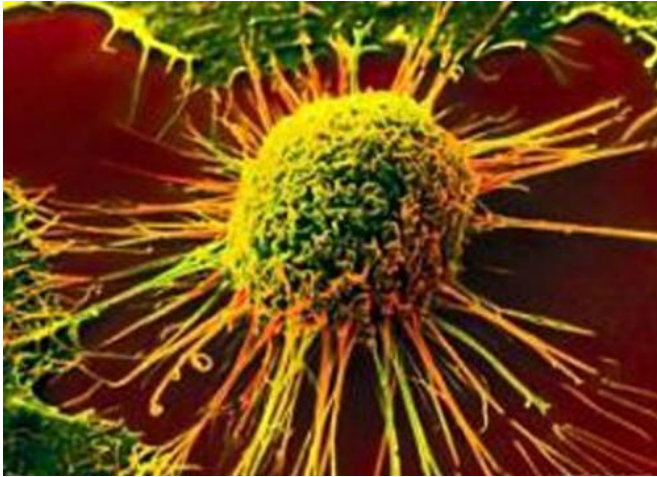


# New target could eliminate lurking cancer stem cells

27 November 2015



Scientists from Trinity College Dublin have identified a novel target that could help to identify 'cancer stem cells' while they are in their inactive state. The scientists could then jolt these cells into action so that they could be eliminated by radio or chemotherapeutic approaches.

The team discovered that a specific protein (PCL1) kicks a famous cancer-associated protein (p53) into action in our bodies. The p53 protein suspends cells in a dormant, non-dividing state called 'quiescence'. When cells are in this state, they are much harder to target therapeutically.

As a result, the scientists hope that blocking PCL1 will set a chain of events in motion that will cause [cancer cells](#) to leave the cover of quiescence so that they can be targeted and eliminated.

Assistant Professor in Medical Molecular Genetics at Trinity, Dr Adrian Bracken, led the team whose work has just been published in the journal *Genes and Development*.

He said: "Often, treating a cancer patient with chemotherapy or radiation doesn't work out as planned. The tumour shrinks at first, but the cancer [stem cells](#) within can survive and eventually seed the growth of new, more aggressive cancers. When cancer stem cells are in this state of 'cellular quiescence', the treatments can really only be partially effective."

Therefore, a key challenge in medicine has been to develop a means to target cancer stem cells and knock them out of their dormant, quiescent state, so they can then be killed by standard cancer therapies.

The team's research encompasses multiple disciplines including cancer cell biology, computer-predictive chemistry and evolutionary genetics.

The study's lead author, Dr Gerard Brien, demonstrated that PCL1 binds to – and boosts – the function of the p53 protein, and that this is required for p53 to activate cellular quiescence.

Dr Elisa Fadda, in NUI Maynooth's Department of Chemistry, was then instrumental in pin-pointing the structural basis of how PCL1 and p53 interact. Then, with Professor Aoife McLysaght, also at Trinity's Smurfit Institute of Genetics, the team determined that minor differences in PCL1 compared to its sister proteins, PCL2 and PCL3, only emerged during the recent evolution of mammals.

Dr Bracken added: "Our discovery that PCL1 has acquired a new function during the relatively recent evolution of mammals was very interesting, while the realisation that it teams up with the famous [p53 protein](#) represented an important breakthrough in the field of cancer biology."

"We are now excited about using this new knowledge to develop a strategy to target [cancer stem cells](#) by knocking them out of their dormant

state, thereby making them more amenable to standard chemotherapy and radiotherapy."

The research was supported by funding from Science Foundation Ireland and the Irish Cancer Society Collaborative Cancer Research Centre, Breast-Predict.

The full title of the paper is: 'A chromatin-independent role of Polycomb-like 1 to stabilize p53 and promote cellular quiescence'.

**More information:** Gerard L. Brien et al. A chromatin-independent role of Polycomb-like 1 to stabilize p53 and promote cellular quiescence, *Genes & Development* (2015). [DOI: 10.1101/gad.267930.115](https://doi.org/10.1101/gad.267930.115)

Provided by Trinity College Dublin

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