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## Population genetic studies conducted among Roma people

*„You and I, in fact everyone all over the world, we're literally African under the skin; brothers and sisters separated by a mere two thousand generations.”*  
(Spencer Wells)

One of the most important scientific results of the 20-21st century are the discovery of the double helix of the DNA – the material storing genetic information – (Watson & Crick, 1953), and the nearly complete mapping of the human genome (Human Genome Project, 2001). This means the beginning of a whole new chapter of medicine; the discovery of genes – that define the functioning of the human body – and gene defects – responsible for lesions and dysfunctions – opened great potential both for prevention and treatments.

### The importance of population genetic studies

Today we know for certain that besides environmental and lifestyle factors, genetic causes are also responsible for the development of several diseases such as cardiovascular disorders, diabetes mellitus, certain autoimmune diseases, asthma bronchial, some neurological and psychiatric disorders, tumors, osteoporosis, etc. Identifying genes responsible for these lesions enables us to study their functioning, providing the opportunity for the correction of those medical conditions in addition to diagnostics.

As a result of the above mentioned discoveries, genetic causes for the aggregation of certain diseases in a given ethnic group can be identified. It is well known that due to geographical, social-political isolation, religious reasons, or traditional endogamy, typical spectrums of diseases developed in homogenic groups. Genetic diseases of Finnish people, Ashkenazi Jews, French-Canadians, and Amish people of Pennsylvania are well mapped, and besides research institutions, clinics have been established for treatment. It is also widely known that there are more than thirty diseases specific only to Finnish people, and that certain metabolic diseases occur only to Ashkenazi Jews. The list of similar results of population genetics studies goes on.

The identification of the origin and the relationship of ethnic groups is also due to the genetic researches. Between 2005 and 2015 a worldwide research –*The Genographic*

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*Projekt* – was performed about the origin and the migration of the world population to the initiative of American geneticist Spencer Wells. Hungary also joined the research in addition to 139 more countries.

### The study of Gypsies'/Roma people's genetics

Population genetic researches in the 1980's proved that genetically Gypsies have closer relationships with Indian people than Europeans; the rate of blood type "B" is very high similarly to ethnic groups in the subcontinent. According to former studies, blood type „0" and „A" are typical in Europe, while „B" is typical in Asia. The further we go from Europe towards Asia, the rate of type „B" increases. The most common group of Y chromosomes and mitochondrial DNA in the genes of studied European gypsies was *H haplogroup* (50%) in case of men, *H and M haplogroup* (35% and 26%) in case of women. These are very rare in case of other European people but similarly common in India. However, certain haplogroups are completely missing in case of European gypsy people that are considered common in India (e.g. *U2i* and *U7* with the rate of 11-35% in case of Indian women). This means that European gypsy population has mixed with the surrounding European ethnic groups.<sup>1</sup>

In addition to blood type, genetic similarities are rather conspicuous between the Gypsy population and Indian people. Luba Kalaydjieva, an Australian professor of Bulgarian origin – who has been conducting researches about the genetics of Roma people for 15 years – compared the DNA of both populations, and in addition to the unambiguous relationship, she believes that the ancestors of today's Gypsy population emigrated from India 32-40 generations earlier, approximately 1000 years ago, and their number certainly did not exceed one thousand.<sup>2</sup> By studying their diseases and genetics, she determined that gypsy people are genetically multicolored and more heterogeneous than European population.

Studies about Hungarian ethnic groups, specifically the genetic structure of Gypsies were conducted by Béres Judit and her contributors. During the 1980's and 1990's they studied the genetic variations and relationship possibilities of nine populations in Hungary (Jász, Kiskun, Nagykun, Székely, Csángó, Palóc, Matyó, Roma, Ashkenazi Jew).<sup>3</sup> Special disease spectrums different from the European average were found only in the case of Roma people and Ashkenazi Jews. In addition to exploring and describing typical diseases, significant results were obtained regarding the origin and the relationship of Hungarian ethnic groups by joining the above mentioned worldwide researches in the 2000's.

- 1 GRESHAM, D. – MORAR, B. – Underhill, A. P. et al.; Origins and Divergence of the Roma (Gypsies) (The Eurasian Heartland: A continental perspective on Y-chromosome diversity, Wells et al.) *Am J Hum Genet.* 2001 Dec; 69 (6): 1314–1331.
- 2 KALAYDJIEVA, L. – MORAR, B. – CHAIX, R. –TANG, H.: A newly discovered founder population: the Roma/Gypsies. *BioEssays*, 27 2005 (10):1084-1094
- 3 BÉRES JUDIT: Hazai népcsoportjaink eredete és eltérő betegségsprektuma. In: Dr. Józsa László-Dr. Pálfi György-Szikossy Ildikó szerk.: A FORDULAT. A magyarság és a Kelet II. őstörténeti konferencia. A Magyarok VI. Világkongresszusának kötetei. Magyarok Világszövetsége, Budapest, 2008. 71-72.



