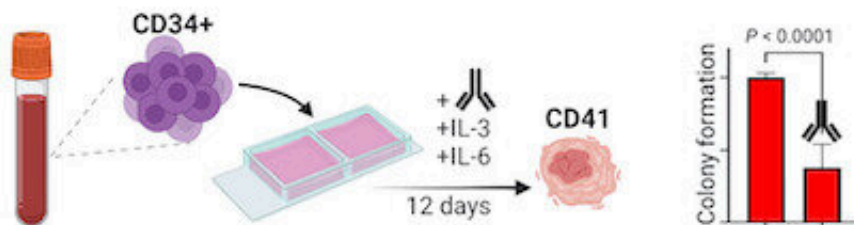
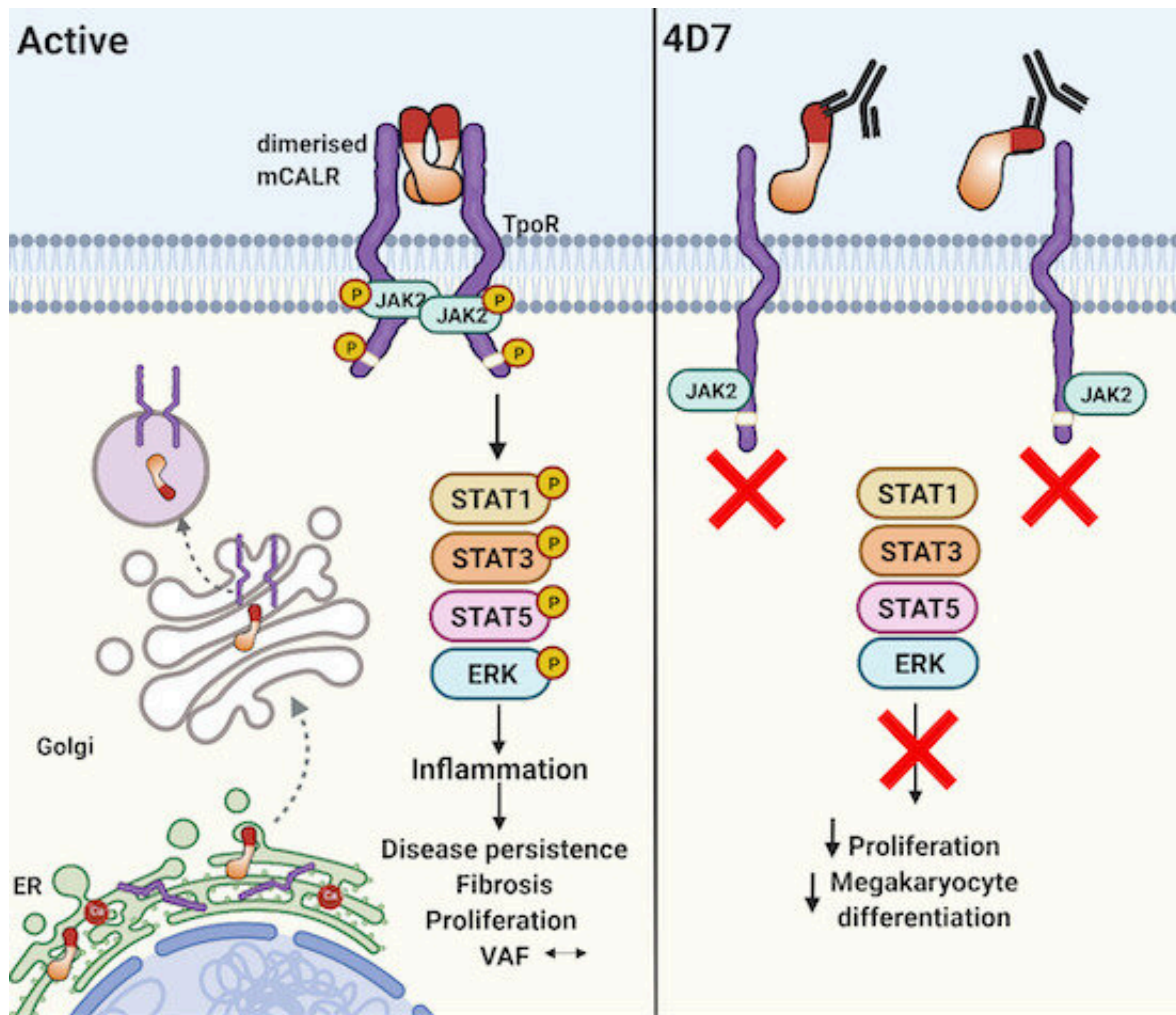


