Urinary levels of miR-491-5p and miR-592 as potential clinical biomarkers in female aging patients with OAB.

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Background: Overactive bladder syndrome (OAB), a common condition associated with aging, is characterized by a decrease in the ratio NGF/proNGF in urine of patients. In order to reinforce the clinical value of this observation, we measured the relative amount of several urinary microRNAs (miRNAs) involved in the processing of these neurotrophins and their receptors.

Methods: Urine and blood samples from women with OAB ad controls between the age of 50 and 80 years old were gathered together with validated questionnaires. Results were adjusted for age, sex, medication and insulin sensitivity. MiRNAs were measured by RT-qPCR.

Results: Levels of miRNAs (miR-98-5p, let-7b-5p and let-7d-5p) implicated in the translational control of proNGF were similar between groups. On the other hand, levels of miR-491-5p was strongly decreased in OAB. The latter directly controls the translation of matrix metalloproteinase-9 (MMP-9), the main enzyme hydrolysing NGF into peptides. MiR-885-5p, associated with indirect translational control of MMP-9, was expressed at similar levels between groups. The microRNAs MiR-92a-3p and 221-5p that control expression of the survival receptor TrkA were unchanged between groups. However, lower levels of miR-592 were measured in OAB group, which suggests an increase in the pro-inflammatory receptor p75NTR synthesis as miR-592 normally downregulates it. Finally, no change was observed for markers of nerve integrity (miR-21-5p, miR-132 and miR-212-5p). ROC curves confirmed a high sensitivity of miR-491-5p and miR-592 for diagnosis.
Conclusions: Together, our results suggest that OAB is associated with enhanced inflammatory pathways through: 1) elevated proteolysis of NGF consecutive to high MMP-9 activity; and 2) increased expression of the proinflammatory receptor p75NTR. These results may prove useful for diagnosis and treatment of OAB.