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The Impact of the Sociodemographic Structure of Deaf People Communities on the Prevalence of Hereditary Hearing Loss

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Abstract—Hearing loss caused by environmental or genetic factors concerns more than 10% of the world's population, leading to disability and considerable deterioration of the quality of life for deaf people. On the average, one in 1000 children is born deaf with 50–60% of the cases having a genetic cause. Nonsyndromic hereditary deafness is a monogenic disease with uniquely high genetic heterogeneity. The prevalence of some forms of genetic deafness varies in different regions of the world and is determined, as for many other monogenic diseases, by the ethnic composition, isolation, founder and bottleneck effects, rate of consanguineous marriages, and potential heterozygote selective advantage. It is assumed that some social factors (a long-standing tradition of assortative marriages between deaf people combined with an increase in their social adaptation and genetic fitness) have contributed to a high prevalence of hearing loss caused by mutations in the *GJB2* (C×26) gene. The breach of deep social isolation of the deaf some 300 years ago in Europe (and later in the United States) with the establishment of schools for the deaf teaching sign language as a common communication tool (linguistic homogamy) triggered these events. Computer simulation and comparative retrospective studies have shown that these social processes could have doubled the rate of *GJB2* deafness in the United States over two centuries. The information about the sociodemographic structure of deaf communities in the past is extremely limited by the almost complete lack of the relevant archival data. Nevertheless, studies of the sociodemographic and medical genetic characteristics of deaf communities are now important for both predicting the prevalence of various hereditary deafness forms and understanding the impact of social factors on evolutionary processes in human populations.

Keywords: hereditary deafness, social processes, assortative marriages, *GJB2* (C×26) gene mutations, agent-based modeling

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The hearing loss determined by either environmental or genetic causes concerns a considerable part of the population, leads to disability and a significant deterioration of the quality of life. The rate of genetic deafness is at least one per 1500–2000 births (Marazita et al., 1993; Morton and Nance, 2006), exceeding the rates of the monogenic diseases included in the programs for mass neonatal screening (phenylketonuria, approximately one per 10000 newborns; congenital hypothyroidism, one per 4000–5000; galactosemia, one per 15000–20000; cystic fibrosis, one per 3000–6000; and adrenogenital syndrome, approximately one per 5000–15000 newborns), which makes this pathology a serious social problem.

The research into genetically determined forms of hearing loss mainly focuses on (1) the diversity of the genetic control of hearing impairments; (2) prevalence of hereditary hearing loss forms in different regions of the world; and (3) factors that determine the accumulation of particular forms of hearing pathologies.

DIVERSITY OF THE GENETIC CONTROL OF HEREDITARY HEARING LOSS FORMS AND THEIR PREVALENCE IN DIFFERENT REGIONS OF THE WORLD

Clinical diversity and unique genetic heterogeneity are characteristic features of hereditary hearing loss. At least 300–400 syndromes are known with a hearing impairment/loss as its clinical symptom (Toriello and Smith, 2013); however, nonsyndromic (isolated) sensorineural hearing loss is the prevalent form (~70%).

Most cases of nonsyndromic hearing loss (75–80%) are inherited in an autosomal recessive manner; 15–20% cases, in an autosomal dominant manner; and 3–5% cases are either linked to the X chromosome or determined by mtDNA mutations (Morton and Nance, 2006). About 140 genetic loci are currently known to be associated with nonsyndromic hearing loss and several tens of genes encoding various proteins that are diverse in their structure and function (ion transport, extracellular matrix, and cytoskeletal proteins; various structural proteins; components of cell membranes; adhesive proteins; transcription factors; and other proteins with unknown functions) have been identified (Van Camp and Smith, 2015). In addition, mtDNA mutations associated with hearing impairments have been detected in the mitochondrial genome; they mainly affect the genes that control the mitochondrial protein-synthesizing machinery, tRNA and rRNA (MITOMAP: http://www.mitomap.org). The data on mapping the loci and identification of the genes responsible for hearing loss have been accumulated at the Hereditary Hearing loss Homepage (http://hereditaryhearingloss.org), currently the most complete database in the world on the genetic control of hearing impairments (Van Camp and Smith, 2015).

Despite the wide diversity in the genetic control of hearing impairments, it is known that the most prominent pathogenetic contributor to the development of nonsyndromic hearing loss in many populations of the world is the *GJB2* gene (13q11–q12, MIM 121011). In particular, mutations in the *GJB2* gene account for ~30–50% of the hearing loss cases in most European countries (Morton and Nance, 2006) and for ~5–20% in Asian populations (Park et al., 2000; Liu et al., 2002; Ohtsuka et al., 2003; RamShankar et al., 2003; Wattanasirichaigoon et al., 2004; Dai et al., 2009; Tekin et al., 2010). *GJB2* encodes connexin 26 (Cx26), a gap junction protein; its expression has been observed in the inner ear's tissues and skin, as well as in some other tissues. Connexin 26 molecules form intercellular channels for ion exchange in the inner ear's tissues that are necessary for normal sound perception. Mutations in gene *GJB2* damage the connexin 26 structure and function eventually impairing sound perception and causing irreversible hearing loss. Currently, over 300 mutations, polymorphisms, and unclassified variations of this gene sequence are known (Stenson et al., 2014; Van Camp and Smith, 2015). The ethnic and regional specificities of the *GJB2* mutation rates, as well as the prevalence of private mutations in different populations of the world, have been clarified. Several major recessive mutations in this gene prevalent in individual populations have been identified. For example, the c.35delG mutation is widespread in Europe (Gasparini et al., 2000; Rabionet et al., 2000); mutation c.235delC, in several Asian countries (Park et al., 2000; Liu et al., 2002; Ohtsuka et al., 2003; Dai et al., 2009); c.167delT is characteristic for Ashkenazi Jews (Morell et al., 1998; Lerer et al., 2000); p.Arg143Trp, for several Western African populations (Brobby et al., 1998; Hamelmann et al., 2001); p.Val37Ile is prevalent in Southeast Asia (Wattanasirichaigoon et al., 2004); p.Trp24*, in India (RamShankar et al., 2003); c.–23+1G>A, among the Yakut (Barashkov et al., 2011; Pshennikova et al., 2015); and the p.Trp172Cys mutation is observed at a high rate among the Tuvinians (Bady-Khoo et al., 2014a).

Since *GJB2* gene mutations are the most important cause of hereditary deafness, the molecular diagnostics of hearing loss cases based on the search for mutations in this gene have been elaborated in many countries.

Genetic and epidemiological studies in Russia have succeeded in detecting ethnic and regional distinctions in the prevalence of hereditary hearing loss cases (Puzyrev et al., 1999; Zinchenko et al., 2003, 2007, 2009a, 2009b, 2012a, 2012b; Tarskaya et al., 2004; Shokarev et al., 2005; Bady-Khoo et al., 2014b; Pshennikova et al., 2015).

