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AB74. MicroRNAs fuels cancer growth through the RNAa mechanism

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Abstract: MicroRNAs (miRNAs) are master regulators of gene expression and have been known to be involved in cancer by acting either as tumor suppressors or oncomiRs. It is widely accepted that the miRNAs carry out their functions in the cytoplasm via targeting the 3' UTR region of mRNAs leading to downregulation of gene expression. However, whether and how miRNAs function in the nucleus remains largely unknown. We showed that both exogenous and endogenous miRNAs are able to induce the expression of genes whose promoters contain the targets of the miRNAs, a phenomenon known as RNA activation (RNAa). In mouse prostate cancer cells, two miRNAs (miR-744 and miR-1186) are able to stimulate cell cycle progression and cause chromosomal instability by inducing the expression of Cyclin B1, a gene critical for mitosis. Genome-wide analysis of potential miRNA binding in human prostate cancer cells further revealed that the miRNA machinery interacts with the transcriptional apparatus to sustain the expression of hundreds of genes which are important for cell proliferation, evading apoptosis, angiogenesis and DNA damage repair. These findings suggest that miRNAs could be implicated in carcinogenesis through a non-canonical miRNA targeting mechanism.

Keywords: MicroRNAs (miRNAs); cancer growth; RNA activation

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AB75. Lower urinary tract dysfunction in a pink1 gene knockout rat model for Parkinson’s disease

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Abstract: Bladder dysfunction is a common non-motor disorder on Parkinson’s disease (PD) patients. A new transgenic Pink1 gene knockout rat model of PD has been developed recently. To explore lower urinary tract function in this newly established PD model and provide possible therapeutic base for PD urinary complications. Twelve Pink1 KO rats (pink1-/-, LEH-pink1tm 1sage, 40 weeks old) and twelve wide type rats (pink1+/+, LEH, 40 weeks old) were used in this project. After acclimation, the rats underwent 24 hours metabolic cage test, conscious cystometry, and leak point pressure test. Their bladders were harvested, weighted and then fixed for histological study. Total volume, micturition times, and voided volume per micturition were calculated for 24h metabolic cage test. Pressure parameters, micturition frequency, bladder capacity/compliance, volume parameters, leak point pressure (LPP) were analyzed according to the result of cystometry and LPP test. Body weight, bladder weight, and the general pathologic changes in bladder were also checked. Continuous variables were compared between groups using t-test. Categorical variables were compared using Chi-square test. P< 0.05 was set as statistical significant.
Pink1 KO rats acquired the functional disorder of detrusor over activity compared to wild type rats. Hyperplasia of smooth muscle and nerves were noted in the bladder wall of Pink1 KO rats. More specific nerve changes and specific causality among dopaminergic neuron loss, pathologic alterations of bladder, and functional changes should be investigated in the future. Pink1-/- rat model of PD exhibited bladder dysfunction at the age of 40 weeks old. Detrusor over activity was the main change. Smooth muscle and nerves in bladder wall displayed the alteration of hyperplasia. This is a better transgenic rat model of PD induced detrusor over activity for future study.

**Keywords:** Lower urinary tract dysfunction; Parkinson’s disease; pink1 gene knockout

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**AB76. Adipose-derived stem cells improve erectile function through secretion of growth factor in aged rat**

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**Introduction & objectives:** Adipose-derived stem cells (ADSCs) have been recently considered promising therapy for erectile dysfunction (ED). However, the mechanism of ADSCs-based therapy remains to be elucidated. The aim of this study was to determine whether transplantation of ADSCs was capable of resolving aging-related ED, and to investigate its underlying mechanisms.

**Materials & methods:** Hepatocyte growth factor (HGF), angiopoietin-1 (ANG-1), angiopoietin-2 (ANG-2), insulin-like growth factor (IGF-1), vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) secreted by ADSCs were assessed in vitro by means of neutralization of VEGF, bFGF or both using CCK-8. Sixteen 24-month-old male Sprague-Dawley rats were used for comparative analysis of 2-week treatment regimens with CM-DiI labeled ADSCs or PBS. Eight additional 5-month-old rats were used as young rats group. At 2-week post-transplantation, all the rats were analyzed for erectile function, cavernous VEGF and bFGF levels, and penile histology. The VEGF and bFGF levels of ADSCs-conditioned medium and penile tissues were determined by an enzyme-linked immunosorbent assay (ELISA). The ratio of maximal intracavernous pressure (ICP) to mean arterial blood pressure (MAP) was measured to evaluate erectile function. Immunofluorescence staining was used to evaluate the number of ADSCs, and the contents of cavernous smooth muscle and endothelium.

**Results:** ADSCs could secrete a large amount of VEGF and bFGF in culture medium compared to basal medium (P<0.05). Rat corpus cavernosum smooth muscle cells (CCSMCs) grew more slowly due to oxidative stress. However, conditioned DMEM of ADSCs played a protection role. Neutralization of VEGF, or both of VEGF and bFGF could significantly attenuate the effect. bFGF played a less important role in the protective effect. Compared to the young rats, the untreated aged rats showed significantly lower Max ICP/MAP (P<0.05) and ADSCs treatment significantly increased the ratio (P<0.05). Immunofluorescence staining demonstrated that there was only a small number of CM-DiI labeled ADSCs found in corpus cavernosum. The corpus cavernosum of untreated aged rats showed decreased VEGF and bFGF levels, and the contents of cavernous smooth muscle and endothelium compared to young rats (P<0.05). ADSCs treatment partially normalized these alterations (P<0.05).

**Conclusions:** ADSCs treatment may improve aging-related ED partially through secretion of VEGF and bFGF.

**Keywords:** Adipose-derived stem cells; erectile dysfunction (ED); vascular endothelial growth factor (VEGF); basic fibroblast growth factor (BFGF)

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