

Systemic tryptophan and kynurenine catabolite levels relate to severity of rhinovirus-induced asthma exacerbation: a prospective study with a parallel-groups design

Koenraad F. van der Sluijs PhD ^{1,2,3}, Marianne A. van de Pol MSc ^{1,2}, Wim Kulik PhD⁴, Annemiek Dijkhuis MSc ², Barbara S. Smids BSc ^{1,2}, Hetty W. van Eijk BSc ⁵, Jos A. Karlas BSc ⁵, Richard Molenkamp PhD ⁵, Katja C. Wolthers PhD ⁵, Sebastian L. Johnston MD PhD ⁶, Jaring S. van der Zee MD PhD^{1,7}, Peter J. Sterk MD PhD ¹, René Lutter PhD ^{1,2} and the RESOLVE research team.

Departments of ¹ Respiratory Medicine and ² Experimental Immunology, ³ Laboratory of Experimental Intensive Care and Anesthesiology ⁴ Department of Genetic Metabolic Disorders and ⁵ Medical Microbiology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands, ⁶ Airway Disease Infection Section, National Heart and Lung Institute, Imperial College London, London, United Kingdom, ⁷ Department of Respiratory Medicine, Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands.

Corresponding author: K.F. van der Sluijs, Laboratory of Experimental Intensive Care and Anesthesiology (current address), P.O. box 22700, 1100 DD, Amsterdam, the Netherlands, phone: +31 20 5668224, fax: +31 20 6979441, e-mail:

kvandersluijs@amc.uva.nl

Online repository

Supplemental figure 1: Tryptophan metabolome in EBC and serum

Tryptophan, kynurenine, anthranilic acid and quinolinic acid were determined in serum (day -1 and day 6) and exhaled breath condensate (day -1 and day 4) of healthy individuals and allergic asthma patients with confirmed lower respiratory tract infection. Concentrations are provided as nmol/L or $\mu\text{mol/L}$ (mean \pm SE). * $p < 0.05$, ** $p < 0.01$ and *** $p < 0.001$ vs healthy individuals. Detection limits are: Tryptophan (5 nmol/l), Kynurenine (1 nmol/l), Quinolinic acid (1 nmol/l) and Anthranilic acid (5 nmol/l).