Until recently, the molecular diagnostics of hearing loss in Russia was limited to screening of a single *GJB2* mutation, c.35delG (Markova et al., 2002, 2008; Nekrasova et al., 2002; Khidiyatova et al., 2002; Zinchenko et al., 2003; Shokarev et al., 2005; Zhuravskii et al., 2009; Sharonova et al., 2009), which is the major cause of hearing loss in European countries. This approach could hardly be an adequate diagnostic methodology taking into account the specific ethnic and geographic features of the *GJB2* mutation spectrum among the multinational population of Russia. The recent advent of DNA sequencing in molecular diagnostics has allowed the detection of a wider range of *GJB2* mutations. As has been shown, the share of hearing loss cases determined by *GJB2* mutations in several Russian populations may reach 40–50% depending on particular region (Posukh et al., 2005; Osetrova et al., 2010; Bozhkova et al., 2011; Bliznets et al., 2012; Bady-Khoo et al., 2014a; Pshennikova et al., 2015).

Mutations in the *SLC26A4* gene (pendrin, 7q22–q31, MIM 605646) are likely to be the second most prevalent in the list of genetic deafness causes, at least in Asian populations, accounting for up to 10% of all genetic hearing loss cases (Park et al., 2003; Tsukamoto et al., 2003; Lee et al., 2008; Du et al., 2013).

The information about the prevalence of genetic deafness caused by mutations in other genes is rather scarce. Consecutive Sanger sequencing of the overall totality of genes controlling hearing impairments is still unfeasible; only a few laboratories can perform molecular diagnostics of the several other genes associated with hearing loss (*SLC26A4*, *MYO15*, *TMC1*, *CDH23*, and *OTOF*) besides *GJB2*. The etiology of hereditary hearing loss still remains unsolved in many cases after testing the most significant deafness genes. Nonetheless, the next generation sequencing technologies, including whole exome sequencing (Brownstein et al., 2011; Diaz-Horta et al., 2012; Sirmaci et al.,

2012; etc.) have been recently used to solve the "many genes–one phenotype" problem. Thus, new data on the genes associated with hearing loss and specific features in the prevalence of various hereditary deafness forms in different regions of the world are expected.

It has been already clarified for some hereditary hearing loss forms that, similar to many other monogenic diseases, their accumulation in a particular population is determined by several factors, such as the ethnic composition, isolation, rate of consanguineous marriages, as well as the founder and bottleneck effects (Groce, 1985; Scott et al., 1995; Winata et al., 1995; Van Laer et al., 2001; RamShankar et al., 2003; Ben Arab et al., 2004; Lezirovitz et al., 2008; Sirmaci et al., 2009; Barashkov et al., 2011; etc.).

However, it is postulated that unlike most hereditary monogenic diseases, certain social factors, namely, a long-standing tradition of assortative marriages between deaf people (choice of the mating parther according to pathological phenotype) combined with an increase in their social adaptation and genetic fitness, have also contributed to a high prevalence of *GJB2* deafness (Nance et al., 2000; Nance, 2003; Nance and Kearsey, 2004).

SOCIAL FACTORS IN THE PREVALENCE OF GENETIC DEAFNESS

In the past, hearing loss, interfering with the perception of warning and alarming information, orientation, and social communication, drastically decreased the fitness of a deaf individual; correspondingly, the share of genetic deafness was comparatively small.

Currently, the trend of a steady increase in genetic deafness determined by the *GJB2* (C×26) gene is observed in several European countries and the United States (Morton and Nance, 2006). Computer simulation has shown that the number of individuals with deafness caused by recessive mutations in this gene could have doubled over two centuries if the rate of assortative matings between the deaf had increased from 0 to 0.9 and their genetic fitness had increased from 0 to 1 (Nance and Kearsey, 2004). It is assumed that the establishment of schools for the deaf some 300 years ago in several European countries (somewhat later in the United States) (Bender, 1981) triggered these processes, as well as the further active development of the sign language, a universal tool for communication of the deaf (Nance and Kearsey, 2004).

General information. Sign language (also signed language) is an independent language that emerged naturally or was elaborated artificially, which simultaneously combines hand shapes, orientation, and movement of the hands, arms, or body and facial expressions. Sign language is not international: at least 121 sign languages are recognized in the world (*Ethnologue*..., 2015). The first educational centers for children with hearing impairments were established in France (1760) and Germany (1778). The background for the taught sign languages was natural sign languages that developed in national deaf communities. This allowed elaborating the sign variants of the French and German languages supplemented with special methodical signs for prepositions, grammatical genders, etc. The French and German sign languages formed the background for many other national sign languages. For example, the American Sign Language (ASL) was developed based on the French school. Note that the national sign languages now have their own structure and history and are almost independent of the corresponding spoken languages. The first special school for deaf children in Russia was opened in 1806 in Pavlovsk and, similar to those in the United States, used the French methodology. Later (1860), the special school for the deaf utilizing the German methodology was opened in Moscow. The modern Russian sign language was formed based on these two schools and was centrally disseminated in the former Soviet republics by organizing schools and institutions for the deaf. This explains the prevalence of a common sign language on the territory of the former Soviet Union (Prozorov, 2007).

THE DEAF COMMUNITIES—DEAF CULTURE

The common linguistic space (sign language) enhanced the improvement of living conditions and consolidation of the deaf people. In European countries and the United States, this brought about special micro communities, the Deaf Culture, with their own sign language, traditions, and culture (Padden and Humphries, 1988; Andersson, 1991; Arnos et al., 1991; Christiansen, 1991; Ruben, 1991; Prezioso, 1995; Stern et al., 2002; etc.). Deafness in these communities is considered in a sociocultural aspect rather than as a disability. In particular, the self-determination of the deaf people affiliating themselves with the Deaf Culture appears in writing the word *Deaf* with an uppercase letter (Arnos et al., 1991). Among the important sociodemographic characteristics of these micro communities are a high rate of assortative marriages between deaf partners, which is based on the linguistic homogamy (use of sign language) and the positive attitude of deaf couples to the birth of deaf children (Middleton et al., 1998, 2001; Stern et al., 2002).

For example, a structured, self-completion questionnaire was given to delegates at an international conference on the "Deaf Nation" in the United Kingdom. The questionnaire had been designed to assess attitudes towards genetic testing, interest in prenatal diagnostics for deafness, and preference for having deaf or hearing children (Middleton et al., 1998). According to this questionnaire, 55% of the respondents believed that genetic testing would do more harm than good and 46% thought that its potential use devalued deaf people. In addition, 60% of the respondents would refuse to pass prenatal DNA diagnostics;

16% were not sure; 8% did not answer, and only 16% would agree to pass such testing. As for the preferred hearing status of their child, 15% of the respondents said that they would prefer to have deaf children; 74% were not sure; 5% did not want to answer this question; and only 6% would like to have a hearing child. In a later study (Middleton et al., 2001), three cohorts of respondents—(1) deaf, (2) hard of hearing or late deafened, and (3) hearing individuals with either a deaf parent or deaf child —were questioned for their attitude to prenatal diagnostics for inherited deafness and termination of pregnancy due to hearing status of fetus. The results were that 21, 39, and 49% of the listed cohorts, respectively, would consider the prenatal DNA test for deafness. However, only 6% of the deaf respondents, 11% of the hard of hearing or late deafened individuals, and 16% of the hearing respondents would consider terminating a pregnancy if the future child was found to be deaf. Of the deaf persons, 2% preferred to have deaf children and would terminate pregnancy if the fetus was found to be hearing (Middleton et al., 2001).

