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New breast cancer genetic mutation found in Chinese population

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A genetic mutation that appears to be associated with a high breast cancer risk has been identified by researchers from Hong Kong. It is likely to be important enough to be included in genetic screening for people of Chinese origin with a family history of breast cancer, they say.

Carriers of the genetic mutations BRCA1 and BRCA2 are at high risk of contracting breast cancer, but these mutations are only involved in between 10-15% of inherited breast cancers, and there are many other candidates waiting to be discovered. Speaking at the 10th European Breast Cancer Conference (EBCC-10) today (Wednesday), Dr Ava Kwong, Assistant Dean and Clinical Associate Professor at the University of Hong Kong and Director of the Hong Kong Hereditary and High Risk Breast and Ovarian Cancer Programme, will describe a genetic mutation that appears to be associated with a high breast cancer risk in the Chinese ethnic population.

Dr Kwong and her team undertook genetic testing on 1114 patients selected from the Hong Kong Hereditary Breast Cancer Family Registry. Their family history showed that they were at high risk for breast cancer, but they were all negative for four of the best known breast cancer-causing mutations: BRCA1 and 2, TP53, and PTEN.

"We decided to test for the RECQL mutation, recently identified as being associated with an increased risk of the disease," she will say. "We found that RECQL was present in 0.54% of the women in our group (Southern Chinese), and we also know that a similar group of Northern

Chinese women, from Beijing, had a RECQL incidence of 2%."

This level of incidence means that the RECQL mutation may be an important enough factor to be included in genetic screening for people of Chinese origin with a family history of breast cancer. "We need to do further work in order to be able to understand whether we are looking at founder mutations, which occur in the DNA of one or more individuals who were founders of a distinct population, since even within the two Chinese groups two RECQL mutation loci, or specific positions on a chromosome, were seen more than once in different families," Dr Kwong will say.

When a newly formed colony is small, its founders can strongly affect the population's genetic makeup well into the future. For example, there are known to be three founder BRCA mutations among Ashkenazi Jews. "The scale of the Chinese diaspora means that the RECQL mutation is most likely to be fairly prevalent in countries outside Asia," says Dr Kwong. "For example, in 2010 there were nearly 3.5 million people of Chinese origin living in the USA, as well as over 400,000 in the UK.

"In the Hong Kong patients studied we identified two potential recurrent mutations on which we need to do more work in order to prove that the families carrying them are founders. In a previous study of BRCA mutations in our locality, we discovered, unexpectedly, seven founder mutations. It is likely that we would find similar effects in other inherited mutations, given the migration history of ethnic Chinese people. If they are identified as such, and their relationship to breast cancer risk is confirmed as being high, they should be included in genetic testing in the future," Dr Kwong will say.

In an era where the utility of breast screening in the general population is increasingly controversial, the ability to identify and screen women at high risk has become more important. However, a better understanding

of the exact clinical implications of these gene mutations will be needed before effective screening programmes can be developed. "And, of course, we should also be concentrating on those mutations where treatment and preventive strategies exist," Dr Kwong adds.

The RECQL mutation has been associated with a poor prognosis in liver, pancreatic and head and neck cancers across all populations, and it was commonly associated with cardiovascular disorders in the study patients' families.

"However, cardiovascular disease is also common in this group of mutation carriers in Hong Kong, so this is another area that merits further study as, at present, the numbers are still too small to enable us to draw definitive conclusions. We do not think that the RECQL mutation is unique to the Chinese population, since other RECQ and RECQL mutations have been described in other ethnic populations; for example, their association with breast cancer has been described in Poland and Quebec. Our previous work on other mutations associated with breast cancer has led us to believe that the loci do vary between different ethnicities. In our work on BRCA 1 and 2, for example, we found that over 40% of the BRCA mutations in our Chinese study group were novel.

"We hope that our work will enable screening programmes for high risk women to be better targeted, and also lead to the development of new drugs aimed exclusively at patients carrying specific mutations," Dr Kwong will conclude.

Chair of the conference, Professor Fatima Cardoso, Director of the Breast Unit of the Champalimaud Clinical Centre in Lisbon, Portugal, said: "This is an interesting finding which, if confirmed by further research, could lead to the inclusion of the RECQL mutation into genetic screening for breast cancer for those from families at high risk. From

clinical practice, we are all aware of patients and families where the genetic risk appears to be very high but where no known mutation is found in the four genes that are usually tested for. Knowing where the loci are situated in people of ethnic Chinese origin makes it easier and quicker to check for the mutation, and will enable those who are found to carry it to consider and discuss possible preventive strategies."

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