

## DETECTION OF CHAT-CONTAINING CYTOPLASMIC VESICLE-LIKE STRUCTURES IN THE MOUSE BLADDER UMBRELLA CELLS

### Hypothesis / aims of study

Cell adhesion molecules (CAMs) are essential for maintenance of tissue integrity and to regulate cell to cell adhesion and cell to extracellular matrix interactions. Cadherins and catenins are CAMs located on the cell membrane and are important for adherens junction formation. This study aims to verify if hypercholesterolemic diet (HCD) promotes structural bladder wall modifications, regarding cadherins and catenins expressions

### Study design, materials and methods

Forty-five 4 week-old female Wistar rats were divided into three groups: 1) control fed on a normal diet (ND); 2) bladder outlet obstruction (BOO) model fed on a ND and 3) control fed on a HCD (1.25% cholesterol). Initially, serum cholesterol, LDL-cholesterol and body weight were determined. Four weeks later groups 1 and 3 underwent a sham operation while group 2 underwent a partial BOO, with a suture tied around the urethra with a 22G needle beside it. Six weeks later, all animals had their bladders removed and previous exams were repeated. The N-, P-, OB-, E-cadherins and  $\alpha$ -,  $\beta$ - and  $\gamma$ -catenins expressions were evaluated by immunohistochemistry and a semiquantitative analysis was performed for all antibodies. Statistical analysis was done comparing groups with significance considered when  $p < 0.05$ .

### Results

Wistar rats fed on a HC diet (group 3) showed a significant increase of LDL-cholesterol levels ( $p < 0.001$ ) and body weight ( $p = 0.017$ ), compared to both groups fed on normal diet in ten weeks period. Catenin analysis showed a similar overexpression pattern in  $\beta$ - and  $\gamma$ -catenin in groups 2 and 3 when compared to group 1 ( $p = 0.02$  and  $p = 0.04$ , respectively). OB-cadherin was also overexpressed in the group 3 compared to groups 1 and 2 ( $p = 0.001$  and  $p = 0.016$ , respectively), as demonstrated in the next table.

| CAM               | Expression  | GROUPS      |         |         | P      |
|-------------------|-------------|-------------|---------|---------|--------|
|                   |             | Control (1) | BOO (2) | HCD (3) |        |
| E - cadherin      | Normal (%)  | 40          | 42.9    | 33.3    | 0.863  |
|                   | Reduced (%) | 60          | 57.1    | 66.7    |        |
| N - cadherin      | Normal (%)  | 0           | 21.4    | 33.8    | 0.056  |
|                   | Reduced (%) | 100         | 78.6    | 66.2    |        |
| P - cadherin      | Normal (%)  | 6.7         | 0       | 33.3    | 0.169  |
|                   | Reduced (%) | 93.3        | 100     | 66.7    |        |
| OB - cadherin     | Normal (%)  | 20          | 35.7    | 80      | 0.003* |
|                   | Reduced (%) | 80          | 64.3    | 20      |        |
| $\beta$ -catenin  | Normal (%)  | 20          | 66.7    | 71.4    | 0.021* |
|                   | Reduced (%) | 80          | 33.3    | 28.6    |        |
| $\alpha$ -catenin | Normal (%)  | 40          | 58.3    | 42.9    | 0.717  |
|                   | Reduced (%) | 60          | 41.7    | 57.1    |        |
| $\gamma$ -catenin | Normal (%)  | 10          | 50      | 57.1    | 0.044* |
|                   | Reduced (%) | 90          | 50      | 42.9    |        |

### Interpretation of results

A hypercholesterolemic diet in Wistar rats promoted, besides higher body weight gain and serum LDL-cholesterol increase, overexpression of  $\beta$ - and  $\gamma$ -catenins in the detrusor muscle cells, similarly in the HCD and BOO rats groups. OB-cadherin overexpression was seen only in the HCD rats.

### Concluding message

These findings induced by a HCD may be associated with bladder dysfunctions (1) occurring under such situations.

### References

- Yoshida M, Masunaga K, Satoji Y, Maeda Y, Nagata T, Inadome A: Basic and clinical aspects of non-neuronal acetylcholine: Expression of non-neuronal acetylcholine in urothelium and its clinical significance. Journal of pharmacological sciences 2008;106:193-198.
- Hanna-Mitchell AT, Beckel JM, Barbadora S, Kanai AJ, de Groat WC, Birder LA: Non-neuronal acetylcholine and urinary bladder urothelium. Life sciences 2007;80:2298-2302.
- Tallini YN, Shui B, Greene KS, Deng KY, Doran R, Fisher PJ, Zipfel W, Kotlikoff MI: Bac transgenic mice express enhanced green fluorescent protein in central and peripheral cholinergic neurons. Physiological genomics 2006;27:391-397.

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Is this a clinical trial?

No

What were the subjects in the study?

ANIMAL

Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?

Yes

