Objective: The objective of this study was to evaluate the efficacy of vitamin D supplementation as a treatment of asthma and atopic dermatitis in children taking into account the presence of FLG and MTOR gene polymorphisms.

UV-B exposure declines progressively with distance from the Equator, creating a gradient that reduces intracutaneous VD3 production. Evolutionary differences in cutaneous structure and function are more likely to provide an explanation for the observed increase in circulating 25-(OH)D3 levels in northern Europeans. A strong genetic component that links epidermal structure to VD3 status was shown, that further correlates the individual’s ability to generate VD3 during summer months’ UV exposure.

Filaggrin is a histidine-rich protein, generated in epidermal differentiation, that plays an initial structural role in the formation of the cornified envelope, and in promoting filament aggregation in corneocytes. Higher in the stratum corneum, FLG detaches from the cornified envelope, followed by its humidity-dependent hydrolysis into its constituent amino acids including trans-urocanic acid (t-UCA). t-UCA is the major endogenous UV-B filter of the stratum corneum, interdicting at least 50% of incident UV-B in lightly-pigmented skin. Accordingly, down-regulation of FLG expression in organotypic human keratinocyte cultures yields lower-than-normal levels of t-UCA. The relationship between FLG mutation prevalence, 25-OH D3 serum levels and latitude shows a high degree of statistical correlation [Man L., 2015]. It was proposed that an increased prevalence of FLG mutations evolved relatively recently to insure adequate VD3 status in northern Europeans, who lived at high latitudes, and in cultures where seafood was not extensively consumed. A decrease in FLG results in a corresponding reduction in levels of t-UCA, the principal endogenous UV-B filter in lightly pigmented individuals.

Researchers have shown that 1,25(OH)2D is able to regulate the mammalian target of rapamycin (MTOR) signaling pathway by stimulating expression of DNA damage-inducible transcript 4 (DDIT4), a potent suppressor of MTOR activity [Lisse TS, et al., 2011]. The MTOR system forms part of a pathway that integrates signals from environmental nutrients, energy, stress and growth factors and therefore plays a crucial role in directing cell proliferation, growth and differentiation. Given the role of MTOR as a “master regulator” of cell function, it seems likely that DDIT4-mediated inhibition of this pathway will also play a pivotal role in mediating cellular responses to 1,25(OH)2D, as well as provide new strategies for its use in allergic disease therapy.

Materials and methods: The study includes patients with asthma, N = 99; ages 5-18 years (8 ± 2,1): five children with minor rs11204981 genotype polymorphism in FLG gene and 50 children with polymorphism rs11121704 risk genotype in the gene MTOR. In order to study the
effect of cholecalciferol addition to the clinical course of AD and asthma in children with FLG and MTOR genotype risk genes patients were divided into 2 groups. Children in the first group received basic therapy and cholecalciferol supplementation 1000 IU 1 time per day for 3 months. Dose of cholecalciferol was conditioned by the results of previous studies, conducted by Camargo CA Jr, Amestejani [Camargo CA Jr, 2014]. Children of the II-nd group received basic therapy for 3 months. Evaluation the efficacy of treatment was carried out on the following criteria: frequency of asthma exacerbation, severity of exacerbations, spirometry parameters (FEV$_1$), PEF daily variations, the use of salbutamol to relieve symptoms of asthma, index SCORAD. $\chi^2$ test was performed to investigate if there was any difference in the treatment efficacy between two groups before and after therapy. A $p$-value of less than 0.05 ($p<0.05$) was considered statistically significant.

Results: Supplementation of cholecalciferol to the basic treatment of asthma leads to improved controllability ($\chi^2 = 14.42; p < 0.05$). The analysis of data comparing the efficacy of treatment in the I-st and II-nd groups showed a statistically significant difference ($\chi^2 = 5.34; p < 0.05$).

Cholecalciferol addition to the basic treatment at a dose of 1,000 IU for 3 months leads to the use of lower doses of IGCS in patients with asthma ($\chi^2 = 3.74; p > 0.05$), thus reducing the risk of side effects of IGCS. In I-st group results after treatment have shown significantly reduced relapse rates ($\chi^2 = 14.91; p < 0.05$) and duration of exacerbations ($\chi^2 = 8.71; p < 0.05$), in contrast to the II-nd group ($p > 0.05$). Also cholecalciferol addition significantly reduces the index SCORAD. After the therapy SCORAD index improved in 12 children (54.54%) in the first group ($\chi^2 = 9.053; p < 0.05$) compared with 6 (28.57%) in the II-nd group ($\chi^2 = 1.921; p > 0.05$). Thus, the addition of cholecalciferol reduces symptoms of AD, improving the status and function of the epidermal barrier.

Addition of cholecalciferol to the basic treatment of asthma and atopic dermatitis in a dose of 1,000 IU for 3 months resulted in significant reduction in the frequency and duration of exacerbations, reduced number of night attacks and attacks that require hospitalization, improved values of pulmonary function tests, decreased use of salbutamol and reduced the index SCORAD.

Conclusions: Our study showed that cholecalciferol supplementation to the basic treatment of asthma and atopic dermatitis in a dose of 1,000 IU per day for 3 months will likely be of clinical use, since beneficial effects were reported in asthmatic and atopic dermatitis patients treated with cholecalciferol.