Personalized Rheumatic Medicine

three approaches to personalized rheumatic medicine

by

Michael Kruse Meyer

Rheumatic diseases are high-incident inflammatory diseases with unknown etiology and with limited knowledge regarding occurrence and pathogenesis. These diseases are inherently associated with progressive disability and reduced quality of life. During the last decade, several new anti-rheumatic drugs have been developed and introduced into the clinic. This has significantly improved the quality of life for rheumatic patients and these drugs are crucial in maintaining low disease activity. However, the new biological drugs are the historically most expensive drugs and have allegedly resulted in dramatically increased hospital budgets in Denmark.

Personalized or individualized rheumatic medicine is in its infancy and we expect that overall treatment costs will decrease as this field develops. In this thesis, the initial aim is to address the intriguing question: Is it possible to optimize rheumatic medication strategies with modern omics technology and data-driven approaches? The secondary aim is to provide new understanding into the pathogenesis of especially rheumatoid arthritis and polymyalgia rheumatica and translate results from the basic research into clinical and treatment applications.

These questions are addressed in this PhD thesis and have been divided into three approaches. The first study is based on investigating the impact of an empirically approach, which utilizes disease activity score and remission criteria to dose down patients in biological treatment. To our knowledge, this is the first attempt that reports empirical dose-down strategy. The investigation substantiated that a dose reduction did not reduce treatment quality. Moreover, it was shown that the strategy reduced medication cost. The second approach involves a proof-of-concept to assess patient treatment response to biological drug treatment using discovery technologies. One substudy provided insight to immunometabolomic changes of leucocytes as a consequence of biological treatment of rheumatoid arthritis using mass spectrometry. A similar discovery approach was performed to assess the patient response to corticosteroid treatment in the serum of polymyalgia rheumatica patients. This study utilized both mass spectrometry and multi array electrochemiluminescence to overcome difficulties in serum analysis. This enabled us to propose new treatment options for polymyalgia rheumatica patients. The third approach, involves the development of mass spectrometry based assay to monitor the concentration of biological drugs in patients. It was especially interesting to develop the assay for one drug because no alternative methods have been published or made available. This study was then designed to observe the body uptake of that particular drug over the course of one week.

This thesis is inherently experimental and mainly based on the application and development of next-generation proteomics technologies. We successfully developed novel assays, which can be applied to address important questions of individualized patient response to treatment with anti-rheumatic drugs. One method was developed to explain patient response to treatment by evaluating the individual cellular response of peripheral leucocytes. An extensive study of patient sera was developed to evaluate treatment response to corticosteroid treatment. An assay was developed to measure pharmacokinetics of one biological drug in patients. The socioeconomically study, though somewhat distant from the experimental work, marks an important transition in rheumatology, where biological drugs are not only developed, but also put in the context of cost versus treatment efficiency. The results from this study highlight a potential for optimization of treatment, which is likely to adverse effects and reduce treatment costs, which is beneficial for the patient and for society. As a final comment, it should be noted that all these three approaches could be combined in future studies to enable more precision based medical research.

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PhD lecture

by

Michael Kruse Meyer

Thursday 5 October 2017

Department of Rheumatology & Center for Clinical Science

NORTH DENMARK REGIONAL HOSPITAL

DEPARTMENT OF HEALTH SCIENCE AND TECHNOLOGY

AALBORG UNIVERSITY

This thesis is based on
Michael Kruse Meyer's research work at:

Department of Health Science and Technology
Aalborg University, Denmark

To fulfill the requirements for the PhD degree, Michael Kruse Meyer has submitted the thesis Personalized Rheumatic Medicine – three approaches to personalized rheumatic medicine, to the Faculty Council of Medicine at Aalborg University.
The Faculty Council has appointed the following adjudication committee to evaluate the thesis and the associated lecture:

Professor Ole Nørregaard Jensen
Department of Biochemistry and Molecular Biology
University of Southern Denmark
Denmark

MD, PhD, Professor Per-Johan Jakobsson
Department of Medicine
Karolinska Institutet
Sweden

Chairman:
Associate Professor Jacek Lichota
Department of Health Science and Technology
Aalborg University
Denmark

Moderator:
Associate Professor Allan Stensballe
Department of Health Science and Technology
Aalborg University
Denmark

The PhD lecture is public and will take place on:

Thursday 5 October 2017 at 13:00
Auditoriet at Regionshospital Nordjylland,
Bispensgade 37, 9800 Hjørring

Program for PhD lecture on

Thursday 5 October 2017

by

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Chairman: Associate Professor Jacek Lichota
Moderator: Associate Professor Allan Stensballe

13.00	Opening by the Moderator
13.05	PhD lecture by Michael Kruse Meyer
13.50	Break
14.00	Questions and comments from the Committee Questions and comments from the audience at the Moderator's discretion
16.00	Conclusion of the session by the Moderator

After the session a reception will be arranged