Cyclophosphamide (CYP) is a prodrug chemotherapeutic agent that ultimately leads to the formation of acrolein, which damages the bladder urothelium and causes haemorrhagic cystitis. The resulting bladder overactivity is due to C-fiber afferent stimulation. This rat model is a valuable tool for evaluating the effect of treatments on bladder inflammatory processes such as interstitial cystitis associated with painful bladder syndrome (IC/PBS).

Pathophysiological features

A single or multiple cyclophosphamide administration can be performed depending on the specific experimental design or goal of each study, each resulting in:

- Abnormal bladder function: spontaneous micturition patterns are being disturbed as well as urodynamic evaluation by cystometry displaying a decrease in intercontraction interval and an increase in maximal and baseline pressures (figures 1 A&B).
- Haematuria and bladder wall oedema, characterized by the Gray score.
- Increase in bladder weight and histological modification of the bladder wall (histomorphometry).
- Inflammatory cell infiltration (polymorphonuclear neutrophils) in the bladder lamina propria (figures 2 A&B).
- Increase C-Fos positive cells in the spinal cord at L6 level.
- Increase in bladder pain score evaluated by Von Frey experiment (figure 3).

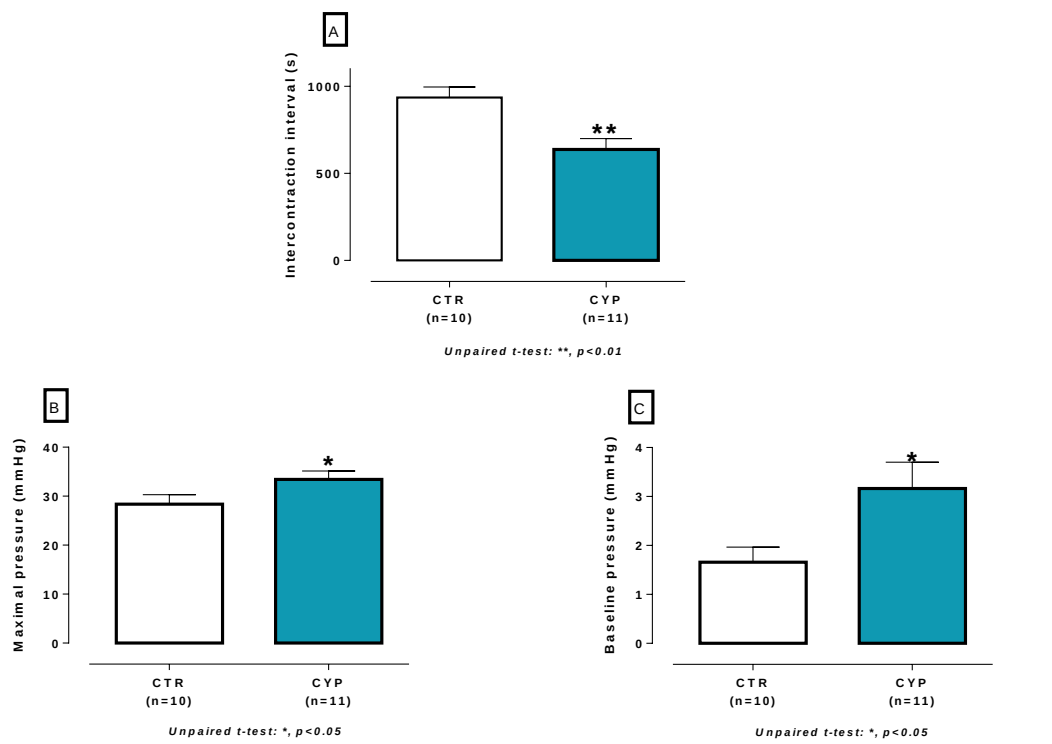

Figure 1: Representative urodynamic results on A) intercontraction interval, B) maximal pressure and C) baseline pressure parameters in control (CTR) and CYP treated rats chronically (Pelvipharm, internal data).

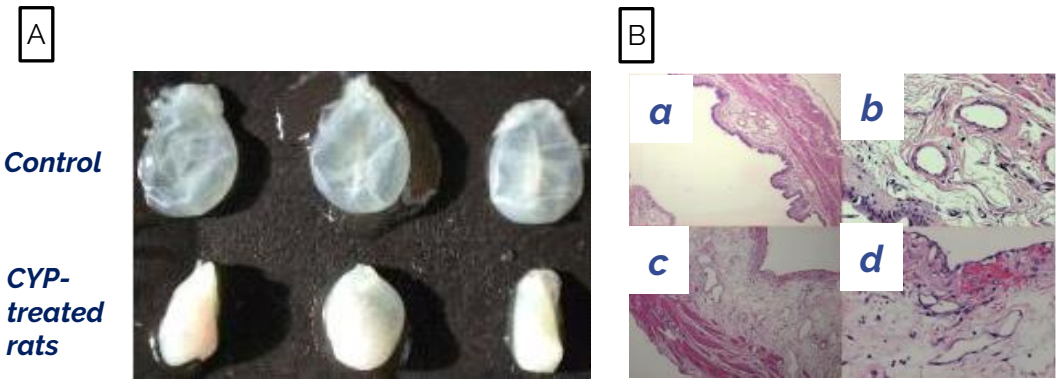

Figure 2: A) Representative images showing the inflammatory effect of CYP on bladders of CYP-treated rats versus control rats (adapted from Giuliano F et al. 2006). B) Representative HE staining in control rats with an intact urothelium (a,b) and in CYP-treated rats with an accumulation of inflammatory cells, oedematous changes, and urothelium haemorrhage (c,d). a,d ×40; b, c, ×200 (Pelvipharm, internal data).

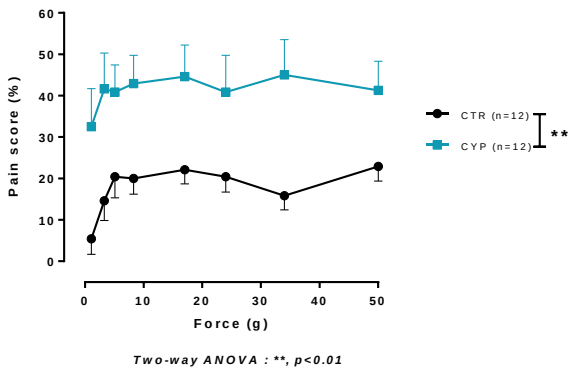

Figure 3: Representative Von Frey results on pain score in control and CYP-treated rats (Pelvipharm, internal data).

Related Pelvipharm bibliography:

Giuliano F *et al.* **BJU Int** (2006):97(2):386-92.

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