Evaluation of the ability of drugs at modulating prostatic urethra smooth muscle tone:

- on adrenergic contractile responses elicited by alpha-adrenergic pharmacological stimulation (phenylephrine/norepinephrine) or by electrical field stimulation (EFS) which stimulates efferent nerve terminals
- on KCl response
- on other relevant physiological precontracted states (endothelin-1, thromboxane agonist: U46619…)

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 prostatic urethra samples are obtained from control patients undergoing cystoprostatectomy for infiltrating bladder cancer.Combined increase in both prostate cell number (DNA content) and size (protein content).

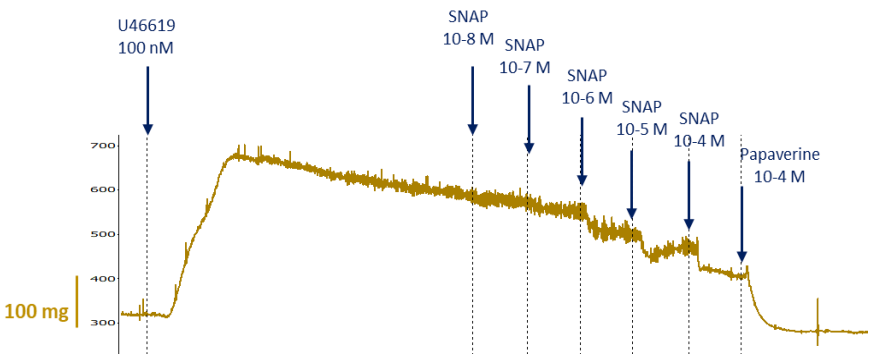
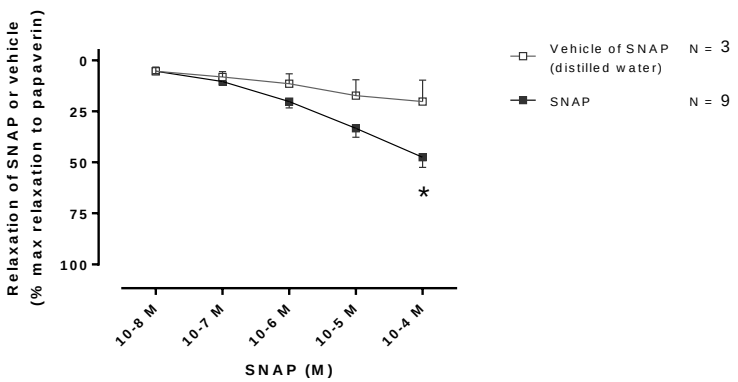


Figure 1: Original tracing showing the effect of cumulative addition of increasing concentrations of a NO donor (SNAP, 10-8 M to 10-4 M) on 100 nM U46619-induced contractions of human prostatic urethra. (Pelvipharm, internal data).



**p=0.0002 vs. vehicle of SNAP, Student's t-test with Holm-Sidak correction for multiple comparisons following two-way repeated measures ANOVA with interaction.*

Figure 2: Effect of S-Nitroso-N-acetyl-DL-penicillamine (SNAP) on U46619-induced contractions on human prostatic urethra. Data are expressed in % of maximal relaxation to papaverine. (Pelvipharm, internal data).

Endpoints

- Evaluation of the capacity of a drug to inhibit prostatic urethra smooth muscle contractions.
- Determination of potency **(EC50)** and efficiency **(Emax)** of a drug.
- Determination of the affinity **(pA2)** of a drug for a human prostatic urethra receptor.

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