Populations of various ethnic groups are often characterized by particular genetic profiles, which result from the past evolutionary and demographic processes. For example, the frequency of genetic variants in a particular group may differ significantly as compared to the general population. The awareness of such peculiarities is of importance not only for historians and anthropologists studying particular ethnic groups, but above all, for a primary physicians working in the region.

The proposed study aims to evaluate the profile of genetic diversity in Kashubians, a unique ethnic population from Pomerania region of Poland. Kashubian people are descendants of the fraction of the old West Slavic tribe, who have settled along the southern cost of the Baltic Sea between the Oder and Vistula Rivers, after the Migration Period in the middle of the first millennium period (5th to 7th century A.D.). Despite a substantial cohabitation of the region by both Poles and Germans over the following centuries, this ethnic group has preserved its cultural identity. Classical genealogy tools allow tracking back family and population origins to a limited extend only, as well-documented (written) sources of information before 17th century are scarce. Therefore, ethnographic studies have to be assisted by the advanced genetic analyses. The recent studies suggest that Kashubians are genetically different from the general Polish population, but little is known about their early genetic history. Based on the Y-chromosome profiling (a male genetic "finger-print"), the genetic diversity of Kashubian males can be traced back to the pre-WorldWarII ethnically distinct Slavic population inhabiting this region. So far, no systematic studies of the female genetic "finger-print" (which can be approached i.e. through analysis of mitochondrial DNA and X-chromosome) have been performed. It is generally acknowledged that female DNA profiles better reflect permanent inhabitation of a given region, as male genetic material is usually spread in the neighboring populations as the result of short stays such us trade visits or military invasions. However, this was not always the case, the Vikings being a well-known paradigm (analysis of the Norse line of descent from a female ancestor to a descendant revealed that woman also set sail on Viking voyages and colonized new lands).

The study of the neutral genetic diversity shall allow shedding light on the past history of the Kashubian people. The studies of mitochondrial and X-chromosome profiles will be supported by the analysis of the copy-number variants (CNV) genomic profile. The latter is the fastest evolving aspect of human DNA studies. CNVs are gains and losses of large chunks of DNA sequence. For a number of recurrent CNVs, there is marked variation in copy number among populations.

The recently reported increased prevalence of a number of diseases and/or pathogenic mutations in Kashubians further supports the notion of the genetic distinctiveness of this Polish ethnic group. Accordingly, the second part of our study will be evaluation of the origin of altered mutation frequencies in five genetic disorders. These include mutations in 1. *LDLR* gene (familial hypercholesterolemia); 2. *BRCA1* gene (high risk for breast/ovarian cancer development); 3. *CFTR* gene (cystic fibrosis); 4. *HADHA* gene (the long-chain fatty acid dehydrogenase deficiency – a metabolic disorder); 5. *NPHS2* gene (steroid-resistant nephrotic syndrome – a hereditary kidney disease).

Estimating the age of mutations (time to the most recent common ancestor), combined with the available knowledge on the origins of Slavic Pomeranians, should help answering, whether the mutations originated in Kashubians or were already present in the ancient founding population. The third possible solution on the origin of mutations comes from trade exchange and/or military invasions. This has been already postulated with respect to the *BRCA1* mutation, present in Kashubians and Czechs, but not in Polish inhabitants of lands separating these two geographical regions. Ethnologists suggest that either the mutation was brought to Kashuby by Czech regiments during Teutonic reign of Pomerania or by Czech immigrant craftsmen, who introduced the technique of window-making to this area.

The proposed study will go beyond helping to elucidate the past history of the Kashubian people. It has also a potential for a substantial practical application. As in any other population, disclosing the genetic profile of Kashubians is important in light of mutation screening strategies, forensic medicine, pharmacology, and genetic counselling. The increased frequency of certain pathogenic mutations in northern Poland is a premise for the implementation of new region-specific diagnostic procedures and genetic tests, which will lead to a faster diagnosis and more efficient patient-tailored treatment.

It should be underlined that for most of the diseases studied in the project some sort of preemptive management and/or pre-symptomatic treatment is already available. However, so far, there is no Kashubian-specific panel for carrier screening. Availability of such a panel would facilitate presymptomatic diagnosis, which may lead to improved medical outcomes; it would also aid cascade screening and facilitate informed reproductive decisions. This goal has already been achieved with respect to LCHAD deficiency – its analysis was introduced to neonatal screening program of all children born in the Pomeranian region since 2010.