

# Taking a closer look at eye cancer: Research offers new insight into high rate of metastasis

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Credit: Marc Schulte from Pexels

New research from Edith Cowan University (ECU) is one step closer to understanding why uveal melanoma, the deadliest form of eye cancer,

has such a high rate of metastasis.

Uveal melanoma is a rare cancer type with an incidence of 7.6 per million adults in Australia and represents around 5% of all melanomas. Patients presenting with [uveal melanoma](#) have a 50% chance of the disease metastasizing or spreading from the eye, commonly to the liver, even after successful treatment of the tumors within the eye.

Metastases of uveal melanoma could develop up to 20 years after the primary tumor treatment, and the median survival in patients after a diagnosis of metastases, is between 5 to 18 months.

ECU Vice Chancellor's Research Fellow, Dr. Vivian Chua noted that after diagnosis of the disease in the liver, patient survival is often short due to the lack of effective treatment options.

"The metastatic tumors respond poorly to many treatment options that had been shown to be effective in other cancer types including skin melanoma. It is unclear how and why uveal melanoma spread or metastasize to the liver.

"Identifying the mechanisms that drive uveal melanoma metastasis will likely uncover strategies to prevent uveal melanoma spreading or the development of metastatic uveal melanoma, which is the cause of death of patients."

Dr. Chua's most recent research focused on alterations in the BRCA1-associated protein 1 (BAP1) gene. The BAP1 gene is functionally involved in modulating the characteristics of cancer cells, particularly uveal melanoma. The work is [published](#) in the journal *Science Signaling*.

Alterations in the BAP1 gene lead to loss of the BAP1 [protein function](#)

and expression and are associated with an increased risk of metastasis of uveal melanoma and poorer patient survival. BAP1 alterations have also been reported in other cancer types such as mesothelioma and cholangiocarcinoma.

"However, the roles of BAP1 loss or deficiency in uveal melanoma remains unclear," Dr. Chua said.

Dr. Chua, who recently returned to Australia following eight years at Thomas Jefferson University, in Philadelphia, engineered human uveal melanoma cell cultures that are BAP1-deficient to re-exhibit BAP1, to allow for a comparison between the BAP1-deficient and BAP1-proficient uveal melanoma cells.

"We found that BAP1-deficient cells are slow-growing, and this was associated with the cells exhibiting low activity of the S6 protein. This is consistent with the known function of the S6 protein to regulate [cancer](#) cell growth. These characteristics were also associated with the BAP1-deficient cells surviving better under conditions deprived of [amino acids](#).

"Overall, we have uncovered a role of BAP1 deficiency in uveal melanoma," said Dr. Chua.

Cancer cells require lots of nutrients to survive and grow but during metastasis or spreading, the surrounding environment, such as in the bloodstream, can often be deprived of nutrients. Results identified by this ECU researcher suggest that BAP1-deficient uveal melanoma cells can survive or thrive under conditions that are deprived of nutrients, particularly, amino acids, thereby allowing them to spread successfully.

"My research is now aimed at investigating what mechanisms support BAP1-deficient cell survival under amino acid deprivation and

identifying co-players of S6. I expect findings from these studies to uncover strategies to effectively treat uveal [melanoma](#) or prevent the development of metastatic disease," Dr. Chua said.

**More information:** Vivian Chua et al, Slow proliferation of BAP1-deficient uveal melanoma cells is associated with reduced S6 signaling and resistance to nutrient stress, *Science Signaling* (2024). [DOI: 10.1126/scisignal.adn8376](https://doi.org/10.1126/scisignal.adn8376)

Provided by Edith Cowan University

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