

Hepcidin-22 produced in urinary space

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Introduction

Hepcidin, a key regulator of iron metabolism, is expressed in the liver, distributed in blood, and excreted in urine. In previous report, molecular peaks of hepcidin-25, -22 and -20 are detected in urine (1) and it is speculated that urinary hepcidin could pass through glomerular basement membrane because of its small molecule. Recently, it is reported that hepcidin is also produced in the kidney (2) and the heart (3). We hypothesized that cleavage of hepcidin in urinary space could provide insight into the early pathophysiology of human interstitial nephritis (IN).

Methods

Here, we used surface-enhanced laser desorption ionization time of flight mass spectrometry (SELDI-TOF MS) with IMAC-30 distinctive serum and urine proteomic patterns of patients with IN. MALDI-TOF/TOF (AXIMA, SHIMAZU) analysis utilizes only 0.1 ml of urine samples were extracted with trichloroacetic acid. The extract was evaporated to dryness and target molecules were analysed by MALDI-TOF/TOF.

Results

In the normal urine, about 20 peaks are expressed in almost all volunteers'™ urine profiling by SELDI. The profiling pattern showed almost same patterns during 12 months in one volunteer, and the peaks at 2192 and 2789m/z were excreted at trace levels. In urine from patients with IN, these peaks were expressed highly compared with their sera and the peak at 2436m/z was detected only in the urine. When the peaks at 2192, 2436 and 2789m/z in extracted urine samples were analyzed by MALDI-TOF/TOF, same patterns of 8 repeated peaks were detected from each peak. Each interval was 32m/z which means the size of sulfur molecule which is constructed in disulfide binding. These findings imply that these fragments were induced from one precursor; hepcidin-25 which has 4 disulfide bindings. Hepcidin-22 may be cleavage from hepcidin-25 or prohepcidin by endopeptidase activated by IN and could work in inflammation and innate immunity.

Innovative Aspects

- #1 hepcidin-22 as biomarker for IN
- #2 8 peaks with 32 m/z interval from hepcidin
- #3 innate immunity in urinary space

References

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