

Multiple urinary peptides display distinct sex-specific distribution

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Abstract

Previous studies have established the association of sex with gene and protein expression. This study investigated the association of sex with the abundance of endogenous urinary peptides, using capillary electrophoresis-coupled to mass spectrometry datasets from 2008 healthy individuals and patients with type II diabetes, divided in one discovery and two validation cohorts. Statistical analysis using the Mann-Whitney test, adjusted for multiple testing, revealed 143 sex-associated peptides in the discovery cohort. Of these, 90 peptides were associated with sex in at least one of the validation cohorts and showed agreement in their regulation trends across all cohorts. The 90 sex-associated peptides were fragments of 29 parental proteins. Comparison with previously published transcriptomics data demonstrated that the genes encoding 16 of these parental proteins had sex-biased expression. The 143 sex-associated peptides were combined into a support vector machine-based classifier that could discriminate males from females in two independent sets of healthy individuals and patients with type II diabetes, with an AUC of 89% and 81%, respectively. Collectively, the urinary peptidome contains multiple sex-associated differences, which may enable a better understanding of sex-biased molecular mechanisms and the development of more accurate diagnostic, prognostic or predictive classifiers for each individual sex.

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