

Amino acids as modulators of allergic immune responses

Dr. Leon Knippels - Division of Pharmacology, Utrecht Institute of Pharmaceutical Sciences (UIPS), Faculty of Science

Prof.dr. André Knulst - Department of Dermatology/ Allergology, University Medical Centre Utrecht

The intestine and the gut-associated lymphoid tissue (GALT) are essential components of whole body immune defense, protecting the body from pathogens and foreign substances while, allowing tolerance to commensal bacteria and dietary antigens. Recent studies indicate that not only the total protein intake, but also the availability of specific dietary amino acids is essential to optimizing immune development and functions of the intestine and the proximal resident immune cells. These amino acids, including glutamine, glutamate, arginine, cysteine, threonine and glycine, have each unique properties that include maintaining the integrity, growth and function of the intestine, as well as supporting immune development and fitness. Mechanisms underlying the effect of amino acids on immune function are diverse and include mTOR activation, NO and glutathione synthesis, tryptophan catabolism, normalizing inflammatory cytokine secretion, improving T-cell numbers and function, and secretion of IgA by the lamina propria cells.

We hypothesize: *that the high levels of glutamate as present in human milk, potentially in collaboration with other amino acids, modulate antigen presenting cell and T cell function in supporting tolerance development in the infant.*

With the FFU seed grant we aim to study the possible immune modulatory effect of glycine and glutamate on cow's milk protein induced cytokine production by specific cow's milk responsive T cell lines. The T cell lines are derived from allergic and healthy infants. The cell lines and the specific techniques for activating the T cells are available at the department of dermatology and allergology (Knulst). Cytokine production will be studied with multiplex analysis to study the effect of the amino acids on the production of Th1, Th2, regulatory and pro-inflammatory cytokines (Knippels). These data can be used as pilot data for future grant proposals.