Lucky find could hold key to beating rare blood cancer

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Graphical abstract. Credit: DOI: 10.15252/embr.202152904

Adelaide researchers have discovered a new method to treat the rare and crippling blood cancer, myelofibrosis, that could have the potential to greatly extend lifespan while also significantly improving quality of life.

Myelofibrosis affects 1 in 100,000 Australians and while symptoms can currently be controlled with the use of oral tablets, they cause side effects and do not actually remove the [cancer cells](#).

Over time the disease commonly evolves into leukemia or complete marrow fibrosis, with deadly impact on patients. Dr. Daniel Thomas, leader of the Myeloid Metabolism Lab at SAHMRI and Associate Professor of Medicine at the University of Adelaide, led the study recently published in *EMBO Reports*, in collaboration with Professor Angel Lopez at SA Pathology. Dr. Thomas says it was a stroke of luck that led to the extraordinary find.

"We were actually trying to make a tool to study myelofibrosis. We didn't realize the antibody we made would have therapeutic properties," Dr. Thomas said.

"Our drug blocked the growth of [cancer](#) cells in a very aggressive live model of the disease, significantly increasing survival rate without noticeable negative side effects," Dr. Thomas said.

Co-lead author and biochemist Dr. Denis Tvorogov generated antibodies using a [peptide fragment](#) called "neoepitope" that's only present within the cancer and not on any normal tissues.

What he didn't expect was for the antibody to kill cancer cells when he tested it on patient samples, working with an early career scientist Dr. Chloe Thompson-Peach. "What is really exciting is that many other cancers have similar peptide fragments that we could also target by harnessing the immune system," Dr. Tvorogov said.

"These fragments are created by the insertion or deletion mutations within the cancer. We've found they not only drive cancer growth but also vulnerable for targeting without side effects." It's become [standard practice](#) to treat myelofibrosis with the drug Ruxolitinib. However, it hasn't proven effective at destroying cancer and is known to cause uncomfortable side effects. The new antibody is currently being prepared for early phase [clinical trials](#) set to run in South Australia later this year, supported by local biotech company, AusHealth. Managing Director, Greg Johansen says the group is excited to be supporting Prof. Lopez and Dr. Thomas through the next phase of the process.

Pre-clinical models have shown the drug is effective at shrinking tumors and Dr. Thomas is confident the [antibodies](#) will prove to be safe and effective in humans.

"We estimate there are at least 12,000 Australians living with cancer or having had cancer that express a recurrent neopeptide similar to what is found in myelofibrosis, that could be curable with an immunotherapeutic approach," Dr. Thomas said.

"This discovery brings us a fresh perspective. We need to build cell therapies and antibody therapies against these fragments as fast as possible."

Dr. Thomas is now building a computational algorithm to detect the fragments that will help pathology companies and doctors to link to clinical trials.

"With the new proton therapy facility being built, a raft of Biotech companies and an outstanding track record in clinical trial recruitment, South Australia is poised to lead in a new wave of life changing cancer therapeutics," Dr. Thomas said.

More information: Denis Tvorogov et al, Targeting human CALR-mutated MPN progenitors with a neoepitope-directed monoclonal antibody, *EMBO Reports* (2022). [DOI: 10.15252/embr.202152904](https://doi.org/10.15252/embr.202152904)

Provided by South Australian Health and Medical Research Institute (SAHMRI)

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