Metabolomic study of inflammatory mediators by high resolution mass spectrometry in a cyclophosphamide-induced cystisis model

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INTRODUCTION

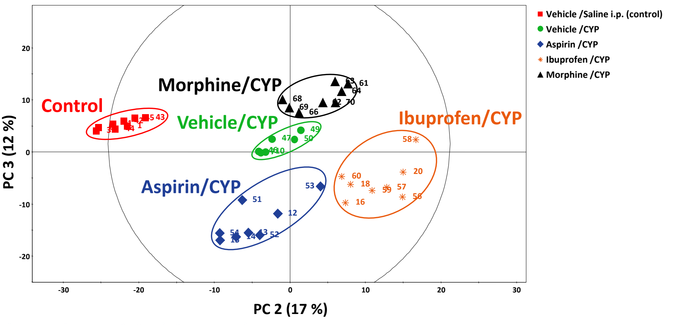
- **Cyclophosphamide** (CYP)-**induced acute bladder hypersensitivity** is a pathophysiological model of interstitial cystitis, a chronic clinical syndrome affecting the urinary tract.
- In a first set of experiments, **urinary inflammatory biomarkers** of this CYP-induced cystitis model were identified in conscious female rat. In a second set, **the efficiency of different analgesics** or **anti-inflammatory drugs** (aspirin, ibuprofen or morphine) following CYP intra-peritoneal injection were evaluated.

MATERIAL & METHODS

- Urinary samples from five different groups (n = 8) provided by UROsphere were studied : vehicle/saline (control), vehicle/CYP (n = 6), aspirin/CYP, ibuprofen/CYP and morphine/CYP.
- Acquisition of urinary metabolomic profiles was performed by **high resolution mass spectrometry** (Orbitrap™ technology) and electrospray ionization fitted with a fast liquid chromatography device.

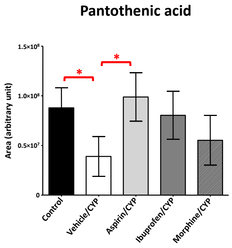
RESULTS

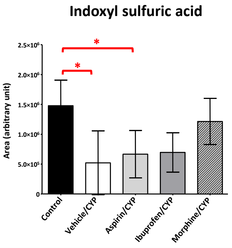
- Principal component analysis

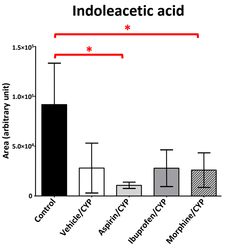


- Highlighted urinary CYP-induced cystitis biomarkers

** p < 0.05 (Kruskal-Wallis test)*







CONCLUSION

- PCA revealed obvious clusterization of different groups according to drugs/CYP variables. PLS-DA was used to highlight pathological biomarkers.
- **Pantothenic acid** (vitamin B5) and **indoxyl sulfuric acid** are **putative urinary biomarkers** for this model of CYP-induced cystitis. Moreover, they could be relevant **biomarkers** of **therapeutic efficiency**. Pantothenic acid level was fully recovered by aspirin treatment and partially recovered by ibuprofen or morphine treatments, whereas indoxyl sulfuric acid level was almost recovered by morphine treatment.
- Indoxyl sulfuric acid and indoleacetic acid variations revealed an **alteration of tryptophan metabolism** in this CYP-induced cystitis model.

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