Hormones and their link to microbiome and immune system

Summary

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Supervisor: Prof. Dr. Barbara Obermayer-Pietsch
Availability: This position has been occupied.
Offered by: Medical University of Graz
Application deadline: Applications are accepted between August 02, 2017 00:00 and September 17, 2017 23:59 (Europe/Zurich)

Description

Background:
Hormonal and metabolic changes are known to be associated in women with polycystic ovary syndrome (PCOS), affecting up to 20% of women worldwide and adding to the incidence of diabetes, obesity, fertility problems, depression and related long-term problems [1]. We recently published the first evidence of an interaction of stool microbiome with hormonal and metabolic features in women with PCOS diagnosed according to the Rotterdam criteria, with potential links to gut endotoxinemia and immunological changes [2].
A significant reduction in phylogenetic diversity and the number of observed operational taxonomic units (OTUs), accompanied by characteristic phylogenetic microbiome profile shifts between samples from PCOS women and controls has been demonstrated based on lower relative abundance of certain bacterial taxa. We have shown evidence for the hypothesis that diet-induced gut bacterial dysbiosis and subsequent gut barrier dysfunction and endotoxemia may drive the chronic inflammation and subsequent insulin resistance and androgen hypersecretion associated with PCOS [2]. Intestinal epithelial barrier damage, potential changes in phytoestrogen metabolism and (auto)immunological and genetic profiles in PCOS women may promote insulin resistance and lipid storage through an up-regulation of pro-inflammatory and auto-immune signaling. As this model is not only important for women, but also for men with metabolic syndrome and/or diabetes and/or gonadal dysfunction, this hypothesis might have a significant impact on our knowledge about both hormonal as well as metabolic dysregulations via (auto)immunological and microbiomal links in a large proportion of women and men.

Hypothesis and Objectives:
Based on our recent results that hormonal secretion and metabolic changes are associated and/or modulated by certain microbiomal and immunological profiles, we want to add novel insights to the unclear etiology and treatment options of PCOS and related clinical problems and generate new diagnostic and potential therapy concepts based on our human and animal pilot studies.
Furthermore, associations between host genetics and certain members of the gut microbiome will be investigated, since some bacteria predisposing to a healthy or unhealthy metabolic state may be heritable, thus explaining familiar components not only in PCOS.
Probiotic intervention might decrease gut permeability in systemic and functional tests as well as systemic inflammation, and increase gut microbiome diversity analysed by NGS techniques. Thus, intervention studies will define the potential impact of the gut microbiome on glucose, lipid, and hormone metabolism via and the translocation of bacterial products across the intestinal barrier by the investigation of gut barrier integrity, endotoxemia, and inflammation. In addition, recent approaches in the clarification of autoimmune changes of endocrine regulation will be conducted in our established large PCOS-, pregnancy-, and cardiovascular cohorts in context with these findings.

Methodology:
The PhD candidate will be involved in the planning and performance of clinical studies and biobanking. Besides insights into enzyme-linked and radioimmunological assays for hormonal and metabolic measurements, hormone and phytoestrogen metabolites will be assessed by HPLC-MS. Microbiome analyses based on MiSeq sequencing after DNA extraction from samples will be processed using open-source software according to published protocols.

with established adaptations and bioinformatic tools. Real-time quantitative PCR will be used for the confirmation of relative abundances of bacteria, whole blood gene expression and immunological changes in PCOS patients and controls as well as functional tests and flow cytometry. Studies will be complemented by cell culture models of hormonal and immunological interaction.

References:


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