The All-Russia Society of the Deaf (http://www.voginfo.ru/) was founded in the Russian Soviet Federative Socialist Republic (Soviet Union) in 1926, currently comprises about 90000 persons with hearing impairments, and has 79 regional and over 800 local offices over the territory of the Russian Federation. The main goals of the All-Russia Society of the Deaf are to protect the rights and interests of people with hearing impairments, their social rehabilitation, integration in the community, and equalization of opportunities.

As far as we know, the research focused on integrated sociodemographic characterization of deaf communities and the role of local and regional offices of the All-Russia Society of the Deaf in the consolidation of people with hearing loss have never been performed in Russia.

ASSORTATIVE MARRIAGES AND MARRIAGE RATE OF THE DEAF

The distinct trend of an increase in the rate of assortative marriages between deaf people observed in many regions of Europe and the United States is most likely determined by better social adaptation and consolidation of the deaf using sign language (Schein and Delk, 1974; Rose, 1975; Arnos et al., 2008; Blanton et al., 2010)

One of the relatively few integrated studies of the sociodemographic characteristics of deaf communities in Europe by Carlsson et al. (2004/2005) has analyzed and compared the two largest deaf communities in Sweden, living in Närke and Värmland counties. These counties, similar in the main demographic characteristics (total population and the number of adults), differ in the degree of development of their deaf communities. The association of the deaf in the former county comprises 450 members and 82% of them live in a large city, Örebro. As for the community of Värmland, it has about 100 members and only 33% of them live in the city of Karlstad, whereas the remaining persons are dispersed over the county. Both the preschool facilities and higher school education are available for the deaf children in Närke, which has the largest number of deaf university students in Sweden. The opportunities for the deaf children in Värmland are limited to preschool education. Thus, Närke has a well-developed social infrastructure for the deaf, and their consolidation is considerably higher compared to Värmland. The degrees of assortative matings in these two counties are in contrast to each other despite the almost equal marriage rates of the deaf (37.1% of deaf people were married in Närke and 35.1% in Värmland): 99% of the deaf had a deaf mate in Närke and only 10% of such marriages were recorded in Värmland (Carlsson et al., 2004/2005).

Blanton et al. (2010) have analyzed the data on the alumni from Gallaudet University, the oldest university for education of the deaf in the United States, and report a high marriage rate of deaf people (0.88), which is similar to the rate observed for their hearing siblings (0.89), while the share of deaf-to-deaf marriages (assortative marriages) was 79% (Blanton et al., 2010). The 1970 National Census of the Deaf Population in the United States recorded an 80–90% level of assortative marriages among the deaf, which matches the data from other sources (Rapin, 1978; Schein, 1978). Thus, a certain increase in this characteristic is observed relative to the beginning of the 19th century (75%) (Schein and Delk, 1974; Rose, 1975).

A significantly lower rate of assortative marriages between the deaf has been observed in a few studies covering other regions of the world (Chaabani et al., 1995; Tekin and Arici, 2007, Tekin et al., 2010). For example, the rate of assortative marriages between deaf people in Tunisia is about 10–30% (Chaabani et al., 1995); in Turkey, 46.8% (Tekin and Arici, 2007); and in Mongolia, 37.5% (Tekin et al., 2010).

The rate of the *GJB2* (Cx26) genetic deafness, which is correlated to the rate of assortative marriages of the deaf in Europe and the United States, may reach 40–50% (Nance, 2003; Morton and Nance, 2006). The contribution of *GJB2* mutations to the etiology of hearing loss in some Asian regions is considerably smaller. For example, it does not exceed 5% in Mongolia, which, according to Tekin et al. (2010), is determined by the lower levels of consolidation and assortative marriages there (37.5%), where teaching of sign language commenced relatively recently. Indeed, the first school for deaf children was opened in Ulan Bator at the beginning of the 20th century but the sign language remained rather primitive until 1995, when volunteers of the American Peace Corps developed a structured sign language corresponding to Mongolian

language (Tekin et al., 2010). Some indirect evidence for the traditional absence of deaf-to-deaf marriages in China were obtained by the segregation analysis of familial deafness in Shanghai: both parents were deaf in only eight of 260 parental pairs of the examined deaf probands (Hu et al., 1987).

REPRODUCTION OF THE DEAF

The parameters of reproduction are an important measure for assessing the genetic fitness of both the general population and groups of individuals with genetic diseases. Several research teams have attempted to compare the parameters of reproduction of the deaf people (average number of children) with the corresponding characteristics of the general population or their healthy siblings (Schein and Delk, 1974; Hu et al., 1987; Liu et al., 1994; Carlsson et al., 2004/2005; Blanton et al., 2010; Tekin et al., 2010). In particular, Blanton et al. (2010) have shown that the average number of children in the married alumni from Gallaudet University was statistically significant smaller as compared with corresponding parameter in their siblings (2.06 and 2.26, respectively). However, as for the mating types of the deaf, the average number of children was higher in the deaf-to-deaf couples (2.11) as compared with the marriages between a deaf and hearing mate (1.85). Nonetheless, the general genetic fitness of the deaf people independently of their marital status and taking into account childless individuals was reduced (0.88) (Blanton et al., 2010). Analyzing the data of the 1970 National Census of the Deaf Population in the United States, Schein and Delk (1974) demonstrated that the genetic fitness of women varied from 0.31 to 0.77 (depending on the age cohort) as compared with the general population of the United States (Schein and Delk, 1974). Analysis of the reproduction parameters of the deaf in two Sweden counties showed a lower average number of children per woman (1.16 in Värmland and 1.33 in Närke) as compared with the data for the general population of these counties (1.63–1.65). Note that the difference between these counties was most likely determined by a statistically significant prevalence of childless deaf women in Värmland as compared with Närke (43.7 versus 38.5%) taking into account the population's share of childless women, amounting to 18.8 and 19.7 in Värmland and Närke, respectively (Carlsson et al., 2004/2005). A considerable decrease in the genetic fitness of the deaf as compared with their normal siblings (0.6 and 0.78) has also been demonstrated by two studies in China (Hu et al., 1987; Liu et al., 1994). As for Mongolia, the relative genetic fitness of the deaf (independently of their marital status and taking into account childless individuals) was 0.62 at a statistically significantly decreased average number of children in the married deaf (2.7) relative to their hearing siblings (3.6) (Tekin et al., 2010).

Thus, the different approaches used in a few studies of the parameters of reproduction of the deaf people have shown that their genetic fitness expressed as the average number of children varies, similar to other human cohorts, depending on the geographical localization, as well as sociocultural and ethnic environments, but still remains lower than for hearing individuals.

