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EUROPEAN RESPIRATORY SOCIETY
INTERNATIONAL CONGRESS 2023
MILAN Italy, 9-13 September

Prediction of severe asthma clinical phenotypes using molecular profiles of urine eicosanoids

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Introduction: Urine eicosanoid concentrations increase with asthma severity, and eicosanoid profiles associate with known clinical phenotypes including type 2 asthma. We test the hypothesis that phenotypes can be independently predicted by urine eicosanoid profiles.

Methods: We quantified urinary excretion of eicosanoids in the U-BIOPRED study of mild to severe asthmatics, including baseline (n=497) and longitudinal (n=302) follow-up visit. Consensus clustering of baseline urine eicosanoid concentrations was performed. An elastic net prediction model was built using eicosanoid profiles at baseline (80/20 training/test split) and applied to the longitudinal timepoint to evaluate association with significant clinical variables observed in the consensus cluster model.

Results: Clustering defined 5 groups (termed U1-U5) of asthmatics: female-high BMI (U1), Type II (U2), late onset obstructive (U3), male-eosinophilic (U4), and female-early onset (U5). Ranked importance of eicosanoid pathways defining the 5-cluster prediction model (test set accuracy=94%) was: isoprostanes>PGD2>PGF2a>LTE4>TXB2. The elastic net model evidenced excellent performance for the longitudinal timepoint (93% probability). Clinical associations observed in terms of FEV1(%), ACQ-5, AQLQ, BMI, CRP, blood/sputum eosinophils and FENO between baseline and predicted longitudinal clusters evidenced reproducible median distributions in the order U1-U3>U5>U4.

Conclusion: The prediction of longitudinal sample-to-cluster probability was high, reproducing the baseline association between clinical presentation and eicosanoid concentrations. These findings support the use of urine eicosanoid profiles for identifying asthma phenotypes.

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