Public Abstract

BRMS1 MSD: A potential new inhibitor of breast cancer metastasis

One of the challenges of treating metastasis is that cells spread early, even before the original tumor is detected. Those disseminated cells can become dormant and can resume growth months to years later. The growth at secondary sites of disseminated cells is called colonization. One of the metastasis suppressor genes discovered by my lab, BRMS1, blocks colonization. Many believe blocking colonization is the most reasonable step of the complex process of metastasis to target clinically. And it has the advantage of being able to prevent metastases as well as stabilize already existing metastases. By blocking growth after tumor cells have already disseminated, the possibility of rendering cancer a chronic, but controllable, disease becomes a practical reality.

Metastasis suppressors are typically lost, or the genes are ‘turned off’ when cancer becomes metastatic. Therefore, strategies to restore function of these suppressors represent a promising and novel avenue for metastatic therapy. Gene therapy (replacing the gene) is currently not practical. And size limitations of the proteins made by metastasis suppressor genes restrict their use as therapeutics (i.e., they’re too big and unstable for use as drugs). However, smaller pieces have advantages from the perspective of drug development. We propose that small pieces (called peptides) of some suppressor molecules could overcome these limitations to block metastasis.

Preliminary data suggest that we have identified a piece of BRMS1 that suppresses metastasis. We have also discovered that cells alter that piece by adding a phosphate group to it. We will first test whether addition of that phosphate group is required for metastasis suppression. We will also test whether the piece of BRMS1 containing that phosphate group can suppress metastasis by itself.

At the same time, we will explore which other molecules interact with the BRMS1 peptide fragments. The latter information will help us understand the mechanism underlying the metastasis suppressing ability. So, this project has the potential to identify new anti-metastatic therapies as well as deepen our understanding of the metastatic process, both of which will eventually lead to even more effective cancer therapies.