NONCOMPLEMENTARY MARRIAGES

The probability to bear a deaf child varies in different variants of marital pairs with genetic and nongenetic causes of deafness. Parents whose deafness is determined by recessive mutations of the same gene (noncomplementary marriages) can give birth only to children with hearing loss caused by the same genetic defect. Consequently, such marriages can considerably increase the rate of a recessive mutation causing deafness in the subsequent generations.

Arnos et al. (2008) have analyzed the marital structure of the deaf based on the monumental treatise titled *Marriages of the Deaf in America* (Fay, 1898), a unique collection of pedigrees of the deaf over 1801–1894, and the corresponding data for the 20th century, involving the data on the alumni from Gallaudet University and demonstrated a statistically significant increase in the number of noncomplementary marriages over the past 100 years (4.2% and 23.0%, respectively) (Arnos et al., 2008). In addition, the comparative analysis of the mutation rates for the *GJB2* (C×26) gene in the patients of three age cohorts (born in 1921–1940, 1941–1960, and 1961–1980) demonstrated a statistically significant increase in the rate of *GJB2* mutations over this comparatively short time span (60 years) (Arnos et al., 2008).

COMPUTER SIMULATION OF THE IMPACT OF SOCIAL FACTORS ON THE PREVALENCE OF HEREDITARY HEARING LOSS FORMS

Mathematical and computer simulations are widely used when studying epidemic (Sattenspiel and Dietz, 1995; Hethcote, 2006; Mossong et al., 2008) and nonepidemic (Di Rienzo and Hudson, 2005; Peng et al., 2007; Hoban et al., 2012) diseases in order to analyze and predict their prevalence in populations. Agent-based simulation is currently among the most popular approaches for the construction of computer models in biology, including the simulation of various diseases. Such approaches make it possible to construct composite hierarchical (multiscale) models, now regarded as one of the major tools in systems biology (Ayton et al., 2007; Ferrer, 2007; Ferrer et al., 2008; Martins et al., 2010; Twycross et al., 2010; Qu et al., 2011). The agent-based simulation allowed it to be demonstrated for the first time that the significant growth in the share of the genetic deafness caused by GJB2 (Cx26) gene mutations can be determined by the long-term tradition of the assortative matings of

the deaf people and their increased genetic fitness (Nance and Kearsey, 2004).

Along with the known factors influencing the rate of many monogenic genetic diseases (ethnic composition of the population, isolation, founder and bottleneck effects, and the rate of consanguineous marriages), it is assumed that certain social factors—a long-term tradition of assortative marriages between the deaf people combined with an increase in their social adaptation and genetic fitness—have also significantly contributed to the prevalence of genetic hearing loss, at least its most frequent form caused by the *GJB2* (C×26) gene mutations.

Deaf communities are present in many countries of the world; however, their structure and degree of consolidation in individual populations are different. The attitude of society towards the deaf also varies in a wide range from recognizing the Deaf Culture as a special sociocultural community and the sign language as an official language to pronounced social discrimination of people with lost or impaired hearing. The sociodemographic characteristics (the rate of marriages, marital structure, reproduction, communicative opportunities, quality of life, social status of the deaf, and degree of isolation/inner consolidation) of deaf communities are actively studied in European countries and the United States. Such studies involving the contemporary data are very rare in other regions of the world and the retrospective analysis of the corresponding information is confined to a few studies in the past. No such studies have been conducted in Russia.

Assessment of the potential role of the sociodemographic structure of the currently existing communities of the deaf people in combination with molecular genetic studies of the hereditary hearing loss and computer simulation of potential cause–effect relationships between the sociodemographic parameters of these communities and rates of certain genetic deafness forms is of both basic and applied importance. These data will significantly clarify the role of social factors in evolutionary processes taking place in human populations and can be useful for the long-term prediction of the prevalence of hereditary hearing loss in the regions of interest.

Our research team is involved in obtaining the structured data on the level of mating, specific features in the marital structure, and parameters of reproduction of the people with severe hearing impairments in several Siberian regions (Tuva, Altai, and Yakutia) to compare these data with the distribution of *GJB2* genotypes in deaf individuals revealed by epidemiological and molecular genetic studies (Posukh et al., 2005; Barashkov et al., 2011; Bady-Khoo et al., 2014a, 2014b; Pshennikova et al., 2015). We believe that this integrated approach will give a unique opportunity to estimate, for the first time, the potential impact of sociodemographic factors reflecting the current state of the communities of the deaf people in various Siberian regions on the specificity of the genetic component and its contribution to the etiology of hearing loss. An agent-based simulation utilizing the totality of the obtained sociodemographic, molecular genetic, and population genetic data will make it possible to clarify the potential trends in the prevalence of hereditary hearing loss in the examined regions of Siberia.

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CONFLICT OF INTEREST

The authors state that they have no conflict of interest.

REFERENCES

Andersson, Y., Sociological implications of genetic deafness, *Am. J. Hum. Genet. Suppl.*, 1991, vol. 49, p. 5.

Arnos, K.S., Israel, J., and Cunningham, M., Genetic counselling for the deaf: Medical and cultural considerations, *Ann. N. Y. Acad. Sci.*, 1991, vol. 630, pp. 212–222. doi 10.1111/j.1749-6632.1991.tb19590.x

Arnos, K.S., Welch, K.O., Tekin, M., Norris, V.W., Blanton, S.H., Pandya, A., and Nance, W.E., A comparative analysis of the genetic epidemiology of deafness in the United States in two sets of pedigrees collected more than a century apart, *Am. J. Hum. Genet.*, 2008, vol. 83, no. 2, pp. 200–207. doi 10.1016/j.ajhg.2008.07.001

Ayton, G.S., Noid, W.G., and Voth, G.A., Multiscale modeling of biomolecular systems: In serial and in parallel, *Curr. Opin. Structr. Biol.*, 2007, vol. 17, no. 2, pp. 192–198. doi 10.1016/j.sbi.2007.03.004

Bady-Khoo, M.S., Bondar', A.A., Morozov, I.V., Zytsar', M.V., Mikhal'skaya, V.Yu., Skidanova, O.V., Barashkov, N.A., Mongush, R.Sh., Omzar, O.S., Tukar, V.M., and Posukh, O.L., The study of inherited forms of hearing loss/deafness in the Republic of Tyva. Part II. Assessment of the spectrum of *GJB2* (Cx26) gene mutations and their contribution to the etiology of hearing loss, *Med. Genet.*, 2014a, vol. 13, no. 11, pp. 30–40.

Bady-Khoo, M.S., Posukh, O.L., Zorkol'tseva, I.V., Skidanova, O.V., Barashkov, N.A., Omzar, O.S., Mongush, R.Sh., Bamba, O.M., Tukar, V.M., Zytsar', M.V., and Mikhal'skaya, V.Yu., The study of inherited forms of hearing loss/deafness in the Republic of Tyva. Part I. Epidemiology of hearing impairment in the Republic of Tyva, *Med. Genet.*, 2014b, vol. 13, no. 1, pp. 17–26.

