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Study Design for Gene Mapping: Korean Migration History as a Natural Experiment to Study Gene-environment Interaction in Man

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In human genetics, researchers can never design their own experiments the way one can when working with a model organism. The reason studies of mouse and *Drosophila* are powerful to uncover the phenotypic effects of heritable genetic variation is because of our ability to manipulate the mating structure of the population and their environmental exposures to test hypotheses in a directed manner. In human studies, the only thing we may do is look for naturally occurring experiments that approximate the sort of study designs that might be optimal to answer certain questions. To this end, we must be detectives looking for populations with mating patterns and environmental exposures which fit our scientific needs, which have occurred naturally without our intervention. To this end, in an effort to dissect the relative contributions and interrelationships between genetic and environmental influences on human biological variation, we have focused on the natural experiment which has resulted from the past century and a half of Korean emigration history. Prior to 1860, the vast majority of ethnic Koreans lived within the Korean peninsula, but starting around that time, due to famines in the Northern parts of the country, Koreans began to migrate to border regions of Russia and shortly thereafter, to Manchuria. With the Japanese occupation in the early 20th century, the migration increased, and by 1937 there were hundreds of thousands of Koreans in the Russian Far East, who were forcibly resettled to Kazakhstan by Stalin's Soviet Union, in the first of many resettlements of ethnic populations to regions disconnected from their homeland. They were stripped of the culture, diet, language and so on, and today are culturally much more similar to Russians than to Koreans, while being biologically Korean. Another example of a biologically Korean population which is culturally orthogonal to Koreans is the population of roughly 200,000 children who have been adopted by families in Northern Europe and North America in the time since the end of the Korean War. Because of such unfortunate historical events, the Korean diaspora has an enormous range of cultural and environmentally variable populations without genetic admixture, compared to other populations, and thus has provided an ideal natural experiment to look for evidence of gene-environment interaction in quantitative traits related to human health. In this talk I will present some discussion of our ongoing studies of this population, focusing on some preliminary data from our initial pilot studies of two populations of Koreans in Kazakhstan - a group living on a collective farm in a rural part of the country, and a second group from Almaty, the major urban center of the country. I will also discuss our ongoing research efforts with the adopted Korean community in Sweden, and other work we are pursuing in other overseas Korean groups.