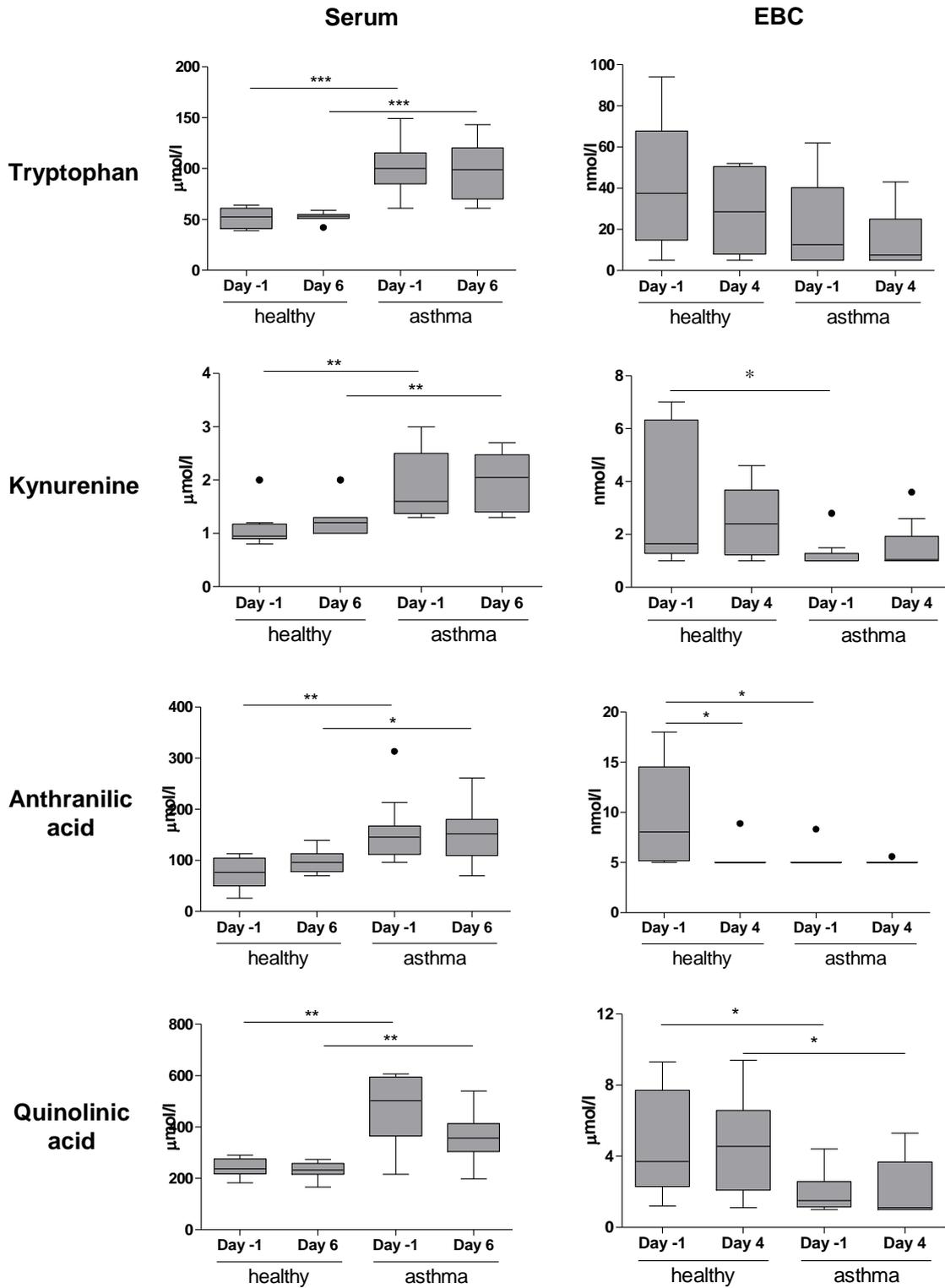
Supplemental figure 2: Arginine metabolome in EBC and serum

Arginine, Citrulline, Ornithine, Proline and urea were determined in serum (day -1 and day 6) and exhaled breath condensate (day -1 and day 4) of healthy individuals and allergic asthma patients. Concentrations are provided as nmol/L, $\mu\text{mol/L}$ or mmol/L (mean \pm SE). * $p < 0.05$, ** $p < 0.01$ and *** $p < 0.001$ vs healthy individuals. Detection limits are: Arginine (25 nmol/l), Ornithine (100nmol/l), Citrulline (25 nmol/l) and Proline (50 nmol/l).

Supplemental figure 3: Association between tryptophan metabolism and eosinophilic inflammation.