Barashkov, N.A., Dzhemileva, L.U., Fedorova, S.A., Teryutin, F.M., Posukh, O.L., Fedotova, E.E., Lobov, S.L.,

and Khusnutdinova, E.K., Autosomal recessive deafness 1a (DFNB1A) in Yakut population isolate in Eastern Siberia: Extensive accumulation of the splice site mutation IVS1+1G>A in *GJB2* gene as a result of founder effect, *J. Hum. Genet.*, 2011, vol. 56, pp. 631–639. doi 10.1038/jhg.2011.72

Ben Arab, S., Masmoudi, S., Beltaief, N., Hachicha, S., and Ayadi, H., Consanguinity and endogamy in Northern Tunisia and its impact on non-syndromic deafness, *Genet. Epidemiol.*, 2004, vol. 27, pp. 74–79. doi 10.1002/gepi.10321

Bender, R., *The Conquest of Deafness: A History of the Long Struggle to Make Possible Normal Living to Those Handicapped by Lack of Normal Hearing*, Danville, Ill., Ed., Interstate Printers & Publishers, 1981, 3rd ed.

Blanton, S.H., Nance, W.E., Norris, V.W., Welch, K.O., Burt, A., Pandya, A., and Arnos, K.S., Fitness among individuals with early childhood deafness: Studies in alumni families from gallaudet university, *Ann. Hum. Genet.*, 2010, vol. 74, no. 1, pp. 27–33. doi 10.1111/j.1469-1809.2009.00553.x

Bliznetz, E.A., Galkina, V.A., Matyushchenko, G.N., Kisina, A.G., Markova, T.G., and Polyakov, A.V., Changes in the connexin 26 gene (*GJB2*) in Russian patients with hearing loss: Results of long-term molecular diagnostics of hereditary nonsyndromic hearing loss, *Russ. J. Genet.*, 2012, vol. 48, no. 1, pp. 101–112.

Bozhkova, V.P., Khashaev, Z.Kh., and Magomedov, Sh.M., The study of hereditary hearing impairment in children of the North Caucasus, *Fundam. Issled.*, 2011, vol. 5, pp. 23–27.

Brobby, G.W., Müller-Muhsok, B., and Horstmann, R.D., Connexin 26 R143W mutation associated with recessive nonsyndromic sensorineural deafness in Africa, *N. Engl. J. Med.*, 1998, vol. 19, no. 338, pp. 548–550. doi 10.1056/NEJM199802193380813

Brownstein, Z., Friedman, L.M., Shahin, H., Oron-Karni, V., Kol, N., Abu Rayyan, A., Parzefall, T., Lev, D., Shalev, S., Frydman, M., Davidov, B., Shohat, M., Rahile, M., Lieberman, S., Levy-Lahad, E., et al., Targeted genomic capture and massively parallel sequencing to identify genes for hereditary hearing loss in middle eastern families, *Genome Biol.*, 2011, vol. 12, no. 9, p. R89. doi 10.1186/gb-2011-12-9-r89

Carlsson, P.I., Danermark, B., and Borg, E., Marital status and birthrate of deaf people in two Swedish counties: The impact of social environment in terms of deaf community, *Am. Ann. Deaf*, 2004–2005, vol. 149, no. 5, pp. 415–420.

Chaabani, H., Ben Arab, S., and Chebbi, K., Genetic heterogeneity study of non-syndromic autosomal recessive sensorineural deafness within the Tunisian population, *Ann. Genet.*, 1995, vol. 38, pp. 158–161.

Christiansen, J.B., Sociological implications of hearing loss, *Ann. N. Y. Acad. Sci.*, 1991, vol. 630, pp. 230–235. doi 10.1111/j.1749-6632.1991.tb19592.x

Dai, P., Yu, F., Han, B., Liu, X., Wang, G., Li, Q., Yuan, Y., Liu, X., Huang, D., Kang, D., Zhang, X., Yuan, H., Yao, K., Hao, J., He, J., et al., GJB2 mutation spectrum in 2063 Chinese patients with nonsyndromic hearing impairment, *J. Transl. Med.*, 2009, vol. 7, p. 26. doi 10.1186/1479-5876-7-26

Diaz-Horta, O., Duman, D., Foster, J., Sırmacı, A., Gonzalez, M., Mahdieh, N., Fotouhi, N., Bonyadi, M., Cengiz, F.B., Menendez, I., Ulloa, R.H., Edwards, Y.J., Züchner, S., Blanton, S., and Tekin, M., Whole-exome sequencing efficiently detects rare mutations in autosomal recessive nonsyndromic hearing loss, *PLoS One*, 2012, vol. 7, no. 11. doi 10.1371/journal.pone.0050628

Di Rienzo, A. and Hudson, R.R., An evolutionary framework for common diseases: The ancestral-susceptibility model, *Trends Genet.*, 2005, vol. 21, no. 11, pp. 596–601. doi 10.1016/j.tig.2005.08.007

Du, W., Guo, Y., Wang, C., Wang, Y., and Liu, X., A systematic review and meta-analysis of common mutations of *SLC26A4* gene in Asian populations, *Int. J. Pediatr. Otorhinolaryngol.*, 2013, vol. 77, no. 10, pp. 1670–1676. doi 10.1016/j.ijporl.2013.07.023

Ethnologue: Languages of the World, Lewis, M.P., Simons, G.F., and Fennig, C.D., Dallas, Texas: SIL International, 2015, 18th ed. http://www.ethnologue.com.

Fay, E.A., *Marriages of the Deaf in America*, Washington, DC: Volta Bureau, 1898.

Ferrer, P., Systems biology and biological systems diversity for the engineering of microbial cell factories, *Microb. Cell Fact.*, 2007, vol. 6, p. 35. doi 10.1186/1475-2859-6-35

Ferrer, J., Prats, C., and Löpez, D., Individual-based modelling: An essential tool for microbiology, *J. Biol. Phys.*, 2008, vol. 34, nos. 1–2, pp. 19–37. doi 10.1007/s10867-008-9082-3

Gasparini, P., Rabionet, R., Barbujani, G., Melçhionda, S., Petersen, M., Brøndum-Nielsen, K., Metspalu, A., Oitmaa, E., Pisano, M., Fortina, P., Zelante, L., and Estivill, X., High carrier frequency of the 35delG deafness mutation in European populations. Genetic analysis consortium of *GJB2* 35delG, *Eur. J. Hum. Genet.*, 2000, vol. 8, pp. 19–23.

Groce, N.E., *Everyone Here Spoke Sign Language: Hereditary Deafness on Martha's Vineyard*, Cambridge, Massachusetts: Harvard Univ. Press, 1985.

