

Title: Early-life microbial and immunological characterization of children living in contrasting environments - Finland and rural Malawi

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The prevalence of immune-mediated diseases, such as allergies and type 1 diabetes, is high in Westernized societies and rapidly increasing in urbanizing populations. We analyzed the immune system status, gut microbiota, and microbial infections in early childhood in Northern Europe (Finland) and rural Africa (Malawi) to identify differences which could underlie the contrast in the incidence of immune-mediated diseases in Western urbanized environment versus traditional rural environment. Plasma cytokines, gut microbiota, and stool positivity for several pathogens were analyzed from samples collected according to prescheduled time-points at 6- 18-, and 30-months of age during the longitudinal follow-up of 40 children in both countries. Random forest and elastic net regularization was used to identify most important gut microbial taxa associated with plasma cytokine levels. The level of plasma cytokines and stool pathogen positivity was significantly higher in Malawian children. Also, the gut microbiota differed between the countries already at the age of 6 months and diverging more by age. These results highlight the early emergence of differences in the immune system and gut microbiota between the populations living in extremities of the microbial exposure gradient and emphasize the effect of microbial exposure in the development of immune-mediated diseases.