MedicalXpress

Scientists use Iceland's genealogical database to pinpoint the heritage of a deadly disease

June 20 2008

A collaboration of scientists from Iceland and the United States has used Iceland's genealogical database to trace the ancestors of patients suffering from hereditary cystatin C amyloid angiopathy (HCCAA). Analysis shows that the deadly mutation in the cystatin C gene, L68Q, derives from a common ancestor born roughly 18 generations ago, around 1550AD. Details are published June 20th in the open-access journal *PLoS Genetics*.

This dominantly inherited disease, which is due to a mutation in cystatin C (L68Q), strikes young adults with healthy blood pressure. The disease results in death from repeated brain haemorrhages, on average by the age of 30. The origin of the mutation causing HCCAA was previously unknown, but using DNA haplotype analysis* the scientists have shed light on the history of this autosomal dominant disease that has high penetrance in contemporary Icelanders.

The scientists found that 200 years ago, obligate carriers of the mutation lived a normal life span compared to the control population (their spouses). In carriers born around 1820, however, a trend of shortening life span began, resulting in an average life span of only 30 years in people born around 1900. This 30-year lifespan has stayed constant since then in both men and women.

At the same time, a matrilinear effect appeared whereby those who inherited the mutation from the mother died earlier. For carriers born after 1900, the difference is a loss of 9.4 years for those who inherited

the mutation from their mothers rather than their fathers. Based on this information, the authors propose that the traditional diet of the nation (which in the past consisted largely of whey-preserved offal as well as meat, dried fish, and butter) "protected" the mutation carriers for almost 300 years until the Icelandic diet changed early in the early 19th century, exemplified by drastic increases in imported carbohydrates and salt.

This finding has implications for studies of Alzheimer's disease as cerebral amyloid angiopathy (CAA) is almost universally found in Alzheimer's patients and normal cystatin C protein is one of the proteins found in amyloid in brains of Alzheimer's patients. Studies are underway to try to elucidate the risk factors with the hope of providing a preventive stategy for cystatin L68Q carriers.

Source: Public Library of Science
www.plosgenetics.org/doi/pgen.1000099