

Identification of genetic variants affecting age at menopause could help improve fertility treatment

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Vienna, Austria: For the first time, scientists have been able to identify genetic factors that influence the age at which natural menopause occurs in women. Ms Lisette Stolk, a researcher from Erasmus MC, Rotterdam, The Netherlands, told the annual conference of the European Society of Human Genetics today (Monday 25 May) that a greater understanding of the factors influencing age at menopause might eventually help to improve the clinical treatment of infertile women.

Ms Stolk and her team performed a Genome-Wide Association Study (GWAS) in 10,339 [menopausal women](#). The data analysed were taken from 9 different studies undertaken in The Netherlands (the Rotterdam Study 1 and 2), the UK (the TwinsUK study), USA (the Framingham study, the Cardiovascular Health Study, the ARIC study, the HAPI Heart Study), Iceland (AGES-Reykjavik) and Italy (the InCHIANTI study). The scientists found 20 single nucleotide polymorphisms (SNPs) in four different places on [chromosomes](#) 19 and 20. SNPs are common genetic variants that influence how humans look, behave, develop disease or react to pathogens. In genetics they are used to compare regions of the genome between different groups of individuals and to identify those regions that are associated with a particular disease or characteristic. The SNPs the researchers found had not been identified before, and the part of the body where they might have an effect has yet to be identified, though the researchers speculate that this is likely to be in the ovaries or brain.

"We found that the 20 SNPs were all related to a slightly earlier [menopause](#)", said Ms Stolk, "and women who had one of them experienced menopause nearly a year earlier than others. We know that ten years before menopause women are much less fertile, and five years before many are infertile. In Western countries, where women tend to have children later in life and closer to menopause, age at menopause can be an important factor in whether or not a particular woman is able to become a mother."

In addition to its effect on fertility, earlier menopause has other deleterious effects on women such as an increased risk for osteoporosis, osteoarthritis and cardiovascular disease, while it has a protective effect on the risk of breast cancer. The age of menopause varies greatly among Caucasian women, ranging between 40 and 60 year of age, with an average at around 50. The reasons for this variation are unknown, but there is evidence from studies of twins that this could be due to inheritable genetic factors. However, until now, GWAS had not been used to study the effect of genetic variants on age at menopause.

The scientists intend to follow up their work with an even larger sample of menopausal women to identify more chromosomal loci. "GWAS gives you SNPs connected with menopausal age, and a possible indication of the gene involved, but not a total proof of function", said Ms Stolk. "When we have a larger group of loci we intend to perform functional studies to study the exact biology and effect of this association."

The scientists say that it may be several year before they have enough information to make genotyping for earlier menopause available to patients, and even then this may not be helpful to all women with fertility problems. "However, if these studies give us a better understanding of the function of the genetic variants involved in early menopause, we might one day be able to screen [women](#) who have

problems getting pregnant to see if they have one or more of these variants which might relate to their sub-fertility, and perhaps interfere with the relevant physiological pathways in order to delay their total infertility", said Ms Stolk.

Source: European Society of Human Genetics

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