

Study discovers new molecular mechanism likely involved in cancer metastasis

May 7 2018



Danielle Schmitt (r) and Songon An (l) discuss their research on signaling pathways that are likely involved in cancer cell metastasis in An's lab at UMBC. Their new paper in PLOS ONE found that the PDK1 pathway, known to be active in metastatic cells, regulates the formation of a three-protein complex that facilitates purine biosynthesis. Credit: Marlayna Demond for UMBC

Cancer is most devastating when it metastasizes—when tumor cells break away, travel through the bloodstream, and then attach elsewhere, only to grow another tumor. A significant amount of scientific research has focused on finding ways to prevent metastasis. For some time, scientists have understood that a particular biochemical pathway, known as the PDK1 pathway, is active in metastasizing cancer cells. But no one knew why.

In a new paper published in *PLOS ONE*, Songon An and colleagues have shown for the first time that the PDK1 [pathway](#) regulates the formation of a three-protein complex that facilitates two chemical pathways: One builds purines (two of the four building blocks of DNA) and the other produces thiamine, a B vitamin. While it's still unknown how purine and thiamine levels contribute to metastasis, the authors hypothesize ways they could be related, and they are planning further research to reveal any links.

For example, the three-protein core complex that PDK1 regulates is sometimes joined by three more proteins. Together, the six proteins form a larger complex called the purinosome, which carries out all 10 reactions necessary to build purines. Without the three peripheral proteins, however, purine production only goes halfway, and the molecule the core complex makes is more likely to end up as the vitamin thiamine.

Making purines is an energy-intensive process, so one hypothesis is that decreasing purine production during metastasis helps the cell survive while it is detached from a nutrient source like an organ. "Looking at this metabolic switch—which pathways are in use during metastasis versus when the cell is attached—may be where our research goes in the future," says An.



Danielle Schmitt (l) and Songon An (r) study signaling pathways in cancer cells. Their new paper in *PLOS ONE* found that the PDK1 pathway, known to be active in metastatic cells, regulates the formation of a three-protein complex that facilitates purine biosynthesis. This finding encourages further work on the role of purine biosynthesis and other signaling pathways in metastasis, which An will pursue with a UMBC colleague in biochemical engineering. Credit: Marlayna Demond for UMBC

The team's immediate next step is to validate the function of the three-protein core complex. After that, they'll investigate whether the core complex and the six-protein purinosome are actively coming together and breaking apart in metastatic [cells](#). "Blocking those dynamics could be an alternative way to block metastasis," An says.

A broader goal for An and collaborator Greg Szeto, UMBC assistant professor of chemical, biochemical, and environmental engineering, is to map the various [protein](#) complexes and the signaling pathways they regulate in [cancer cells](#). "We want to put every signaling pathway into the same context," An explains. "Whenever the proteins have different spatial assemblies, we would like to know which pathways are on and which ones are turned down."

So far, the researchers have only looked at one pathway at a time (such as PDK1), but by using a cutting-edge technique that can detect many proteins at once within a cell, "now we are going to target multiple signaling pathways at the same time, so that we can understand the complete picture of the regulatory map for [purine metabolism](#)." That knowledge could provide more new insights into the causes of [metastasis](#) and how to prevent it.

More information: Danielle L. Schmitt et al, Spatial alterations of De Novo purine biosynthetic enzymes by Akt-independent PDK1 signaling pathways, *PLOS ONE* (2018). DOI: [10.1371/journal.pone.0195989](https://doi.org/10.1371/journal.pone.0195989)

Provided by University of Maryland Baltimore County

Citation: Study discovers new molecular mechanism likely involved in cancer metastasis (2018, May 7) retrieved 4 May 2024 from <https://medicalxpress.com/news/2018-05-molecular-mechanism-involved-cancer-metastasis.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.
