Epigenetic regulation of metastatic breast cancer progression may guide prognosis and future therapy

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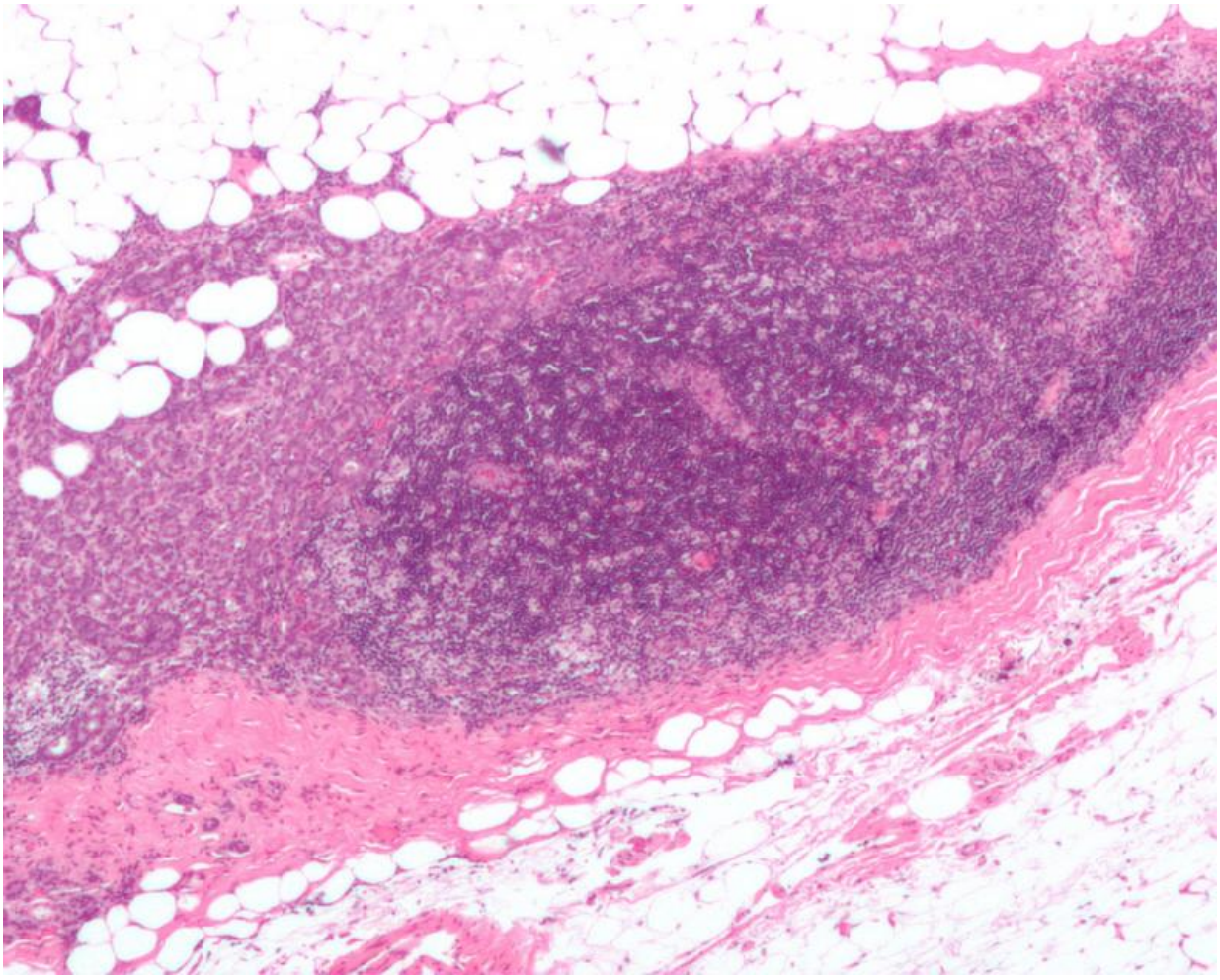

Micrograph showing a lymph node invaded by ductal breast carcinoma, with extension of the tumour beyond the lymph node. Credit: Nephron/Wikipedia

Boston-A gene that plays a role in the development of breast cancer to metastatic disease has been identified which may help to predict disease progression and serve as a target for the development of future breast cancer therapies.

These findings by Boston University School of Medicine (BUSM) researchers currently appear in the journal *Proceedings of the National Academy of Sciences*.

Researchers have identified a gene called serum deprivation response (SDPR) and the mechanisms by which this gene is down-regulated, or silenced, in breast cancer cells promoting tumor spread. Using a breast cancer progression model, the team identified that aggressive, metastatic breast cancer cells had little or no genetic expression of SDPR and furthermore that when it is over-expressed (or turned on) this gene in models of breast cancer cells with propensity for metastasis, there was a significant reduction in the incidence of metastatic disease.

Despite the advent of advanced technologies, the discovery of new metastasis suppressor genes such as SDPR that prevent the spread of breast cancer to distal sites using genomic efforts has been slow potentially due to their primary mode of regulation by epigenetic mechanisms as shown in this case by the researchers at BUSM. The current study reveals the importance of gene regulation by epigenetic rather than genetic mechanisms enabling the cancer cells to readily adapt to new microenvironments of the various organs of the human body at sites away from the initial sites at which the cancer cells formed.

According to the researchers this work is crucial as metastatic dissemination of breast cancer cells represents a significant clinical obstacle to curative therapy and spreading of the cancer is the major cause of death of patients affected by breast and other cancers. "It is of utmost importance to understand the underlying molecular mechanisms

that facilitate/prevent cancer metastasis," explains corresponding author Sam Thiagalingam, BUSM associate professor of medicine, genetics and genomics, pathology and laboratory medicine.

The researchers also found that SDPR loss was not limited to breast cancer, as tumor samples from bladder, colorectal, lung, pancreatic and ovarian cancers as well as sarcomas also exhibited loss of SDPR expression based on in silico meta-analysis of publicly available data, suggesting its functional role as a metastasis suppressor is likely to impact multiple cancers.

"While this is a significant advance in deciphering the molecular basis of the metastatic disease and may help to predict progression to metastatic cancer, its potential importance in the development of future precision cancer therapies have yet to be worked out from the identification of druggable targets regulated by SDPR," added Thiagalingam.

More information: SDPR functions as a metastasis suppressor in breast cancer by promoting apoptosis, *Proceedings of the National Academy of Sciences*, www.pnas.org/cgi/doi/10.1073/pnas.1514663113

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