

Do cathepsins play a role in manifestations of hyper IgE syndrome?

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Introduction: The Hyper-IgE Syndrome (HIES), caused by mutation in *STAT3* gene accounts for the majority of the autosomal dominant (AD) and sporadic forms of HIES. AD-HIES is associated with skeletal and dental abnormalities in addition to immunological defects. Mice deficient in *Cathepsin E* has been observed to spontaneously develop features of atopic dermatitis very similar to human AD while *Cathepsin K* dysregulation has been observed to have similar skeletal defects including double row of teeth.

Objective: To correlate *cathepsin E* and *K* expression with skin and skeletal manifestations in HIES patients.

Material and Methods: Fifteen clinically suspected HIES patients were recruited based on NIH Scoring. *STAT3* sequencing, T_H17 cells (CD4⁺ IL-17⁺ IFN- γ) and phospho-*STAT3* analysis was performed among the patients of HIES and healthy controls. Patients were classified into Mutation negative [n=11] and Mutation positive [n=4]. PBMCs from patients and controls were stimulated with IL-6 (30 ng/ml) for 24 hr followed by total RNA isolation. qPCR was performed for *Cathepsin K* and *Cathepsin E* expression using relative quantification method.

Results: Mutation was found in 4 out of 15 clinical suspected HIES. Mutation positive patients had significantly decreased T_H17 cells compared to healthy controls and Mutation negative patients. *STAT3* phosphorylation was also found to be abnormal in Mutation positive patients. Expression of *Cathepsin K* and *E* was similar in controls and Mutation negative patients after stimulation however Mutation positive patients showed variable expression of *cathepsin K* and *E*.

Conclusion: *STAT3* signaling through IL-6 does not seem to play a role in regulation of *Cathepsin K* and *E* expression.

Biography

Shubham Goel has completed bachelor degree in Microbiology (H) from Delhi University in 2008 and Master degree in Medical Biotechnology from PGIMER, Chandigarh in 2010. Now pursuing PhD in the field of Immunodeficiency at the age of 26 years from the department of Immunopathology, PGIMER, Chandigarh, India. He has been awarded with NET-CSIR (LS), ICMR and PGI fellowship and life member of India Society for Primary Immune Deficiency (ISPID) and Indian Immunology Society (IIS). He has presented posters and oral paper in various national and international conferences. He has published two papers in peer reviewed journals.

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