Hamelmann, C., Amedofu, G.K., Albrecht, K., Muntau, B., Gelhaus, A., Brobby, G.W., and Horstmann, R.D., Pattern of connexin 26 (*GJB2*) mutations causing sensorineural hearing impairment in Ghana, *Hum. Mutat.*, 2001, vol. 18, pp. 84–85. doi 10.1002/humu.1155

Hethcote, H.W., The mathematics of infectious diseases, *SIAM Rev.*, 2006, vol. 42, no. 4, pp. 599–653. doi 10.1137/S0036144500371907

Hoban, S., Bertorelle, G., and Gaggiotti, O.E., Computer simulations: Tools for population and evolutionary genetics, *Nat. Rev. Genet*, 2012, vol. 13, no. 2, pp. 110–122. doi 10.1038/nrg3130

Hu, D.N., Qiu, W.Q., Wu, B.T., Fang, L.Z., Zhou, F., Gu, Y.P., Zhang, Q.H., and Yan, J.H., Prevalence and genetic aspects of deaf mutism in Shanghai, *J. Med. Genet.*, 1987, vol. 24, pp. 589–592.

Khidiyatova, I.M., Dzhemileva, L.U., Khabibullin, R.M., and Khusnutdinova, E.K., Frequency of the 35delG mutation of the connexin 26 gene (*GJB2*) in patients with nonsyndromic recessive deafness from Bashkortostan and in ethnic groups of the Volga–Ural region, *Mol. Biol.* (Moscow), 2002, vol. 36, no. 3, pp. 338–341.

Lee, K.Y., Choi, S.Y., Bae, J.W., Kim, S., Chung, K.W., Drayna, D., Kim, U.K., and Lee, S.H., Molecular analysis of the *GJB2*, *GJB6*, and *SLC26A4* genes in Korean deafness

patients, *Int. J. Pediatr. Otorhinolaryngol.*, 2008, vol. 72, no. 9, pp. 1301–1309. doi 10.1016/j.ijporl.2008.05.007

Lerer, I., Sagi, M., Malamud, E., Levi, H., Raas-Rothschild, A., and Abeliovich, D., Contribution of connexin 26 mutations to nonsyndromic deafness in ashkenazi patients and the variable phenotypic effect of the mutation 167delT, *Am. J. Med. Genet.*, 2000, vol. 95, no. 1, pp. 53–56. doi 10.1002/1096-8628(20001106)95:13.0.CO;2-2

Lezirovitz, K., Pardono, E., de Mello Auricchio, M.T., de Carvalho, E., Silva, F.L., Lopes, J.J., Abreu-Silva, R.S., Romanos, J., Batissoco, A.C., and Mingroni-Netto, R.C., Unexpected genetic heterogeneity in a large consanguineous Brazilian pedigree presenting deafness, *Eur. J. Hum. Genet.*, 2008, vol. 16, no. 1, pp. 89–96. doi 10.1038/sj.ejhg.5201917

Liu, X., Xu, L., Zhang, S., and Xu, Y., Epidemiological and genetic studies of congenital profound deafness in the general population of Sichuan, China, *Am. J. Med. Genet.*, 1994, vol. 53, no. 2, pp. 192–195.

Liu, X.Z., Xia, X.J., Ke, X.M., Ouyang, X.M., Du, L.L., Liu, Y.H., Angeli, S., Telischi, F.F., Nance, W.E., Balkany, T., and Xu, L.R., The prevalence of connexin 26 (*GJB2*) mutations in the Chinese population, *Hum. Genet.*, 2002, vol. 111, pp. 394–397. doi 10.1007/s00439-002-0811-6

Marazita, M.L., Ploughman, L.M., Rawlings, B., Remington, E., Arnos, K.S., and Nance, W.E., Genetic epidemiological studies of early-onset deafness in the U.S. school-age population, *Am. J. Med. Genet.*, 1993, vol. 46, pp. 486–491.

Markova, T.G., Megrelishvilli, S.M., Zaitseva, N.G., Shagina, I.A., and Polyakov, A.V., DNA diagnostics of congenital and neonatal hearing loss/deafness, *Vestn. Otorinolaringol.*, 2002, vol. 6, pp. 12–15.

Markova, T.G., Polyakov, A.V., and Kunel'skaya, N.L., Clinic of hearing loss due to changes in connexin 26 gene, *Vestn. Otorinolaringol.*, 2008, vol. 2, pp. 4–9.

Martins, M.L., Ferreira, S.C., and Vilela, M.J., Multiscale models for biological systems, *Curr. Opin. Colloid Interface Sci.*, 2010, vol. 15, nos. 1–2, pp. 18–23.

Middleton, A., Hewison, J., and Mueller, R.F., Attitudes of deaf adults toward genetic testing for hereditary deafness, *Am. J. Hum. Genet.*, 1998, vol. 63, pp. 1175–1180.

Middleton, A., Hewison, J., and Mueller, R., Prenatal diagnosis for inherited deafness – What is the potential demand?, *J. Genet. Couns.*, 2001, vol. 10, pp. 121–131. doi 10.1086/302060

Morell, R.J., Kim, H.J., Hood, L.J., Goforth, L., Friderici, K., Fisher, R., Van Camp, G., Berlin, C.I., Oddoux, C., Ostrer, H., Keats, B., and Friedman, T.B., Mutations in the connexin 26 gene (*GJB2*) among Ashkenazi Jews with nonsyndromic recessive deafness, *N. Engl. J. Med.*, 1998, vol. 339, pp. 1500–1505. doi 10.1056/NEJM199811193392103

Morton, C.C. and Nance, W.E., Newborn hearing screening – a silent revolution, *N. Engl. J. Med.*, 2006, vol. 354, no. 20, pp. 2151–2164. doi 10.1056/ NEJMra050700

Mossong, J., Hens, N., Jit, M., Beutels, P., Auranen, K., Mikolajczyk, R., and Edmunds, W.J., Social contacts and mixing patterns relevant to the spread of infectious diseases, *PLoS Med.*, 2008, vol. 5, no. 3. doi 10.1371/journal.pmed.0050074

Nance, W.E., Liu, X.Z., and Pandya, A., Relation between choice of partner and high frequency of connexin-26 deafness, *Lancet*, 2000, vol. 356, no. 9228, pp. 500–501. doi 10.1016/S0140-6736(00)02565-4

Nance, W.E., The genetics of deafness, *Ment. Retard. Dev. Disabil. Res. Rev.*, 2003, vol. 9, no. 2, pp. 109–119.

Nance, W.E. and Kearsey, M.J., Relevance of connexin deafness (DFNB1) to human evolution, *Am. J. Hum. Genet.*, 2004, vol. 74, no. 6, pp. 1081–1087. doi 10.1086/420979

Nekrasova, N.Yu., Shagina, I.A., Petrin, A.N., and Polyakov, A.V., 35delG mutation frequency in connexin 26 gene in children with neonatal sensorineural hearing loss, *Med. Genetika*, 2002, vol. 1, no. 6, pp. 290–294.

Ohtsuka, A., Yuge, I., Kimura, S., Namba, A., Abe, S., Van Laer, L., Van Camp, G., and Usami, S., *GJB2* deafness gene shows a specific spectrum of mutations in Japan, including a frequent founder mutation, *Hum. Genet.*, 2003, vol. 112, pp. 329–333. doi 10.1007/s00439-002-0889-x

Osetrova, A.A., Sharonova, E.I., Rossinskaya, T.G., Galkina, V.A., and Zinchenko, R.A., The study of genetic causes of congenital and neonatal deafness in special schools for children with hearing impairment in the Kirov oblast, *Med. Genet.*, 2010, vol. 9, pp. 30–40.

