center Amsterdam (Amsterdam), and Maastricht University (Maastricht). The candidate will first be stationed at the Maastricht University, where you will work in the group of Dr. Gerry Nicolaes, expert in the development of small compounds. You will be trained in drug discovery, design and optimization under the direction of Dr. Gerry Nicolaes. Upon positive identification of novel biologically active compounds, you will be actively involved in the functional characterisation of molecules via in vitro and in vivo assays at the Amsterdam department of Medical Biochemistry, working under the direction of Prof. Esther Lutgens.

4. We offer

You will be employed on the basis of a 36-hour week. Appointment is for four years. Your salary will depend on your qualifications and experience (according to UMC-CAO).

5. Contact details

For more information please contact dr. G. Nicolaes (g.nicolaes@maastrichtuniversity.nl)