

## **HUMAN BLADDER POSSESSES A NETWORK OF N-CADHERIN POSITIVE CELLS; THE SUBSTRATE FOR DETRUSOR OVERACTIVITY?**

### Hypothesis / aims of study

In order to explain detrusor overactivity, one must describe the physiology of the stable bladder. However, this has not been illuminated. The guinea pig bladder incorporates a network of interstitial cells [1]. These non-neuronal cells show neuronal characteristics and are situated in the suburothelial zone and detrusor layer. They most probably play a significant role within the coordination of contraction of the bladder. Such a mechanism of the detrusor demands a cellular interaction between muscle- and interstitial cells, comparable with neuromuscular junctions, in which N-cadherin coordinates the signal transduction between neuronal and striated muscle cells. We investigated the presence of N-cadherin within the human bladder.

### Study design, materials and methods

Bladder biopsies (n=6) were collected from macroscopically non-pathological locations during transurethral resection of bladder tumours. After immuno histochemical staining techniques, specimens were analyzed for presence of N-cadherin and differentiation markers for myofibroblasts and smooth muscle cells (vimentin, smooth muscle actin, desmin and smoothelin). Morphology was confirmed using haematoxylin-eosin staining techniques.

### Results

Detrusor and suburothelial cells expressed N-cadherin in all biopsies. Multiple processes emerged from N-cadherin positive cell bodies. N-cadherin positive cells formed an intramuscular network within the detrusor and surrounded the detrusor smooth muscle cells at three levels: at the surface of the muscle bundles, at the borders of fasciculae and at the surface of individual muscle cells.

### Interpretation of results

Our study reveals a network of N-cadherin positive cells within the human bladder wall. The identity and function of this cellular network remains unknown. However, considering their pattern and localisation, they most probably play an important role in the coordination of bladder contraction.

### Concluding message

To our knowledge this is the first time evidence is provided that the suburothelial tissue of the human bladder possesses an integrated intramural network, positive for N-cadherin. Future research will focus on the role of this network within the stable and overactive bladder, using immuno electron microscopy techniques.

### References

1. Gillespie JI, Markerink-van Ittersum M, de Vente J. cGMP-generating cells in the bladder wall: identification of distinct networks of interstitial cells. *BJU international* 2004 Nov;94(7):1114-24.

**FUNDING:** The Astellas European Foundation 2006 Prize Fund

**HUMAN SUBJECTS:** This study was approved by the CMO region Arnhem-Nijmegen and followed the Declaration of Helsinki Informed consent was obtained from the patients.