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One of the earliest chemotherapy drugs appears to work against a genetic fault that can trigger bowel and other cancers, UK researchers say.

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This raises the hope of targeted treatments for those whose cancer is driven by the faulty gene.

Patient trials have already begun, EMBO Molecular Medicine reports.

The genetic condition HNPCC leaves people with a propensity to develop certain forms of cancer: some 90% of men and 70% of women will have developed bowel cancer by the time they reach 70.

METHOTREXATE
Methotrexate heralded in the modern era of chemotherapy drugs
In the 1940s, doctors reported remarkable results when treating children who were very ill with leukaemia
It works by stopping cancer cells making and repairing DNA and therefore growing and multiplying
Subsequently used as part of chemotherapy regime for many cancers, including breast, bladder and bone
Over the years as medicine has developed other drugs have been preferred
Still used for leukaemia and also now found to be effective for other conditions,
Those who carry the faulty gene have a very high risk of bowel cancer. One of the earliest chemotherapy drugs appears to work against a genetic fault that can trigger bowel and other cancers, UK researchers say. In laboratory tests methotrexate, first administered in the 1940s, was found to destroy cells containing the damaged MSH2 gene. This raises the hope of targeted treatments for those whose cancer is driven by the faulty gene. Patient trials have already begun, EMBO Molecular Medicine reports. The genetic condition HNPCC leaves people with a propensity to develop certain forms of cancer: some 90% of men and 70% of women will have developed bowel cancer by the time they reach 70. About 40% of people with HNPCC carry a faulty MSH2 gene. The gene usually plays a vital role in repairing DNA damage, but if it is damaged, mistakes accumulate in the cells and increase the risk of a cancer developing.

People who develop bowel cancer as a result may have more than one tumour, making the condition harder to treat.

Years after it was first used in the US, methotrexate is still commonly used in the treatment of leukaemia. It works by stopping cancer cells growing and multiplying, but is not normally deployed against solid tumours as newer, better drugs have been developed.

"What's exciting about methotrexate is that it selectively destroys the cells lacking the MSH2 function. This indicates that it may make an excellent treatment for patients with the genetic alteration," said Professor Alan Ashworth, who led the study at the Institute of Cancer Research.

**Tailored treatment**

Dr Lesley Walker of Cancer Research UK, which funded the research, said: "In the past, many treatments were developed which indiscriminately kill dividing cells. With improved scientific understanding, we are starting to be able to offer targeted therapies that are selective for the genetic faults in cancer."

"It's really fascinating that our scientists have discovered that an old-fashioned drug of this type shows new promise for this very specific group of patients."

Independent experts welcomed the findings.

"This is good news from one of our oldest chemotherapy drugs. It won't be for everyone, but it does hold out hope of a tailored treatment for those affected - a form of personalised chemotherapy," said Professor Will Steward, of the charity Beating Bowel Cancer.

Rob Glynne-Jones, chief medical advisor at Bowel Cancer UK, said: "The discovery that the faulty MSH2 gene has been found to be a specific target for Methotrexate is a really exciting development."

"It will probably only be relevant to a small proportion of patients who have bowel cancer, as HNPCC is only responsible for about 5% of bowel cancer cases. However, this is another positive step in using molecular biology and genetics to individualise a patient's treatment."