Padden, C. and Humphries, T., *Deaf in America: Voices from a culture*, Cambridge, MA: Harvard Univ. Press, 1988.

Park, H.J., Hahn, S.H., Chun, Y.M., Park, K., and Kim, H.N., Connexin26 mutations associated with nonsyndromic hearing loss, *Laryngoscope*, 2000, vol. 110, no. 9, pp. 1535–1538. doi 10.1097/00005537-200009000-00023

Park, H.J., Shaukat, S., Liu, X.Z., Hahn, S.H., Naz, S., Ghosh, M., Kim, H.N., Moon, S.K., Abe, S., Tukamoto, K., Riazuddin, S., Kabra, M., Erdenetungalag, R., Radnaabazar, J., Khan, S., et al., Origins and frequencies of *SLC26A4* (PDS) mutations in east and south Asians: Global implications for the epidemiology of deafness, *J. Med. Genet.*, 2003, vol. 40, no. 4, pp. 242–248. doi 10.1136/jmg.40.4.242

Peng, B., Amos, C.I., and Kimmel, M., Forward-time simulations of human populations with complex diseases, *PLoS Genet*, 2007, vol. 3, no. 3. doi 10.1371/journal.pgen.0030047

Posukh, O., Pallares-Ruiz, N., Tadinova, V., Osipova, L., Claustres, M., and Roux, A.F., First molecular screening of deafness in the Altai republic population, *BMC Med. Genet.*, 2005, vol. 6, no. 1, p. 12. doi 10.1186/1471- 2350-6-12

Prezioso, C.T., Cultural aspects of deafness (the Deaf community), in *An Introduction to Deafness: A Manual for Genetic Counselors*, Israel, J., Ed., Washington DC: Gallaudet Research Institute, Gallaudet Univ., 1995.

Prozorova, E.V., Russian sign language as an object of linguistic research, *Vopr. Yazykozn.*, 2007, vol. 1, pp. 44–61.

Pshennikova, V.G., Barashkov, N.A., Teryutin, F.M., Solov'ev, A.V., Klarov, L.A., Romanov, G.P., Gotovtsev, N.N., Savvinova, K.E., Kozhevnikov, A.A., Sidorova, O.G., Vasil'eva, L.M., Fedotova, E.E., Morozov, I.V., Bondar', A.A., Solov'eva, N.A., et al., Analysis of the spectrum and frequency of GJB2 mutations in patients with congenital hearing impairment in the Republic of Sakha (Yakutia), *Med. Genet.*, 2015, vol. 6, pp. 10–21.

Puzyrev, V.P., Erdynieva, L.S., Kucher, A.N., and Nazarenko, L.P., *Genetiko-epidemiologicheskoe issledovanie naseleniya Tuvy* (Genetic and Epidemiological Study of the Population of Tuva), Tomsk: STT, 1999.

Qu, Z., Garfinkel, A., Weiss, J.N., and Nivala, M., Multi-scale modeling in biology: How to bridge the gaps between scales?, *Prog. Biophys. Mol. Biol.*, 2011, vol. 107, no. 1, pp. 21–31. doi 10.1016/j.pbiomolbio.2011.06.004

Rabionet, R., Zelante, L., and López-Bigas, N., D'Agruma, L., Melchionda, S., Restagno, G., Arbonés, M.L., Gasparini P., and Estivill, X., Molecular bases of childhood deafness resulting from mutations in the *GJB2* (connexin 26) gene, *Hum. Genet.*, 2000, vol. 106, pp. 40–44. doi 10.1007/s004399900192

RamShankar, M., Girirajan, S., Dagan, O., Ravi Shankar, H.M., Jalvi, R., Rangasayee, R., Avraham, K.B., and Anand, A., Contribution of connexin26 (*GJB2*) mutations and founder effect to non-syndromic hearing loss in India, *J. Med. Genet.*, 2003, vol. 40. doi 10.1136/jmg.40.5.e68

Rapin, I., Consequences of congenital hearing loss: A long-term view, *J. Otolaryngol.*, 1978, vol. 7, no. 6, pp. 473–483.

Rose, S.P., Genetic studies of profound prelingual deafness, *PhD Thesis*, Indiana Univ., 1975.

Ruben, R.J., The history of the genetics of hearing impairment, *Ann. N. Y. Acad. Sci.*, 1991, vol. 630, pp. 6–15. doi 10.1111/j.1749-6632.1991.tb19571.x

Sattenspiel, L. and Dietz, K., A structured epidemic model incorporating geographic mobility among regions, *Math. Biosci.*, 1995, vol. 128, nos. 1–2, pp. 71–91. doi 10.1016/0025-5564(94)00068-B

Schein, J., The Deaf community, in *Hearing and Deafness*, Davis, H. and Silverman, S.R., Eds., New York: Holt, Rinehart, Winston, 1978, 4th ed.

Schein, J. and Delk, M., *The Deaf Population of the United States*, Silver Spring, MD: National Association of the Deaf, 1974.

Scott, D.A., Carmi, R., Elbedour, K., Duyk, G.M., Stone, E.M., and Sheffield, V.C., Nonsyndromic autosomal recessive deafness is linked to the DFNB1 locus in a large inbred Bedouin family from Israel, *Am. J. Hum. Genet.*, 1995, vol. 57, pp. 965–968.

Sharonova, E.I., Osetrova, A.A., and Zinchenko, R.A., Hereditary hearing loss in the Kirov oblast, *Yakutsk. Med. Zh.*, 2009, vol. 2, no. 29, pp. 28–31.

Shokarev, R.A., Amelina, S.S., Kriventsova, N.V., Khlebnikova, O.V., Bliznets, E.A., Polyakov, A.V., and Zinchenko, R.A., Genetic-epidemiological and molecular-genetic study of hereditary deafness in the Rostov oblast, *Med. Genet.*, 2005, vol. 4, no. 12, pp. 556–567.

Sirmaci, A., A founder TMIE mutation is a frequent cause of hearing loss in southeastern Anatolia, *Clin. Genet.*, 2009, vol. 75, no. 6, pp. 562–567. doi 10.1111/j.1399-0004.2009.01183.x

Sirmaci, A., Edwards, Y.J., Akay, H., and Tekin, M., Challenges in whole exome sequencing: An example from hereditary deafness, *PLoS One*, 2012, vol. 7, no. 2. doi 10.1371/journal.pone.0032000

Stenson, P.D., Mort, M., Ball, E.V., Shaw, K., Phillips, A., and Cooper, D.N., The human gene mutation database: Building a comprehensive mutation repository for clinical and molecular genetics, diagnostic testing and personalized genomic medicine, *Hum. Genet.*, 2014, vol. 133, no. 1, pp. 1–9. doi 10.1007/s00439-013-1358-4

Stern, S.J., Arnos, K.S., Murrelle, L., Welch, K.O., Nance, W.E., and Pandya, A., Attitudes of deaf and hard of hearing subjects toward genetic testing and prenatal diagnosis of hearing loss, *J. Med. Genet.*, 2002, vol. 39, pp. 449–453. doi 10.1136/jmg.39.6.449

Tarskaia, L.A., Zinchenko, R.A., Elchinova, G.I., Egorova, A.G., Korotov, M.N., Basova, E.V., Prokopeva, A.M., Sivtseva, E.N., Nikolaeva, E.E., Banshchikova, E.S., Samarkina, M.V., Sannikova, A.N., Danilova, G.I., Jhelobtsova, A.F., Danilova, A.P., and Popova, G.N., The Structure and Diversity of Hereditary Pathology in Sakha Republic (Yakutia), *Russ. J. Genet.*, 2004, vol. 40, no. 11, pp. 1264–1272.

