Medical Xpress

Epigenetic changes promoting cancer metastasis identified

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Latest University of Otago research is shedding new light on why and how cancer cells spread from primary tumours to other parts of the body. This phenomenon – known as metastasis – causes about 90 per cent of all cancer deaths.

The Otago findings, published in the leading international journal *Oncotarget*, may pave the way for new therapies that prevent melanoma and other cancers from their deadly seeding of secondary tumours.

Department of Pathology researchers Dr Aniruddha Chatterjee and Professor Mike Eccles are lead authors of the study, which investigated epigenetic changes in melanoma cells.

Epigenetics involves changes to the way genes behave – such as their being switched on or off through the addition of methyl groups to a gene's DNA segments.

After comparing primary and metastatic melanoma cells from the same patients, Dr Chatterjee says the research team identified thousands of epigenetic changes – and, crucially, several that were common to all the metastatic cells.

"We believe that these may be the key drivers that allow melanoma to metastasise," he says.

Additionally, the team identified a new function in melanoma of a gene

called Early B Cell Factor 3 (EBF3).

"We found this gene gains more DNA methylation when primary melanoma progresses to its metastatic version, and that the gene expresses itself highly in the latter."

When the researchers used molecular techniques that decreased EBF3 expression, both primary and metastatic melanoma cells grew less aggressively and behaved less invasively.

Dr Chatterjee says earlier searches for genetic – rather than epigenetic – drivers of metastasis had not been very fruitful.

"Over the years, very few genetic mutations have been identified as drivers of metastasis. Instead, our approach looked at the changes in the way genes in cancer cells are expressed, rather than changes to the genetic code itself," he says.

Dr Chatterjee says unlike genetic changes, epigenetic changes are reversible.

"So if we understand the key changes that underpin metastasis, then not only are we potentially able to monitor for their presence, but also to design new therapies to target and correct them to prevent metastasis of tumours."

More information: Chatterjee, A., Stockwell, P., Ahn, A., Rodger, E., Leichter, A., & Eccles, M. (2016). Genome-wide methylation sequencing of paired primary and metastatic cell lines identifies common DNA methylation changes and a role for EBF3 as a candidate epigenetic driver of melanoma metastasis. *Oncotarget*, 5. Retrieved from www.impactjournals.com/oncotar … article&op=view&path %5B%5D=14042&path%5B%5D=44772

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