Post-doc or PhD position Netherlands Metabolomics Center

Prednisolone induced metabolite profiles in human and mouse: Cross-species translation and cross-omics integration.

A 3-years post-doc position or 4 years PhD student position is available within the Netherlands Metabolomics Center, in a joint project between Schering-Plough, Leiden/Amsterdam Center for Drug Research (LACDR), TNO Zeist and Radboud University Medical Center Nijmegen.

Summary of the project

Prednisolone and other glucocorticoids (GCs) are very potent immunosuppressive and anti-inflammatory drugs that are used in more than 300 different indications. Although very effective, prolonged use at high dose is hampered by side effects of which especially metabolic side effects are evident. These metabolic side effects induced by prednisolone include osteoporosis but also, fat redistribution, induction of insulin-resistance and beta-cell dysfunction, leading to a serious condition that is strongly associated with elevated risk for cardiovascular disease and type 2 Diabetes. Despite the fact that prednisolone is a relatively old drug (introduced in the 50's of the last century) the molecular mechanisms by which its side effects are mediated are largely unknown. To allow for a more rational development of an improved GC it is crucial to understand the molecular mechanisms by which prednisolone induces side effects.

In this project human healthy volunteers and mice will be treated with the synthetic glucocorticoid prednisolone. In these studies, urine, blood and serum samples will be taken and analyzed by metabolomics, transcriptomics and proteomics techniques. These data will be integrated to

i) use state of the art techniques to increase our understanding of the biological mechanisms underlying side effects of prednisolone

ii) identify biomarkers of glucocorticoid side effects that translate from mouse to human

iii) allow for a more rational development of an improved GC.

Function description

The project is an Associate Project of the research program of the Netherlands Metabolomics Centre (http://www.metabolomicscentre.nl/). Within this centre, Core Projects are aimed at method development whereas Associate Projects apply these methods within research programs.

The project is a collaboration between teams from Schering-Plough in Oss, the Leiden/Amsterdam Center for Drug Research (LACDR) in Leiden, the Radboud University Medical Center Nijmegen and TNO in Zeist.

You will be responsible for the statistical and biological analysis of the cross-omics data that are produced within the project. Analysis methods to be used include advanced statistical methods for multivariate analysis, data fusion and

experimental design; pathway analysis; sequence homology analysis; text mining; integration of experimental data and prior knowledge. The focus will be on generating biological hypotheses by applying existing methods and methods that will be developed within the core projects of the NMC, rather than independently developing new statistical or bioinformatics methods. You will work together with scientists in Oss, Leiden, Zeist and Nijmegen to identify the methods that are most suitable for the goals of the project. You will discuss and where possible initiate desired new methodology development with project partners and with scientists from NMC Core Projects. You will also be responsible for initiating and analyzing additional in-vitro or in-vivo experiments. You will interact with the NMC groups involved in metabolite quantification and identification, and spend some time at the NMC Demonstration and Competence Lab in Leiden where the metabolomics experiments are performed.

You will be appointed at the LACDR, and will be stationed bi-locally at Schering-Plough in Oss (approx 60-70% of the time) and at the project partners in Leiden and Zeist (30%-40%).

Profile of the candidate
The ideal candidate has a degree in bioinformatics with a strong proven interest in biology, or alternatively a degree in biology or biochemistry with skills in bioinformatics and/or biostatistics. We are looking for a candidate with excellent communication and interpersonal skills to work successfully with the project partners at Oss, Zeist, Leiden and Nijmegen.

More information
For more information you may contact prof. Thomas Hankemeier (Leiden University, principal investigator) or dr. Wynand Alkema (Schering-Plough, project leader).
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