Tekin, M. and Arici, Z.S., Genetic epidemiological studies of congenital/prelingual deafness in Turkey: Population structure and mating type are major determinants of mutation identification, *Am. J. Med. Genet. A*, 2007, vol. 143A, pp. 1583–1591. doi 10.1002/ajmg.a.31702

Tekin, M., Xia, X.J., Erdenetungalag, R., Cengiz, F.B., White, T.W., Radnaabazar, J., Dangaasuren, B., Tastan, H., Nance, W.E., and Pandya, A., *GJB2* mutations in Mongolia: Complex alleles, low frequency, and reduced fitness of the deaf, *Ann. Hum. Genet.*, 2010, vol. 74, no. 2, pp. 155–164. doi 10.1111/j.1469-1809.2010.00564.x

Toriello, H.V. and Smith, S.D., *Hereditary Hearing Loss and Its Syndromes*, USA Oxford Monographs on Medical Genetics, 2013, 3rd ed.

Tsukamoto, K., Suzuki, H., Harada, D., Namba, A., Abe, S., and Usami, S., Distribution and frequencies of PDS (SLC26A4) mutations in Pendred syndrome and nonsyndromic hearing loss associated with enlarged vestibular aqueduct: A unique spectrum of mutations in Japanese, *Eur. J. Hum. Genet.*, 2003, vol. 11, pp. 916–922. doi 10.1038/sj.ejhg.5201073

Twycross, J., Band, L.R., Bennett, M.J., King, J.R., and Krasnogor, N., Stochastic and deterministic multiscale models for systems biology: An auxin-transport case study, *BMC Syst. Biol.*, 2010, vol. 4, no. 1, p. 34. doi 10.1186/1752-0509-4-34

Van Camp, G. and Smith, R.J.H., Hereditary Hearing Loss Homepage. http://hereditaryhearingloss.org.

Van Laer, L., Coucke, P., Mueller, R.F., Caethoven, G., Flothmann, K., Prasad, S.D., Chamberlin, G.P., Houseman, M., Taylor, G.R., Van de Heyning, C.M., Fransen, E., Rowland, J., Cucci, R.A., Smith, R.J., and Van Camp, G., A common founder for the 35delG *GJB2* gene mutation in connexin 26 hearing impairment, *J. Med. Genet.*, 2001, vol. 38, no. 8, pp. 515–518. doi 10.1136/jmg.38.8.515

Wattanasirichaigoon, D., Limwongse, C., Jariengprasert, C., Yenchitsomanus, P.T., Tocharoenthanaphol, C., Thongnoppakhun, W., Thawil, C., Charoenpipop, D., Pho-iam, T., Thongpradit, S., and Duggal, P., High prevalence of V37I genetic variant in the connexin-26 (*GJB2*) gene among non-syndromic hearing-impaired and control Thai individuals, *Clin. Genet.*, 2004, vol. 66, no. 5, pp. 452–460. doi 10.1111/j.1399- 0004.2004.00325.x

Winata, S., Arhya, I.N., Moeljopawiro, S., Hinnant, J.T., Liang, Y., Friedman, T.B., and Asher, J.H., Congenital non-syndromal autosomal recessive deafness in Bengkala,

an isolated Balinese village, *J. Med. Genet.*, 1995, vol. 32, no. 5, pp. 336–343.

Zhuravskii, S.G., Ivanov, S.A., Taraskina, A.E., Grinchik, O.V., and Kurus', A.A., Distribution of "deaf" mutation 35delG in gene *GJB2* among the healthy population of the North-West region of Russia, *Med. Akad. Zh.*, 2009, vol. 9, no. 2, pp. 41–45.

Zinchenko, R.A., Zinchenko, S.P., Galkina, V.A., El'chinova, G.I., Nurbaev, S.D., Polyakov, A.V., Nekrasova, N.Yu., and Ginter, E.K., Prevalence and molecular genetic typing of nonsyndromic sensorineural deafness in Chuvash Republic, *Russ. J. Genet.*, 2003, vol. 39, no. 9, pp. 1076–1084.

Zinchenko, S.P., Kirillov, A.G., Abrukova, A.V., Sorokina, T.V., Sharonova, E.I., Khidiyatova, I.M., Dzhemileva, L.U., Shokarev, R.A., Bliznets, E.A., Khusnutdinova, E.K., Zinchenko, R.A., and Ginter, E.K., Genetic and epidemiological study of hereditary (isolated and syndromic) hearing impairment in the Republic of Chuvashia, *Med. Genet.*, 2007, vol. 6, no. 5, pp. 18–28.

Zinchenko, R.A., El'chinova, G.I., Osipova, E.V., Petrova, N.V., and Ginter, E.K., Population genetics of hereditary diseases in the Udmurt Republic, *Vestn. Udmurtsk. Univ.*, 2009a, vol. 1, pp. 43–57.

Zinchenko, R.A., Murzabaeva, S.Sh., Greenberg, Ya.I., Galkina, V.A., Khlebnikova, O.V., Dadali, E.L., Fedotov, V.P., Hidiyatova, I.M., Khusnutdinova, E.K., and Ginter, E.K., Genetic epidemiological study of Bashkortostan Republic: The diversity of monogenic hereditary diseases in five districts, *Russ. J. Genet.*, 2009b, vol. 45, no. 5, pp. 593–604.

Zinchenko, R.A., Galkina, V.A., Bessonova, L.A., Dadali, E.L., Khlebnikova, O.V., Mikhailova, L.K., Kadyshev, V.V., Petrin, A.N., Sharonova, E.I., Vafina, Z.I., El'kanova, L.A., Gavrilina, S.G., Bolotov, V.A., Polyakov, A.V., Strel'nikov, V.V., et al., Medical and genetic study of the population of the Republic of Tatarstan. Part II. A variety of monogenic hereditary pathologies in three habitats of the Kazan Tatars, *Med. Genet.*, 2012a, vol. 9, pp. 31–40.

Zinchenko, R.A., Osetrova, A.A., Sharonova, E.E., and El'chinova, G.I., Hereditary deafness in Kirov oblast: Estimation of the incidence rate and DNA diagnosis in children, *Russ. J. Genet.*, 2012b, vol. 48, no. 4, pp. 455–462.

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