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Initial studies performed during the 1980's were aimed at the so-called genetic markers (blood type, serum proteins). Based on these, genetic distance i.e. genetic relationship was determined. Subsequent researches analyzed the mitochondrial DNA of maternal inheritance, and the Y chromosome polymorphism of paternal inheritance; 28 classic markers in both cases. The genetic mapping of Hungarian Roma population was performed in two areas with two groups: Vlach Roma groups in Szabolcs-Szatmár-Bereg county, and Boyash in Alsószentmárton of Baranya county.

### Origin and different genetic diseases

According to the studies of classic markers, two unambiguous findings had already been determined; the fact that Roma people originate from North-India is unequivocally traceable, and there are basic genetic differences between the two Gypsy populations.<sup>4</sup> Béres Judit learned that there is significant difference in the prevalence of the four isoenzymes between the two Gypsy groups.<sup>5</sup> It is a genetic difference of such great degree that causes different disease spectrum, and different prevalence of genetic diseases. The difference

- 4 MÉSZÁROS ANITA – DR. BÉRES JUDIT: Hazai etnikumok/populációk genetikai struktúrája. In: Dr. Józsa László-Dr. Pálfi György-Szikossy Ildikó szerk.: A FORDULAT. A magyarság és a Kelet II. őstörténeti konferencia. A Magyarok VI. Világkongresszusának kötetei. Magyarok Világszövetsége, Budapest, 2008. 75-91.
- 5 BÉRES JUDIT: Hazai népcsoportjaink eredete és eltérő betegségsprektuma. In: Dr. Józsa László-Dr. Pálfi György-Szikossy Ildikó szerk.: A FORDULAT. A magyarság és a Kelet II. őstörténeti konferencia. A Magyarok VI. Világkongresszusának kötetei. Magyarok Világszövetsége, Budapest, 2008. 71-72.

can be easily observed in connection with two hereditary diseases; typical lactose intolerance of Vlach Gypsies, and common polycystic kidney disease among Boyash gypsies. Today, it is well-known that lactose intolerance is common among Vlach Gypsies. Lactose – carbohydrate in milk – is digested by lactase enzyme; in the small intestine lactose is transformed into absorbable glucose and sucrose under the influence of lactase enzyme. The quantity of this enzyme decreases with age, therefore a part of adult population becomes lactase deficient; natives from Asia, Africa and South-America lack this enzyme in 100%. They are unable to digest lactose, that causes abdominal distension and diarrhea. The lack of lactase due to hereditary reasons is attributable to genetic causes; the nature of the gene on the LCD locus on chromosome 2 is responsible for the development of lactase. As per the research of Béres Judit and her contributors, 56% of the Hungarian Vlach Roma population is not capable of digesting lactose, similarly to the results of the North-Indian population. Polycystic kidney disease is significantly more common among Hungarian Boyash Gypsies than among Vlach Gypsies or among the non-gypsy population. This hereditary disease affects both kidneys; the kidneys swell and numerous cysts start to grow inside of it, hindering the urination process, leading to severe kidney failure.

In addition to the research of Béres Judit and her contributors, more and more attention is devoted to the genetic diseases of Gypsy/Roma population; at the University of Pécs, genetic similarities between the Gypsy and Indian population were demonstrated by Dr. Orsós Zsuzsanna through a research about allele-polymorphisms in carcinogenesis.<sup>6</sup>

### Common hereditary diseases among Gypsy/Roma population

Thanks to population genetic studies, the following common genetically hereditary diseases among the Gypsy population are registered in the National Register for Birth Defects (NRBD)<sup>7</sup>

– *Primary Congenital Glaucoma*<sup>8</sup> (PCG eye disease). It is rare among ethnic groups of European origin (1:10000) while more common among Gypsies (1:1200). According to domestic studies, it is common among Gypsies in Northern Hungary while unavailable among Boyash Gypsies living in the southern part of the country.

– *Congenital Myasthenic Syndrome*<sup>9</sup> (CMS) Severe congenital muscle weakness. It happens almost only to Gypsy infants; it is a lesion caused by the mutation of the receptor binding acetylcholine. Clinical symptoms: powerless breast-feeding, feeding difficulties, eyelid ptosis, muscle weakness, choking seizures, apnea, cyanosis (hypoxia).

6 ORSÓS, ZS.: *Karcinogenezisben szerepet játszó allélpolimorfizmusok a magyarországi roma populációban. Ph.D. értekezés.* PTE ÁOK Pécs, 2013. <http://docplayer.hu/27785624-Karcinogenezisben-szerepet-jatszoo-allelpolimorfizmusok-a-magyarorszag-i-roma-populacioban.html> [2018.05.29.]