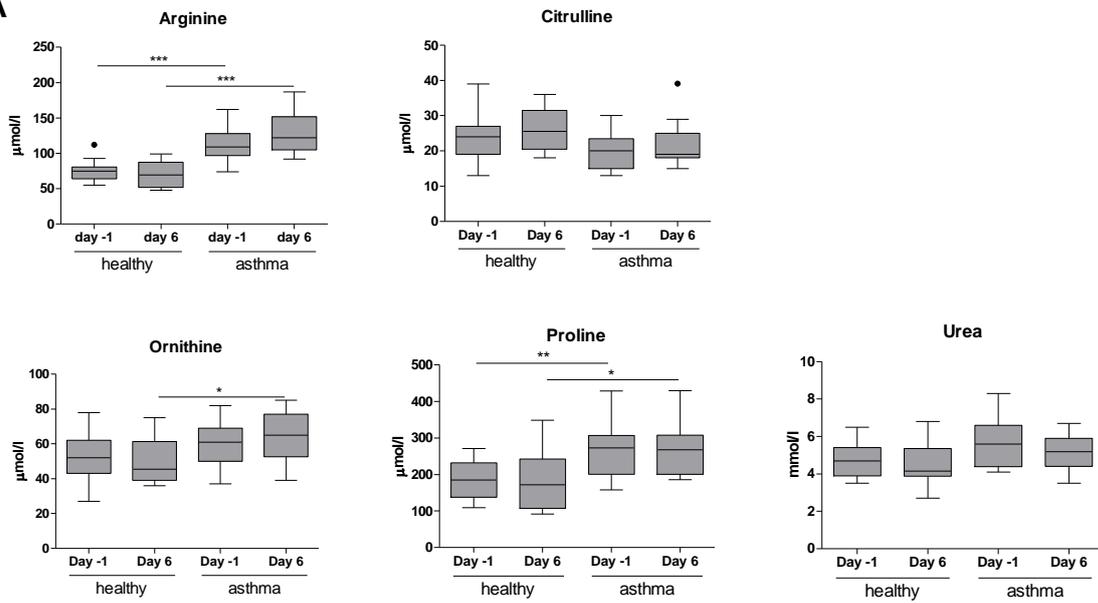
Analyses of the correlation between systemic quinolinic acid (left) and systemic tryptophan (right) with (A) % eosinophils in BAL fluid (B) ECP concentration in BAL fluid and (C) peak asthma symptom scores after rhinovirus exposure in asthmatic (solid dots) and healthy individuals (open dots) with confirmed lower respiratory tract infection. Spearman correlation coefficients (r) and P values are given in each panel.

Supplemental Figure 1:

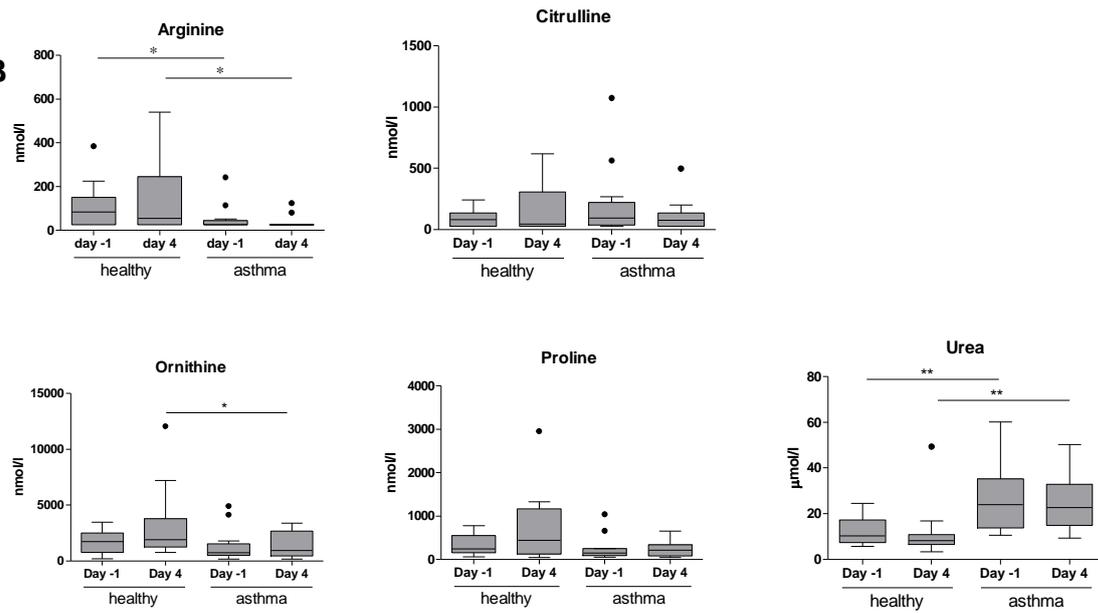


Supplemental Figure 2:

A



B



Supplemental Figure 3:

