PREFACE

Natural selection is the process which, being the most important factor of evolution, promotes rising of adaptability and prevents destructive consequences of all other processes. The concept of natural selection is a discordant problem of evolutionary human genetics. Despite popularity of a hypothesis of "neutral evolution," the majority of scientists consider that selection has played main role in evolution of species and has generated all bio-logical diversity of human populations. This book presents research on natural selection and genetic drift. The author of the first chapter provides an all-embracing macroevolutionary perspective on the processes of the evolution of life and culture on earth. The author investigates a complementary form of natural selection that diverges from the traditional form in that it is acting independently of the external environment. The next chapter discusses natural selection and diabetes mellitus. The last chapter examines how the genetic drift among native people from South American the Gran Chaco region affects interleukin 1 receptor antagonist variation.

Chapter 1 – In the present work, the author gives an all-embracing macroevolutionary perspective on processes of the evolution of life and culture on earth. First, the author investigates a complementary form of natural selection that diverges from the traditional form in that it is acting independently of the external environment. This form of natural selection is found as a result of a mathematical analysis of the conditions for population growth. The author extends the author's investigation as well to other evolutionary processes than the organic, such as the evolution of human language and the evolution of science, thereby suggesting other possible forms of underlying explanatory processes. The author examines the concept of complexity and show that it implies new insights into the ways natural

selection has been acting in forming the evolutionary and developmental processes. Especially, complexity is found to be growing in an accelerating mode, a process that is explained as the combined result of natural selection and a self-reinforcing feedback process. The use of the concept of complexity opens the possibility of construction of a new form of a Tree of Life, which, in contrast to traditional forms, combines complexity and time. Such an illustration of the evolutionary process explains the observation that most species live without great changes over vast periods of time. For species at the highest level of complexity there is no competition from species at still higher levels and these species can therefore, if conditions are beneficent, form new species at still higher levels. The process explains the emergence of new species and the general trend of evolution towards cumulatively higher complexity levels. The cumulative addition of species with successively higher complexity implies that the latest appearing species is the one of the highest level of complexity. At present, this species is the human species.

Chapter 2 – Advances in modern medicine enable a change in the tension of intragroup selection in human populations. Thus, implementation of insulin for type 1 diabetes mellitus (DM) treatment considerably lowered the selection tension for this symptom and converted it from the sub-lethal to the one with a lowered adaptability. Increasing variety of type 1 DM and type 2 DM is being observed recently in different populations. Moreover, recently the heterogeneity of type 1 DM and type 2 DM has also been observed. The investigation was aimed to study the influence of the selection on the evolution of DM clinical forms. Global implementation of insulin therapy into type 1 DM treatment caused the prevalent increase of this disease. Currently, there is a positive selection trend for type 2 DM, which is the original cause for the prevalence increase within the population, and the negative one for type 1 DM determines its prevalence within the population approximately on the same level. Intra-population change of gene frequencies, susceptible for type 1 and 2 DM, predetermined the development of such DM clinical forms as LADA (latent autoimmune diabetes in adults). It also resulted in the increasing number of patients with an absolute insulin deficiency of type 2 DM, which is a more complicated form of this DM type. Polymorphisms association, changing the immune response and forming the susceptibility to type 1 (C1858T of the gene *PTPN22*, A49G of the gene *CTLA4*) and type 2 (E23K of the gene *KNJ11* participating in insulin insufficiency formation) with different DM forms illustrates the result of decreasing the selection tension against type 1 DM after insulin therapy implementation into the public health services practice.

Chapter 3 – Genetic variation is generally responsible for ethnic differences in certain diseases, including inflammatory processes. The antagonist of cytokine IL-1, IL-1Ra, has been widely studied among Caucasian and African populations for genetic polymorphisms, and interethnic differences have been documented. However, the variation and genotype distribution of polymorphisms from these genes among South American Amerindians are thus far unknown. The author's present the results for a VNTR located in the IL-1Ra second intron, in a sample of 169 individuals belonging to 5 Native American populations from Argentina and Paraguay, identified as native according to their self designation, and their geographic location. The author's also compare this data with the results obtained from a sample of non-native Argentinian people. Among the five known alleles of the VNTR, the author's found only two (alleles 1 and 2) in the native populations from Gran Chaco, and heterozygosity was 19%. The allele 2 which is considered proinflammatory (IL-1Ra * 2) has been found in homozygosity at a considerable frequency among native individuals. However, the association of this allele with inflammatory disease previously demonstrated for other populations of the world, might not be acting in the same way for native people, probably due to local adaptation. This would indicate that the allele 2 will probably not have a negative influence on individuals of native origin who have homozygous genotype 2-2. On the contrary, few records on inflammatory disease are available for the native people. It seems that the increment on allele 2 is not related to any adaptive process but to genetic drift, that changes randomly the allele frequencies of different genetic regions along the genome. The effect of genetic drift has already been demonstrated with genetic markers located in autosomes, X and Y chromosomes. These results indicate that the author's must be very cautious when studying populations that passed a process of genetic drift, which can become a confounding factor in epidemiological studies. This information will contribute to a future understanding of the association of this polymorphism with disease, and its incidence in different ethnic groups.