- In vitro investigation of human or animal bladder function in normal or in pathophysiological conditions.
- Unrestricted amount of tissue with animal models.
- Evaluation of the ability of drugs at modulating detrusor smooth muscle tone can be performed:
  - on cholinergic contractile response elicited by muscarinic pharmacological stimulation (carbachol) or by electrical field stimulation (EFS) which stimulates efferent nerve terminals present in the tissue.
  - on beta-adrenergic relaxant response induced by pharmacological agents (norepinephrine).
  - on KCl contractile response.
  - on others non-adrenergic non-cholinergic (NANC) responses (purinergic, nitrergic…)
- Evaluation of the influence of urothelium on the detrusor contractility.
- Useful to investigate the effect of drugs targeting neurogenic detrusor overactivity (NDO) but also overactive bladder whatever its etiology: the NDO bladder is a suitable model for the evaluation of the ability of drugs at modulating increased spontaneous detrusor phasic contractile activity, the hallmark of detrusor overactivity.
- Evaluation of mRNA by RT-PCR or protein expression by, immunohistochemistry (IHC) or western-blot (WB), in parallel of organ bath studies.

Source of human tissues sample

- **Human normal bladder** samples (dome with no macroscopic malignant tissue): obtained from patients undergoing cystoprostatectomy for infiltrating bladder cancer and with no known overactive bladder according to their medical chart.
- **Human neurogenic bladder** samples: obtained from patients who suffer from neurogenic bladder due to damage caused by spinal cord injury, multiple sclerosis or other neurological disease and who underwent partial or total cystectomy. According to their medical chart, patients have urodynamically proven neurogenic detrusor overactivity.

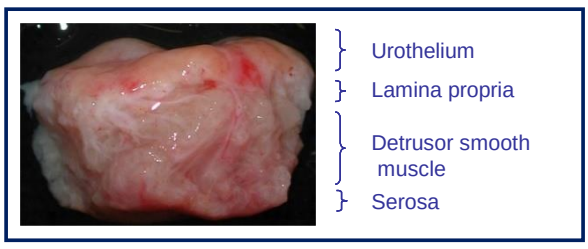

Figure 1: Photography of a section from human bladder wall with all layers (Pelvipharm, internal data)

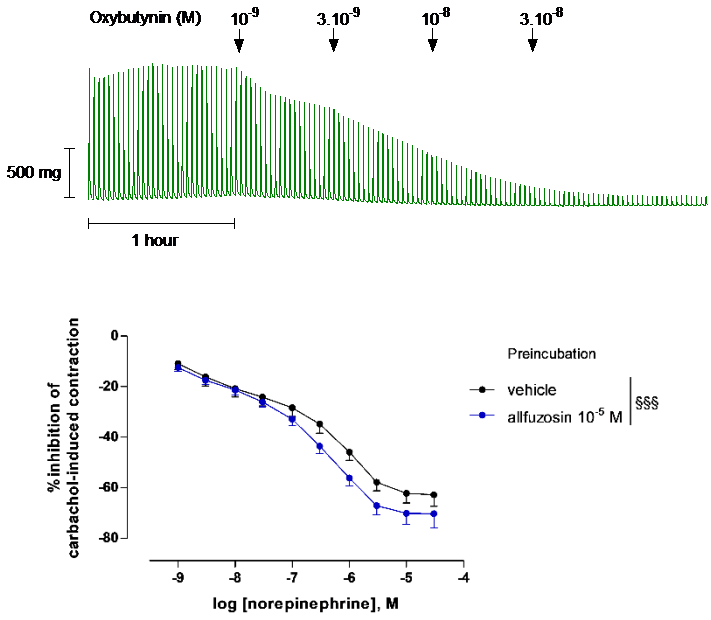

Figure 2: Original recording of contraction developed by human detrusor strips in response to EFS (300 mA, 5 s, 1 ms, 30 Hz). Effect of increasing and cumulative concentrations of the anti-muscarinic, oxybutynin. (From Maignel-Ludop et al., 2017)

Figure 3: Influence of alfuzosin on the relaxation induced by norepinephrine on carbachol-induced bladder contractions from control patients. (From Oger et al., 2010).

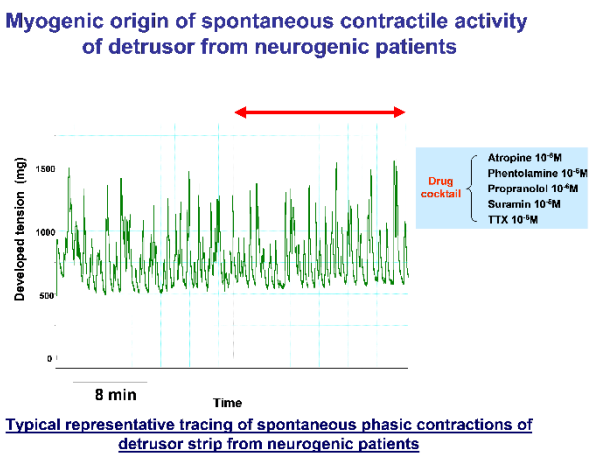

Figure 4: Original recording of myogenic contractile activity developed by human bladder stripfrom neurogenic patient: atropine (1 µM), muscarinic antagonist; phentolamine (1 µM), alpha-adrenergic antagonist; propranolol (1 µM), beta-adrenergic antagonist; suramin (10 µM), purinergic antagonist; tetrodotoxin (1 µM), neuronal Na+ channel blocker). (Pelvipharm, internal data),

Endpoints

- Evaluation of the capacity of a drug to inhibit detrusor smooth muscle contractions or detrusor phasic contractile activity.
- Determination of potency **(EC50)** and efficiency **(Emax)** of a drug.
- Determination of the affinity **(pA2)** of a drug for a bladder receptor.
- Evaluation of the influence of the urothelium.

Related Pelvipharm bibliography:

Oger, S. et al. **BJP** (2010):160(5):1135-43
Oger, S. et al. **Eur Urol Supl** 9(2):73-74 (EAU, 2010)
Oger, S. et al. **Eur Urol** (2010):57 (4):699-707
Oger, S. et al. **Eur Urol** (2007):51(3):772-781
Darblade, B. et al. **Urology** (2006):68(2):442-448
Darblade, B. et al. **World J. Urol** (2005):23(2):147-151

NB: Pelvipharm will gladly study the feasibility to fit this experimental model to its client's needs