



Vacancy for a Ph.D. Student (10-027)

Faculty of Science, LACDR

The Leiden / Amsterdam Center for Drug Research (LACDR) is part of the Faculty of Science. The LACDR is a leading institute which performs fundamental and strategic scientific research in the field of innovative drug research.

In the Division of Biopharmaceutics of the LACDR 3 intertwining research lines focus upon the role of lipids (1), inflammation (2) and atherosclerotic plaque stability (3) for the development of cardiovascular events. Our research aims to identify genes responsible for the occurrence of cardiovascular disease by using genomics, specific gene knock-out technology and vaccination protocols, in order to develop novel experimental therapies to prevent and/or treat cardiovascular disease. The current vacancy is embedded in research line (1).

The division of Biopharmaceutics is looking for a:

**PHD STUDENT,
on the subject:**

The impact of cholesterol metabolism on megakaryopoiesis and platelet production.

Project description

Platelets are key elements in the development of arterial thrombosis. In recent years it has become clear that arterial thrombosis is modulated by lipoproteins, by e.g. altering the platelet response to activating agents. Platelets are formed and released into the bloodstream by megakaryocytes (Mks) that reside primarily in the bone marrow and are formed from pluripotent haematopoietic stem cells in a process called megakaryopoiesis. Mks show a very active cholesterol synthesis during megakaryopoiesis. The high demand for cholesterol is accounted for by endogenous synthesis as well as from LDL endocytosis and degradation. Excess cholesterol may be exported from the Mks by specific cholesterol transporters, including scavenger receptor-BI (SR-BI) and ATP-binding cassette transporters, like ABCA1. Abnormalities in megakaryopoiesis can result in impaired platelet production leading to clinically significant disorders like thrombocytopenia, causing inadequate clot formation and increased risk of bleeding, or thrombocytopenia, resulting in increased risk for thrombotic events, including stroke and myocardial infarction. As platelet properties are defined during megakaryopoiesis, and lipoproteins and thus cholesterol modulate platelet responsiveness, we hypothesize that changes in cellular cholesterol levels in Mks must affect platelet production and functionality. Hence, the aim of the current project, financed by the Landsteiner Foundation for Blood Transfusion Research, is to elucidate the influence of cholesterol metabolism on megakaryopoiesis, platelet production and finally platelet functioning. You will work together in an enthusiastic team studying the different aspects involved in atherosclerotic lesion development. The project will be carried out in close collaboration with the Department of Clinical Chemistry and Haematology of the University Medical Center Utrecht in Utrecht, the Netherlands. The daily tasks are diverse: platelet function studies, cell culture, in vitro lipid efflux assays, bone marrow transplantation, isolation of organs and cell populations, ELISA, FACS analysis, gene expression analysis, immunohistochemistry

and microscopy (bright field and fluorescence), acute arterial injury models to study thrombosis, in-situ knockdown of genes.

Who are we looking for?

We are looking for an enthusiastic, well motivated and ambitious scientist with a Master degree in Biology, Medical Biology, Biomedical Sciences, Biopharmaceutical Sciences or equivalent. Experience with in vivo studies, microscopical techniques and molecular biology is an advantage. This is a collaborative project with the Department of Clinical Chemistry and Haematology of the University Medical Center Utrecht in Utrecht, the Netherlands. Therefore, the candidate is expected to travel to Utrecht for work meetings and to work regularly in the Department of Clinical Chemistry and Haematology in Utrecht. You should display great team spirit and easily communicate in English, both verbally and in writing.

What do we offer?

We offer a temporary full time position for a period of 4 years. Appointment will be under the terms of the Collective Labour Agreement of Dutch Universities (CAO Nederlandse Universiteiten). The position is validated in the University Function Ordering system (UFO) under the profile promovendus. The salary will be set, depending on education and work experience, between the gross minimum of 2042,- and gross maximum of 2612,- Euros per month, based on fulltime employment (salary scale: P). Besides which, Leiden University offers an annual holiday premium of 8% and an end-of-year premium of 8.3%. You will be a member of the Graduateschool of the Faculty of Science and participate in our PhD training programme.

Further information and application

For more information, please contact Dr. S.J.A. Korporaal Telephone: +31 71-527 6213. Additionally, you can check the websites of the Faculty of Science and the division of Biopharmaceutics: www.science.leidenuniv.nl and <http://biopharm.lacdr.gorlaeus.net>

Further information on employment at Leiden University can be found at: www.leiden.edu.

Do you identify with the profile above and are you looking for an interesting job? Please apply by sending your written application before **01-03-2010** using the vacancy number, including a full *Curriculum Vitae*, and a list of publications to:

To the attention of: Dr. S.J.A. Korporaal.
Preferably by e-mail: skorporaal@lacdr.leidenuniv.nl

Or by regular mail:

Dr. S.J.A. Korporaal
LACDR / Division of Biopharmaceutic
Postbus 9502
2300RA
Leiden
The Netherlands