TITLE.

IMMUNE PROTEOME IN HUMAN CERVICAL MUCUS - CLINICAL APPLICATION OF HIGH-RESOLUTION MASS SPECTROMETRY.

AUTHOR/S.

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ABSTRACT.

Context: Proteomic technology has developed identifying potential novel biomarkers for diagnosis, prognosis, and therapy in different clinical aspects.

Objective To analyze the changes in the CM immune proteome through the menstrual cycle.

Methods: Five 25-30 year-old fertile women were enrolled. Cervical mucus samples (n=3 per patient) were obtained by gentle aspiration from the cervical canal with a catheter for intrauterine insemination before (day 7), during (day 12), and after (day 18) ovulation of the same menstrual cycle. Proteomic analysis was performed by an Ultimate 3000 Nano/Micro-HPLC apparatus coupled with an LTQ Orbitrap XL hybrid mass spectrometer; Bioinformatic softwares were used for functional analysis.

Results: 59, 81 and 43 proteins (mean) were respectively identified in the pre-ovulatory, ovulatory and post-ovulatory samples. 38 common proteins were identified including important defense proteins, such as the immunoglobulin chains, neutrophil defensin 1, WAP four-disulfide core (WFDC) domain protein 2 and lactotransferrin.

42, 38 and 17 exclusive proteins were respectively identified in pre-ovulatory, ovulatory and post-ovulatory CM. The comparative analysis of GO annotations for molecular function for the exclusive proteins identified in pre-ovulatory and ovulatory CM reported significative differences in defense/immunity proteins.

The quantitative analysis for the common proteins revealed a significant reduction in the protein abundance index for antileukoproteinase, after the ovulation, and a peak of haptoglobin at the ovulation. Haptoglobin modulate several aspects of the innate and adaptive immune response.

Conclusions: This is the first application of high-resolution MS-based proteomics for the identification of immune protein constituents of CM. This approach might identify putative biomarkers of female reproductive tract.

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