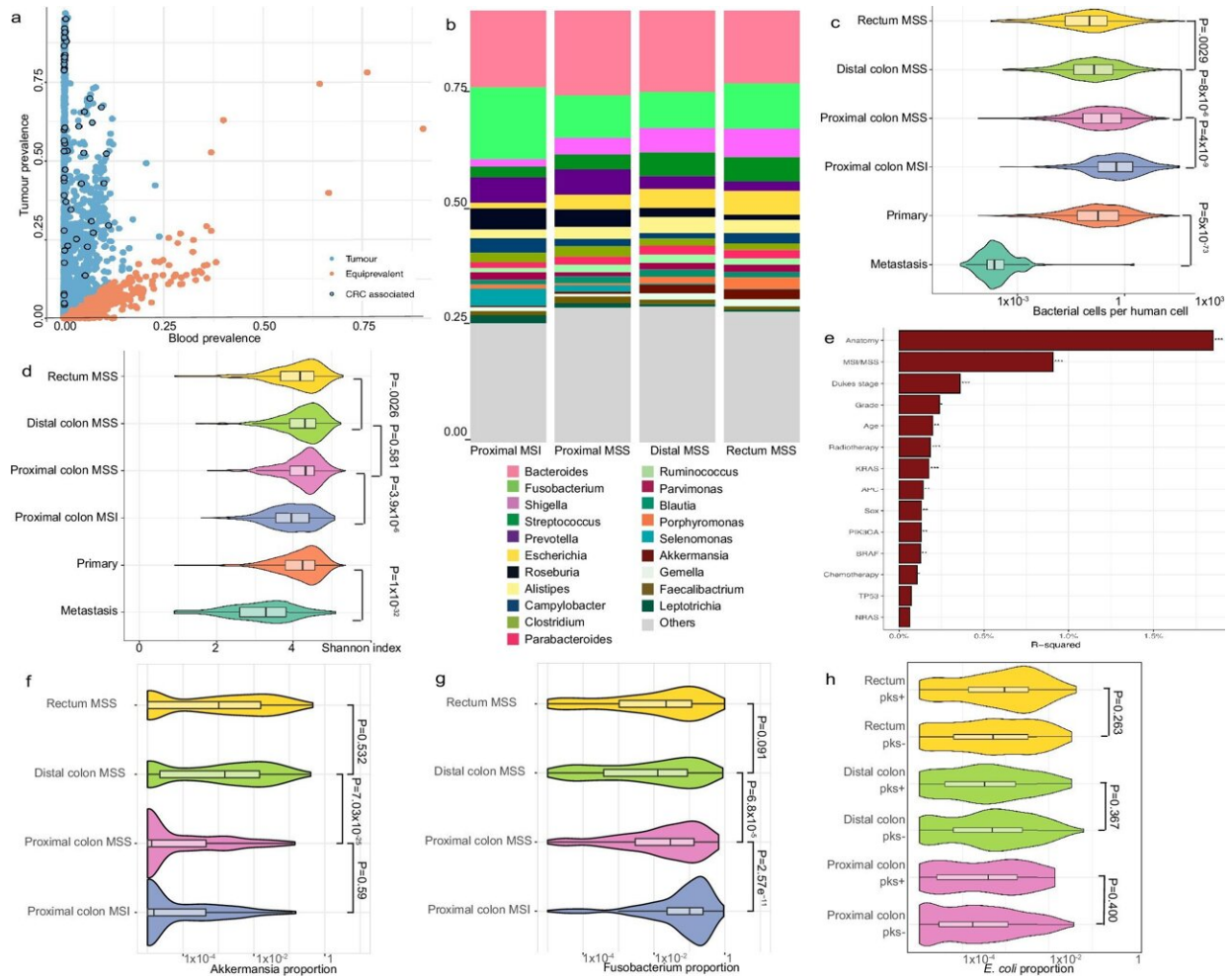


# Study reveals previously unknown genetic causes of colorectal cancer

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The CRC microbiome. Credit: *Nature* (2024). DOI: 10.1038/s41586-024-07747-9

A pioneering study, has provided the most comprehensive analysis to date of the genetic makeup of colorectal cancer (CRC).

Cancers develop partly through genetic abnormalities within cells of the body. Colorectal cancer is a major cause of death worldwide, but we don't yet have a full understanding of the genetic changes that cause it to grow.

The new research—led by U.K. universities, including The Institute of Cancer Research, London, the University of Oxford, and the University of Manchester, and [published](#) today in *Nature*—delivers an unprecedented view of the genetic landscape of CRC and its responses to treatment.

## **The 100,000 Genomes Project**

Utilizing data from 2,023 bowel cancers from the 100,000 Genomes Project led by Genomics England and NHS England, the research team has identified new gene faults that lead to CRC. They've also uncovered new CRC cancer sub-groups (categories of cancer with specific genetic characteristics that affect how cancer behaves and responds to treatment). These findings offer profound insights into the disease's development and potential treatment strategies.

The study has pinpointed more than 250 genes that play a crucial role in CRC, the great majority of which have not been previously linked to CRC or other cancers, expanding our understanding of how CRC develops.

Four novel, common sub-groups of CRC have been discovered based on genetic features. In addition, several rare CRC sub-groups have been identified and characterized. These groups have different patient outcomes and may respond differently to therapy.

The research also reveals a variety of genetic changes across different regions of the colorectum, highlighting differences in CRC causes between individuals. For example, a process has been found that is more active in younger CRC patients' cancers; the cause is unknown, but might be linked to diet and smoking. Many identified mutations could potentially be targeted with existing treatments currently used across other cancers.

Co-lead researcher, Ian Tomlinson, Professor of Cancer Genetics at the University of Oxford, said, "Our findings represent a significant advancement in understanding [colorectal cancer](#). By better understanding the genetic changes in CRC, we can better predict patient outcomes and identify new [treatment](#) strategies, quite possibly including the use of anti-cancer drugs that are not currently used for CRC."

The research provides a vital resource for the scientific community and a promising foundation for future studies. The results from the study are available to other researchers, who are invited to build on the data by undertaking more focused projects based on the CRC genome.

Co-lead researcher, Professor Richard Houlston, Professor of Cancer Genomics at The Institute of Cancer Research, London, said, "This research is a great insight into the biology of colorectal cancer, uncovering the clues as to how it develops, grows, and responds to treatments. I look forward to seeing future studies use these findings to develop tailored treatments for people with colorectal cancer, based on their genetics."

Co-lead researcher, Professor David Wedge, Professor of Cancer Genomics and Data Science at the University of Manchester, said, "This is the first really large study to come out of the 100,000 Genomes Project led by Genomics England and NHS England. In the coming months and years, I expect it to be followed by many more studies of

different types of cancer as well as combined studies across all types of cancer, fueled by the fantastic data resource provided by Genomics England."

Dr. Henry Wood, Lecturer in Translational Bioinformatics from Pathology in the University of Leeds' School of Medicine, said, "This study is the first to provide in-depth, [whole-genome sequencing](#) and characterization of the microbiome—the community of bacteria and viruses that live in the gut—in a large number of cases of bowel cancer.

"This means that we are now in a position to investigate the importance of the microbiome in the development of these cancers, and whether we can change it to influence the tumor and improve patient outcomes."

**More information:** Alex J. Cornish et al, The genomic landscape of 2,023 colorectal cancers, *Nature* (2024). [DOI: 10.1038/s41586-024-07747-9](#)

Provided by Institute of Cancer Research

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