Membrane proteomics for sex differences in renal proximal tubules using Sry gene-modified mice

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It has been shown that the biological sex difference lies not only in gonadal functions but also in physiological or pathophysiological aspects of whole body, including drug efficacy, adverse effects, and pharmacokinetics. Particularly, women experience more adverse events than men. Although it is plausible that the higher risks of adverse events in women could be partly explained by lower renal excretion of drugs, the underlying mechanisms on the sex differences have not been elucidated yet. It is known both hormonal and sex chromosome effects make sex-specific biological factors. Thus, in order to segregate hormonal effects and sex chromosome effects, we employed a murine model system in which the *Sry* gene was moved from the Y-chromosome to an autosome. The renal brush border membrane vesicles (BBMV) were isolated from murine kidney, and were subjected to quantitative membrane proteome analysis using LC/MS/MS (Q Exactive, Thermo Fisher Scientific). We have identified and quantitated 4309 molecules in BBMV and narrow it down to 736 sex specific molecules (80 transporters included). The results of the pathway analysis suggested that gonadal type influences membrane transports and sex chromosome complement influences cell metabolisms, implying that both sex chromosome complement and gonadal sex influence renal excretion of drugs.