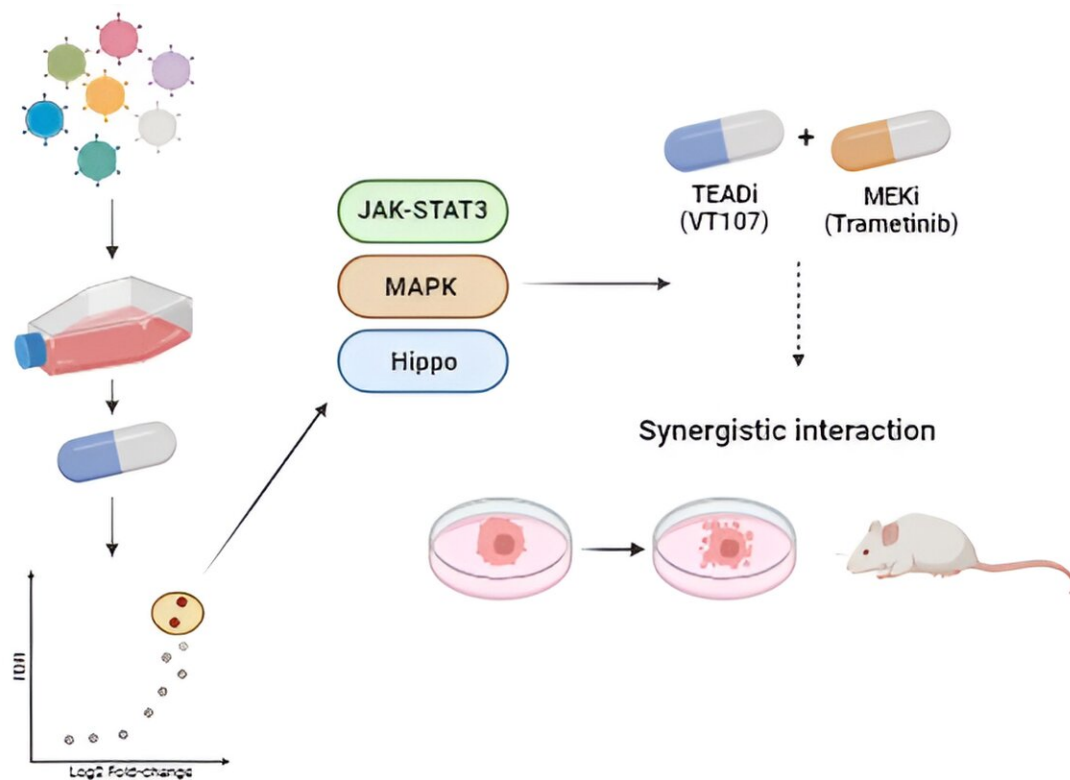


An ancient signaling pathway and 20 years of research offer hope for rare cancer

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Credit: *EMBO Reports* (2024). DOI: 10.1038/s44319-024-00217-3

Researchers at Peter Mac are using their knowledge of an ancient signaling pathway to find new treatments for mesothelioma, a devastating cancer that has few effective treatments and a very poor prognosis.

Dr. Kieran Harvey, Group Leader and Program Head at Peter Mac, helped discover the "Hippo" signaling [pathway](#) 20 years ago and has spent his career trying to understand more about how this pathway controls organ growth and how we can target it to treat cancer.

There are currently five treatments being tested in [early clinical trials](#) that target the Hippo pathway, and most of these are being trialed as [mesothelioma](#) treatments, because the Hippo pathway is the [driving force](#) behind this particular cancer.

Dr. Harvey said that it was incredibly rewarding to see his discoveries lead to potential clinical treatments that were being tested at Peter Mac in patients with mesothelioma, an asbestos-driven cancer with approximately 900 Australians diagnosed each year.

"These new treatments work by inhibiting TEAD, a type of protein that helps control organ growth. However, people will likely develop resistance to the [treatment](#), so we have been researching ways to stop this from occurring," he said.

"In our [study](#) published earlier this month in *EMBO Reports* we conducted genome wide screens in mesothelioma cells and uncovered that the RAS pathway causes resistance to TEAD inhibition. What's exciting is that we already have treatments available that target this pathway.

"In this study we combined the two treatments and found that they worked synergistically to block proliferation of multiple mesothelioma and lung [cancer](#) cell lines and tumors."

Dr. Harvey explained that the next step is to test this treatment combination of a TEAD inhibitor coupled with a RAS pathway inhibitor in people with mesothelioma to verify it works in the real-life setting.

"Peter Mac is in a unique position to be able to undertake informative lab research and apply this knowledge to develop more effective treatments to be tested in clinical trials," he said.

"Peter Mac has been involved in the first two clinical trials of TEAD inhibitors and we hope to apply this knowledge to test a new combination treatment strategy to help people with mesothelioma live longer."

This study was a [collaboration](#) between the Harvey lab, Vivace Therapeutics, U.S. and researchers at Peter Mac, Monash University and the University of Melbourne.

More information: Aishwarya Kulkarni et al, Identification of resistance mechanisms to small-molecule inhibition of TEAD-regulated transcription, *EMBO Reports* (2024). [DOI: 10.1038/s44319-024-00217-3](https://doi.org/10.1038/s44319-024-00217-3)

Provided by Peter MacCallum Cancer Centre

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