How a rogue protein produces 'Dr. Jekyll and Mr. Hyde' cancer cells

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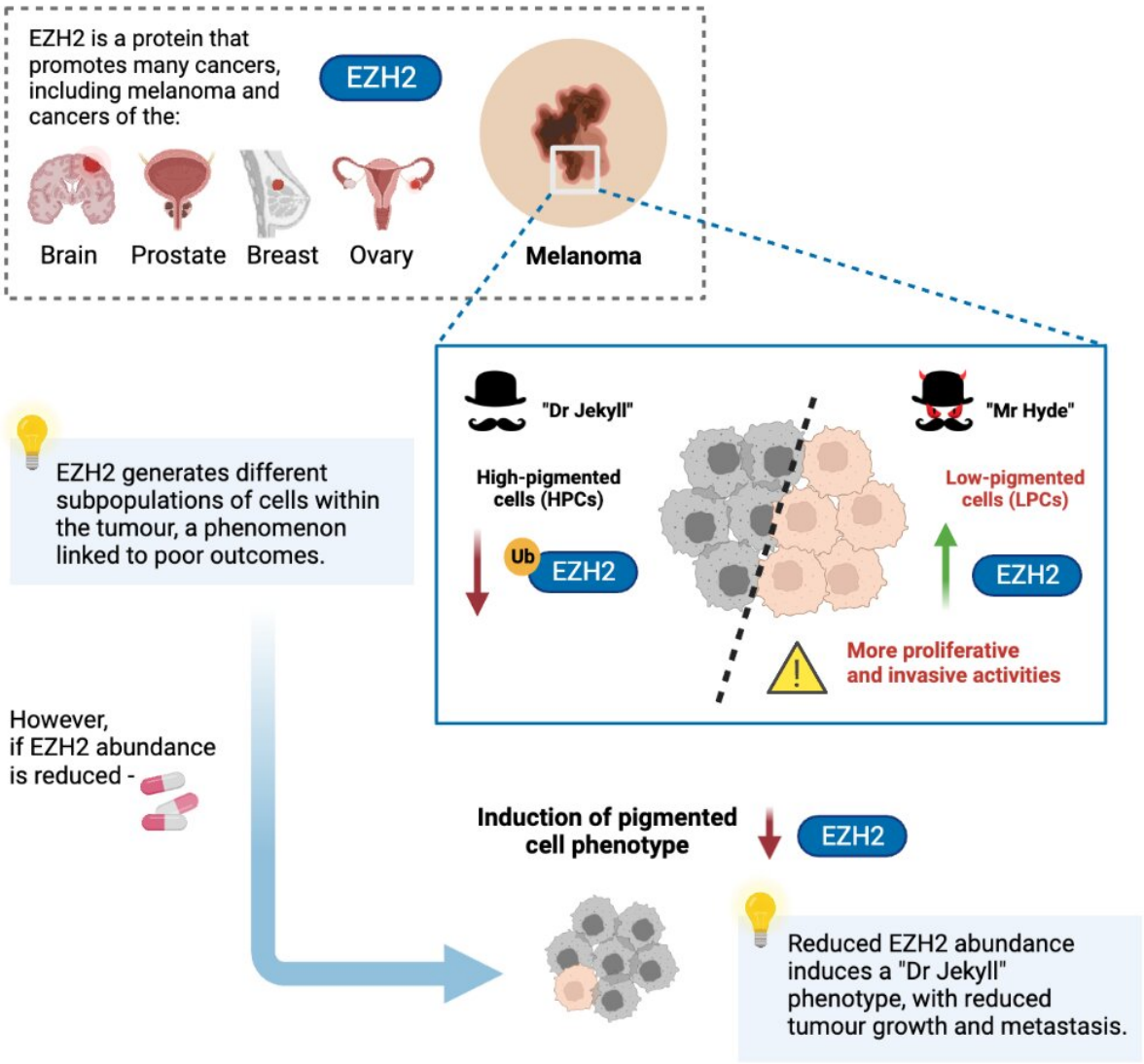

Credit: Monash University

Melbourne researchers have discovered how a rogue protein produces "Dr. Jekyll and Mr. Hyde" cancer cells, which could lead to improved treatments for melanoma and other cancers.

The world-first Monash University-led study, published in the journal *Oncogene*, focused on a protein called EZH2, which is known to promote the development and progression of many cancer types, including melanoma and cancers of the prostate, brain, breast, and ovary.

Using laboratory models and human melanoma samples, Monash University Central Clinical School's Cancer Development and Treatment Group found that EZH2 plays an essential role in generating more aggressive cells within tumors, a phenomenon linked to poor outcomes.

The team, led by Dr. Gamze Kuser-Abali and Professor Mark Shackleton, who is also Alfred Health Director of Medical Oncology and Co-Director of the Monash Partners Comprehensive Cancer Consortium (MPCCC), found that EZH2 causes some cells to produce less melanin, a pigment molecule, resulting in dangerous "Mr. Hyde" cells without color that grow faster and are more likely to spread. Their less aggressive opposite, "Dr. Jekyll" cells in the same tumors are darker.

The researchers now hope that drugs can be developed to reduce the amount of EZH2 in cells to reverse its cancer-promoting effect. This could turn the fast-growing, dangerous Mr. Hyde cells into slow-growing Dr. Jekyll cells, potentially making the tumor less aggressive.

Professor Shackleton, who is also a Laboratory Head at Monash University'sCentral Clinical School, said the discovery could potentially improve some cancer treatments. "We know that not all tumor cells are created equal," he said. "Inside a tumor, there are cells that grow faster

and are more likely to spread than others. Some also look different.

"Our study sheds new light on the role of EZH2 in determining these differences in melanoma, offering a new potential treatment approach. By developing treatments that specifically target EZH2, we hope ultimately to improve cures and the quality of life for people affected by melanoma and other cancers driven by EZH2."

Dr. Kuser-Abali agreed, "This discovery has opened avenues for designing new treatments that could be more effective than current ones. While there are no clinical trials or studies on the horizon yet, this discovery provides hope for those affected by these deadly cancers."

More information: Gamze Kuser-Abali et al, UHRF1/UBE2L6/UBR4-mediated ubiquitination regulates EZH2 abundance and thereby melanocytic differentiation phenotypes in melanoma, *Oncogene* (2023). DOI: 10.1038/s41388-023-02631-8

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