The 22q11.2 deletion syndrome is the most common chromosomal deletion syndrome in humans, with an incidence of 1 in 1-2000 live births, and is a second, after Down Syndrome, cause of intellectual disability in general population. One of the most characteristic features of this syndrome is that it occurs in highly variable phenotypic severity, therefore this disease is very difficult to recognize clinically. Major clinical characteristics are intellectual disability, congenital heart anomalies, velopharyngeal abnormalities, characteristic facial appearance and psychiatric disorders. However, none of these features appears to be fully penetrant, and each exhibits variable expressivity. Therefore, in some patients the clinical recognition of the syndrome is obscured. Most affected individuals have a loss (deletion) on chromosome 22q11.2, which includes at least 48 known genes. Hence, it remains uncertain why individuals carrying identical 22q11 deletions can present with such a wide range of phenotypes. Potential genetics mechanisms underlying this variability include: (1) other chromosome aberration (deletion or duplication on different than 22 chromosome) (2) mutation in one of the genes that play a role in arise of the Syndrome (3) epigenetic (non-genetic) factors like environmental factors.
The aim of this project is to identify the genetic variants and pathways underlying features of 22q11 deletion patients. We hypothesize that the variability is caused by combined occurrence of 22q11 deletion and a “second hit”. We expect to identify genes which act as modifiers in 22q11deletion carriers, located both inside and outside of 22q11 region. These findings will lead to the better understanding of the complex and variable phenotypes of this genetic disorder and will allow us to predict consequences of genetic variations in patients with 22q11 deletion and consequently provide better care.
At the first stage of the project detailed phenotyping of all of 80 patients with 22q11DS is a prerequisite. Phenotyping will be conducted by the clinicians form Institute of Mother and Child.
For investigation of genetics modifiers the state-of-art technology will be applied;
- arry CGH method – for identification of additional copy number change (deletions and duplications) elsewhere in genome (besides deletion of 22q11)
- Full exome sequencing (WES) to identify mutations (small variants) deleterious for significant gene function

Since 2012 I am involved in Polish Association of Patients with 22q11 Deletion Sydrome. Additionally once a year, for a 22q11 Awareness Day (the third Sunday of May) I organize family meeting in Warsaw for Polish patients. Recently we have also established facebook page “22Q11 Syndrom Poland, Di George Syndrome, VCFS” and closed group, only for families with deletion “22q11 Syndrom Poland”. Therefore I’m in constant contact with more than 60 patients and their families, who are willing to collaborate in scientific project. For families it is extremely important to understand the mechanisms of this disease. The leave in constant uncertainty how their kids will develop if the ever will be independent. I believe this project can at least answer on some of their questions.