Old drugs offer new ways of treating bowel cancer

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Old medicines, combined in new ways, are showing promise for treating bowel cancer, a group of University of Auckland researchers has found.

"While there have been advances in treatments for this disease in recent years, the development of new medicines is expensive and time-consuming," lead researcher Professor Peter Shepherd says. "As a possible solution to this problem, our group has been investigating whether using old drugs in new ways could provide a faster and cheaper way of treating this disease."

The scientists investigated several cancer drugs that are coming off patent soon. When they combined two such drugs, they found greatly enhanced overall effectiveness in treating bowel, or colorectal, cancer in their lab-based studies.

Developments in our understanding of how cancers function have paved the way for this research, Shepherd says.

"In recent years, research has led to a rapid increase in our understanding of how colorectal cancer develops. In particular, some sub-types of the disease rely on the development of small blood vessels and on proteins called BRAF and beta-catenin.

"The research group identified existing drugs that target these and investigated the possibility that combining them could have powerful anti-cancer effects."

Studies in the labs at the University of Auckland have shown strong promise for two older drugs. One is an anticancer drug called axitinib. The other is pyrvinium, a low-cost drug that was developed in the 1960s to treat threadworm, which the researchers believe could be reformulated for use in cancer treatment. In one set of studies, the researchers found that the efficacy of another older drug targeting BRAF, called vemurafenib, could be greatly enhanced by adding axitinib. Axitinib works by reducing the growth of small blood vessels.

Both these drugs are used in other contexts to treat other types of cancer and will soon be off patent and so the cost of using them in treatment will drop greatly, Shepherd says.

In a second set of studies, the group found evidence that pyrvinium, which targets beta-catenin, could also increase the efficacy of vemurafenib.

Dr. Khanh Tran who performed most of the experiments says, "This work suggests that existing drugs might be able to be repurposed to treat this type of cancer which could significantly reduce the cost of such therapy."

Tran says, "Since the drugs we used are already in use for other purposes, it makes it much easier to develop clinical trials to see how the findings of our studies will actually translate to improved outcomes for patients with this disease."

Next the researchers are planning a randomized, controlled clinical trial.

More information: Khanh B. Tran et al, Response to BRAF targeted therapy is enhanced by co-targeting VEGFRs or WNT/β-Catenin signaling in BRAF-mutant colorectal cancer models, *Molecular Cancer Therapeutics* (2022). DOI: 10.1158/1535-7163.MCT-21-0941

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