7 BÉRES, J.: Gyakoribb genetikai betegségek a romák körében I-II., in: *Magyar Orvos* (2002.) X/I. X/2.

8 PCG = Primary congenital glaucoma is present at birth. It is usually diagnosed at birth or shortly thereafter, and most cases are diagnosed during the first year of life.

9 CMS = Congenital myasthenic syndrome is a group of conditions characterized by muscle weakness (myasthenia) that worsens with physical exertion.

- *Spinal Muscular Atrophy*<sup>10</sup> (SMA) Spinal neurodegeneration. The second most common, severe autosomal recessive disease.
- *Limb-Girdle Muscular Dystrophy type 2C*.<sup>11</sup> (LGMD2C) It is an autosomal hereditary disease which develops during childhood or middle-age at the latest. It may lead to the complete paralysis of both limbs and the inability to walk within 20 years. Gypsies living in different countries have the same founder mutation!
- *Epidermolysis Bullosa* <sup>12</sup> (EB) Hereditary damage of the structural protein in the basal membrane zone. This disease occurs in changing forms and severity, and results in blistering. According to Spain's NRBD data, the Gypsy population is affected by it 14 times more than any other.
- *Medium chain acyl-CoA dehydrogenase deficiency*.<sup>13</sup> (MCAD) The lack of enzyme is caused by a mutation. It has a high rate of occurrence among Gypsies in Spain. The disease develops below the age of two with a mortality rate<sup>1</sup> of 60%. Every fourth child suffering from this disease dies before the age of 30 months, while 30% of the survivors will develop mental retardation. A study in Hungary concluded with 110 Gypsy children revealed high frequency for the mutation.
- *Hereditary hemochromatosis* <sup>14</sup> (HH). Autosomal recessive hereditary disease of iron metabolism. It is the most frequent monogenic disease in European populations. It is the genetic cause of liver cirrhosis.
- *Galactokinase Deficiency*<sup>15</sup> (GD). Carbohydrate metabolism disorder. Recessive heredity causes early cataracta in homozygotes, and pre-senilis cataracta in heterozygotes between the ages of 25-50. 90% of galactokinase defect occurs among Gypsy population.
- *Glanzmann thrombasthenia*<sup>16</sup> (GT). Typical symptom is increased hemophilia; bleeding time, platelet count and coagulation time are normal, but the adsorption and shape of blood clots is abnormal. Light phenotype and seasonal fluctuation is typical for Gypsy patients, with periodic severe bleeding during spring and summer. It is a common disease among Manush Gypsies in France.

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- 10 SMA = Spinal muscular atrophy is a genetic disease affecting the part of the nervous system that controls voluntary muscle movement.
  - 11 LGMD2C = Limb-girdle muscular dystrophy type 2C is a genetic condition that affects the voluntary muscles around the hips and shoulders
  - 12 EB = Epidermolysis bullosa is a group of genetic conditions that result in easy blistering of the skin and mucous membranes.
  - 13 MCAD = Medium-chain acyl-coenzyme A dehydrogenase deficiency is an inherited metabolic disorder that prevents the body from converting certain fats to energy, particularly during periods without food (fasting).
  - 14 HH = Hereditary hemochromatosis is an autosomal recessive disorder that results from a mutated hemochromatosis (HFE [human factors engineering]) protein.
  - 15 GD = Galactokinase deficiency is an inherited condition in which the body is unable to properly digest galactose, a sugar found in all foods that contain milk and some fruits and vegetables. If a baby with GD eats food containing galactose, undigested sugars build up in the blood.
  - 16 GT = Glanzmann thrombasthenia is a bleeding disorder that is characterized by prolonged or spontaneous bleeding starting from birth



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– *Autosomal Dominant Polycystic kidney disease*<sup>17</sup> (ADPKD). The most common is heredity kidney disease. It is caused by mutations in three different genes. It is almost endemic among Boyash Gypsies in Somogy and Baranya counties. Gene frequency is 2.4% which is 20 times of the rate measured in non-gypsy populations.

It was also shown by genetic studies that *sclerosis multiplex* cannot develop among Gypsies due to the special HLA system.<sup>18</sup>

Learning known and registered genetically defined diseases is crucial; targeted screenings, early diagnosis together with appropriate treatment could be an effective way to improve the unfavourable health condition of the Gypsy/Roma population.

17 ADPKD = Autosomal dominant polycystic kidney disease is an inherited condition that causes small, fluid-filled sacs called cysts to develop in the kidneys.

18 HLA system: Human leukocyte antigens. The HLA gene family provides instructions for making a group of related proteins known as the human leukocyte antigen (HLA) complex. The HLA complex helps the immune system distinguish the body's own proteins from proteins made by foreign invaders such as viruses and bacteria.