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Scientists suggest certain genes boost chances for distributing variety of traits, drive evolution

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Genes that don't themselves directly affect the inherited characteristics of an organism but leave them increasingly open to variation may be a significant driving force of evolution, say two Johns Hopkins scientists.

Their proposed amended view of evolution is based on observations of genetic patterns outside of a cell's DNA and may better explain how organisms, including people, have adapted over hundreds of thousands of years to relatively rapidly changing environments.

This view, which also offers a new explanation for the genetic basis of some persistent, common human diseases, is published the week of Dec. 14 in the early online edition of the Proceedings of the National Academy of Sciences.

"We're proposing that certain gene variants contribute to heterogeneity in populations," says Johns Hopkins professor of medicine Andrew Feinberg, M.D., Ph.D. "In a fluctuating environment, this gives generations more opportunity to survive," he adds.

For more than 100 years, mainstream science has embraced the basic tenets of Darwin's view that characteristics that increase an organism's ability to survive and reproduce will be passed from generation to generation. Scientists later demonstrated that stable, significant traits are indeed inherited in the DNA carried in parental genes on chromosomes

and randomly distributed to offspring.

Characteristics that affect an organism's ability to adapt and survive in times of environmental change have been thought to arise by chance through random mutations in an organism's DNA. However, this view could not explain how such mutations, which arise only rarely, help organisms of every size and variety adapt quickly enough through time. Nor could it explain how diseases that lead to a dramatic loss of survival — such as diabetes, heart disease, autism, and schizophrenia — persist in populations. Indeed, genes that directly contribute to these conditions have been difficult to find.

Feinberg says some scientists have sought to explain gaps in Darwinian theory with epigenetics, the study of changes to genes that don't directly affect the DNA sequence, but do affect which genes are turned on or off and therefore which proteins are produced in cells. Research has shown that environmental conditions, such as diet, sunlight, or viral infections, can bring about epigenetic changes. However, it is unclear whether these changes persist through several generations in a variable environment.

In a new twist on both of these ideas, Feinberg and Johns Hopkins Bloomberg School of Public Health professor of biostatistics Rafael Irizarry, Ph.D., suggest that gene variants or alleles able to take on the challenge and increase random distribution of characteristics might drive the development of the wide variety of traits — from height to skin tone to disease risk — seen in modern populations.

The scientists developed this idea through a series of experiments examining epigenetic patterns in groups of mice littermates that were very similar genetically. From before birth to adulthood, the mice were exposed to the same conditions, living in the same cage and eating the same food. The researchers then examined the animals' livers and brains for methylation, a chemical addition to DNA that is one type of

epigenetic change.

Though Feinberg and Irizarry expected to see similar methylation patterns due to the rodents' identical upbringing, they found regions in the animal's genetic makeup with strikingly different patterns. Moreover, these regions occurred among genes responsible for determining anatomy during early development.

Using samples of human liver, the researchers found that these "variably methylated regions" were the same, suggesting that these genes are affected similarly by epigenetics from species to species.

In another experiment, Feinberg and Irizarry performed a computer simulation in which they calculated the likelihood of a model organism becoming extinct over 1000 generations. This organism had a trait, Y, which affected survival. In some simulations, the researchers allowed Y to behave variably, leading some generations to have more surviving members than others. When the environment in the simulation was static, having a variable Y was a detriment. However, when the environment changed on a periodic basis, generations with a variable Y created organisms with a wider range of characteristics that were more likely to survive in the long run and not become extinct.

The researchers suggest in the study that the presence of genes that contribute to trait variability might help explain the presence of common diseases. Much as having a variable Y aided the model organism in their simulation in the long run but were detrimental in a static environment, variability in traits such as the ability to control blood sugar could have helped human ancestors survive to the present but become detrimental in the current environment.

"In the long run, it might be a good thing to have a large spread of people who handle blood sugar differently. However, in today's environment,

people with a propensity to develop high blood sugar are at a disadvantage," explains Feinberg.

Feinberg and Irizarry suggest that though it's unclear how these variability genes acquire such inconsistent epigenetic changes, one mechanism may be environmental influence.

"The interaction between nature and nurture may be simpler than we've imagined," Irizarry says.

Source: Johns Hopkins Medical Institutions