Primary immunodeficiencies are described with recurrent unusual infections starting from birth through the adolescence and adulthood. There are more than 100 genetically determined conditions that have an identified molecular basis. In Western countries the frequency is defined as 1/10,000-1/100,000. Where as in countries with high frequency of consanguineous marriages, autosomal recessive forms of the disease seem much more frequent. Although there are clear guidelines for the clinical diagnosis of PIDs, sometimes the profile presents itself in a more complex way that the exact diagnosis is not possible. At that point the need for molecular genetic tests come up to clarify the background of the disease. Genetic tests for PIDs are also important for the early diagnosis and/or prenatal diagnosis for the following pregnancies. In PIDs up to date more than 250 gene defects are described. Unfortunately due to the high number of genes, labor intensive techniques and limited experienced laboratory workers it is not possible to run genetic testing for all these genes.

In 2010 with the great support of our beloved Professor Işıl Barlan, the first genetic testing was started as a research project in the Genetics Department of Institute for Experimental Medicine (DETAE) to check the mutations in STAT3 gene for Hyper IgE patients (MÜSBED 2013). With Professor Barlan’s enthusiasm and demanding character the list started to grow gradually. Today DETAE, Genetics Department is running molecular genetic tests for Severe Combined Immune Deficiency (RAG1, RAG2, ADA, IL2RG, Artemis, JAK3), Common Variable Immune Deficiency (TACI, ICOS, CD19 and BAFFR), Agammaglobulinemia (BTK for X-linked and IGHM for Autosomal Recessive form) and Hyper IgE (STAT3) diseases. These are only a few of the most commonly seen mutations in Turkey.

Between 2010-July 2015, in total 144 patients that were clinically diagnosed as PIDs were enrolled for the genetic testing from the Pediatric Allergy and Immunology Departments of, Medical Faculties of Istanbul University, Marmara University and Erciyes University. Among 144 patients 55 of them were screened for BTK, 44 of them were screened for RAG1 and RAG2 and 31 of them were screened for STAT3. The rest 18 patients were screened for Artemis, TACI, IGHM, ICOS, CD19, JAK3 and IL2RG.

Genomic DNA samples were isolated from the peripheral blood samples. The primer sequences, were kindly provided by Professor Jacques van Dongen and Mirijam van der Burg from the Department of Immunology of Erasmus Medical Center. All samples were run with the specific primer sequences of the related gene and positive amplifications were sent to direct sequencing. The samples were analyzed by CLC workbench program. All samples were compared with the wild type sequence of the related gene. All detected variations were analyzed and classified according to the latest standards and guidelines of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology (Genetics in Medicine March 2015).

Genetic testing is a straightforward technique to clarify and confirm the clinical diagnosis but it is an expensive and labor-intensive technique to be used for diagnostic exclusion. The physicians should always include detailed pedigree, clinical findings, blood counts and immunophenotype results of the patients while asking for a genetic test. More over the genetic laboratory should be familiar with the disease and should be experienced both in analyzing the sequencing results and classifying the variation that has been detected. Every variation needs to be analyzed carefully with the help of open access sources and tools. The variations that are detected for the first time, possible changes should be analyzed in detail before reporting.

Prof. Işıl Barlan was a great supporter of research in a very clinic world of physicians. Her support gave our team the power and the courage to start up very hard genetic tests in the field of PIDs. Although she will be missed in every work meeting, her initiation will always be remembered and together with her team it will help us to continue and grow the research of PIDs in Turkey.