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Interaction of the miR-466-699 clusters and Wnt signaling in cell proliferation of the aldosterone-sensitive distal nephron

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Objectives : A small non-coding RNA, microRNA (miRNA), regulates the stability of messenger RNA (mRNA) as part of gene regulatory networks in various biological processes. Functional roles of several miRNAs expressed in the kidney epithelial cells have been studied in renal physiological and pathophysiological processes. Aldosterone, which regulates blood pressure by increasing sodium reabsorption along the renal distal tubule, has been reported to induce proliferation of renal tubular epithelial cells in vivo in mice. However, miRNA-mediated gene regulatory networks of epithelial cell proliferation in response to aldosterone is unknown.
Methods : miRNAs in the kidneys of mice treated with aldosterone for 3 days subcutaneously via osmotic minipumps were profiled using microarray. Differential miRNA expression, bioinformatics, and biochemical analyses for the aldosterone-responsive miRNAs and their targets were performed.
Results : Among 63 miRNAs differentially expressed after aldosterone infusion, 27 miRNAs (17 up-regulated miRNAs and 10 down-regulated miRNAs) were considered as significantly changed miRNAs (> 30% change, $p < 0.05$). The predicted target genes of aldosterone-responsive miRNAs were enriched in various signaling pathways involved in cell proliferation. Particularly, target genes of 10 down-regulated miRNAs were remarkably enriched in Wnt signaling. Among these miRNAs, 4 down-regulated miRNAs of the miR-466-669 miRNA family, localized as clusters in the genome, targets components of the Wnt signaling, including Frizzled-7 (Fzd7) dominantly expressed in the aldosterone-sensitive distal nephron (ASDN).
Conclusions : The clustered miRNAs of the miR-466-699 family decreased by aldosterone are associated with Wnt signaling in the ASDN and are potential regulators of Wnt signaling via the post-translational regulation of Fzd7 expression. The findings could provide novel insights into the miRNA-mediated gene regulatory network for cell proliferation of the ASDN after aldosterone treatment.