A new approach to diagnose urological cancers based on the urinary volatile profile

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**What is metabolomics (or metabonomics)?**

The comprehensive analysis of low molecular weight metabolites involved in the metabolic networks of living organisms and their response to pathophysiological or other stimuli.

Cancer biomarker discovery at UCIBIO (FFUP)

Urological cancers

- Bladder cancer
- Kidney cancer
- Prostate cancer

Bottom-up metabolomics approach

Biomarkers

- Urine
- Tissue
- Cells
Study design

Sample collection

Cells (culture media)  |  Tissue (extracts)  |  Urine (supernatant)

Data acquisition & pre-processing

- HS-SPME-GC-MS
- Filtering, alignment
- Total area normalization
- Pareto scaling

Data analysis

- Principal component analysis (PCA)
- Partial least squares discriminant analysis (PLS-DA)
- Univariate analysis (Student’s t-test, Mann-Whitney U test)
- Variation (%)
- Effect size

Validation

- 7-Fold Cross-validation
- Permutation testing
- Receiver operating characteristic (ROC) analysis

Candidate biomarkers

Electronic nose sensor

In future

HS-SPME-GC-MS – headspace solid-phase microextraction gas chromatography-mass spectrometry
Renal Cell Carcinoma (RCC)

**Urinary volatile organic compounds (VOCs) signature of clear cell RCC (ccRCC) patients**

**PLS-DA model**

- LV=2
- R²X=0.270
- R²Y=0.466
- Q²=0.350

**Candidate 6-biomarker panel**

- p-Cresol
- Octanal
- Benzaldehyde
- 3-Methylbutanal
- 4-Heptanone
- 2-Furaldehyde

**Sensitivity** = 83 %
**Specificity** = 79 %
**Accuracy** = 81 %

**Stage I**

- Sensitivity = 84 %
- Specificity = 73 %
- Accuracy = 76 %

Prostate Cancer (PCa)

Urinary volatile organic compounds (VOCs) signature of PCa patients

Training set
External set

Total=118

Control
PCa
60
58


Sensitivity= 89 %
Specificity= 83 %
Accuracy= 86 %

Serum PSA (normal < 4 ng/mL)

Sensitivity= 21 %
Specificity= 91 %

Conclusions and future perspectives

• The urinary volatile profiling enabled the definition of two multi-metabolite biomarker panels with potential for ccRCC and PCa diagnosis with 81% and 86% accuracy, respectively;

• Further studies should include a larger cohort size in training and external validation sets and prove the translatability across different countries and ethnic groups;

• The biomarker panels will be used to develop sensing materials tuned in specificity and selectivity for those compounds to be applied in an electronic nose sensor in near future.

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