

Lay Summary

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Defining the role of STAT3 in astrocyte adaptation to hypoxia as therapeutic target in brain cancers

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Breast, skin, or lung cancer that has spread to the brain cannot be cured by standard treatment. This cancer is called brain metastases and is associated with terminal diagnosis. The problem with brain metastases is that it does not need oxygen to grow in the brain and oxygen is an important factor in the success of cancer treatment. Just like a plant, we believe that brain metastases begins with a seed and uses food provided by the soil (i.e., normal brain cells called astrocytes) and fertiliser (i.e., the lack of oxygen called hypoxia) to grow. While the roots of the brain metastases start to form under the soil, it will change the primary function of astrocytes, adapting them to the harsh condition (i.e., hypoxia). The stem, leaves and flower of the brain metastases will emerge above the soil and be resilient making the plant difficult to treat because it lacks oxygen in its roots – we know that oxygen is needed in radiotherapy and chemotherapy to kill cancer cells.

Although very limited, some research has shown that specific markers of hypoxia are present in brain metastasis in patients who died of lung cancer. In addition, a limited number of animal and human studies have shown that markers of hypoxia in brain metastasis correlated strongly with tumour spread and poor patient survival. Here, we want to know whether we have the same correlation in astrocytes, which act as a soil in brain metastasis, and whether hypoxia controls a molecule (i.e., STAT3) that adapts astrocytes to this harsh condition. To prove this, we need to identify the active form of STAT3 in the soil (i.e., astrocytes). If we can manipulate the activity of STAT3 in hypoxia, it will have a negative effect on the growth of the plant (i.e., brain metastases) because the soil (i.e., astrocytes) can no longer adapt to hypoxia. This will also have a positive effect on standard treatments and therefore could improve life expectancy of patients with brain metastases.