Scientists discover new drug targets for aggressive breast cancer

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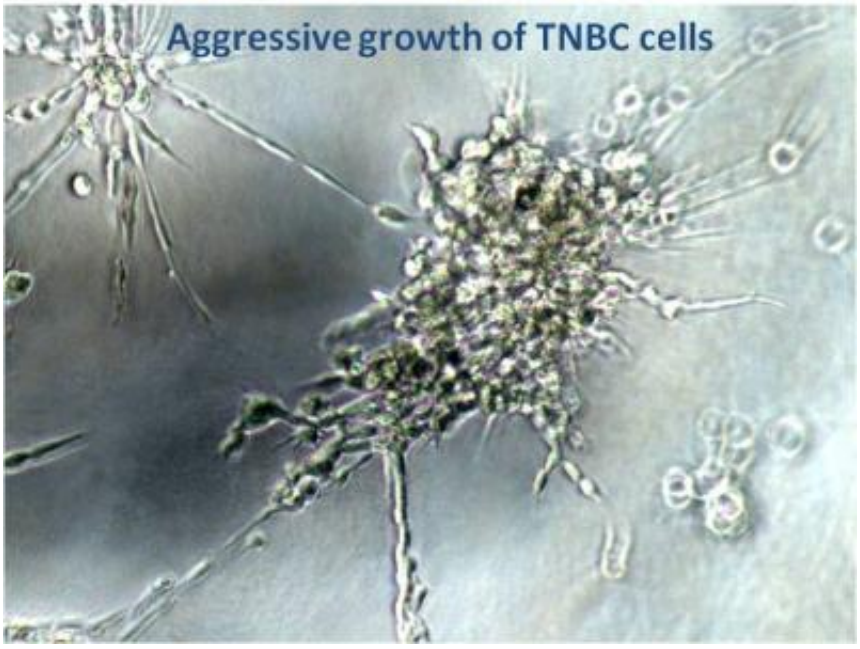

The image shows the aggressive growth of TNBC cells. Credit: Genome Institute of Singapore, A*STAR

Scientists at A*STAR's Genome Institute of Singapore (GIS) led in a study that has identified genes that are potential targets for therapeutic drugs against aggressive breast cancer. These findings were reported in the July 2013 issue of *PNAS*.

Out of the 1.5 million women diagnosed with breast cancer in the world annually, nearly one in seven of these is classified as triple negative.

Patients with triple-negative breast cancer (TNBC) have tumours that are missing three important proteins that are found in other types of breast cancer. The absence of these three proteins make TNBC patients succumb to a higher rate of relapse following treatment and have lower overall survival rates. There is currently no effective therapy for TNBC.

Using integrated genomic approaches, GIS scientists led by Dr. Qiang Yu, in collaboration with local and international institutions, set out to search for targets that can be affected by drugs. The scientists discovered that a protein tyrosine phosphatase, called UBASH3B, is overexpressed in one third of TNBC patients. UBASH3B controls the activity of an important breast cancer gene. The researchers found that deleting this gene expression markedly inhibits TNBC cell invasive growth and lung metastasis in a mouse model. They also showed that patients with TNBC tumours that have high levels of UBASH3B tend to be more likely to have early recurrence and metastasis.

Lead author Dr Qiang Yu said, "The identification of target genes is always the most crucial first step towards treating a disease. It is heartening to know that UBASH3B is an important element of the pro-invasive gene network and targeting UBASH3B not only inhibits TNBC invasive growth, but also significantly reduces metastasis."

Tan Tock Seng Hospital consultant surgeon Dr Tan Ern Yu, a collaborator and co-author of the study said, "Some TNBC patients relapse soon after standard treatment while others remain free of disease for a long time. Being able to predict which patients are more likely to relapse is important since these patients may benefit from more aggressive treatments. But currently, doctors are unable to reliably do so. Further validation will show whether UBASH3B can be developed into a means of identifying these high-risk patients as well as a new form of treatment."

Dr Dave Hoon, Director, Department Molecular Oncology at the John Wayne Cancer Institute, USA, and co-author said, "Recent large-scale genomic analysis of breast cancer show that triple negative breast cancer are highly heterogeneous and patients tumors can have different molecular profiles. Unlike more common breast cancers that often express oestrogen, progesterone or HER2 can be targeted by specific agents such as hormone therapy or Herceptin. TNBC is the most difficult breast cancer to treat. The finding can help us develop new approaches for targeted therapy for this highly aggressive breast cancer."

UBASH3B is expressed in high levels not only in American TNBC patients, but also in local Asian patients. This important information shows that the clinical significance of this finding is not limited to one specific ethnic group.

More information: www.pnas.org/content/early/201 …/19/1300873110.short

Provided by Agency for Science, Technology and Research (A*STAR), Singapore

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