

Genetic mutations differ within a single tumor, study finds

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When researchers looked at different areas within an individual rectal cancer sample, they found cases in which each area contained different genetic mutations. The findings could have significant implications for treatment recommendations.

Researchers from the University of Michigan Comprehensive Cancer Center used next-generation sequencing techniques to sample the genetic landscape of different geographic areas from tissue samples taken from six patients with <u>rectal cancer</u>.

They found that different regions of a single tumor shared as much as 93 percent of genetic mutations and as little as 67 percent.

"Our paper shows that individual parts of a tumor are different. Some tumors have a lot of variation and some don't. This is the first time anyone has shown this in rectal cancer," says lead study author Karin Hardiman, M.D., Ph.D., assistant professor of surgery at the University of Michigan Medical School.

Genetic variation has been found in other types of cancer, including lung cancer, kidney cancer, and some types of leukemia.

Rectal cancer often returns in the area where it was removed, making treatments such as chemotherapy and radiation crucial in addition to surgery. Chemotherapy choices often are determined from the genetic make-up of the tumor.



"When medical oncologists make decisions about targeted chemotherapy, they typically base that off the results of a single biopsy. If they're testing only one biopsy, it may or may not reflect what's in the rest of the tumor," Hardiman says.

The study authors hypothesize that the differences within a tumor might make the cancer more likely to resist targeted therapies. They are studying patient biopsy samples and mouse models to understand why there is variation within a tumor and why that variation is not present in all tumors.

Mouse models of rectal <u>cancer</u> will also allow the researchers to understand whether certain therapies or combinations of therapies can make a <u>tumor</u> more or less likely to respond.

Results of the study appear in the Nature journal *Laboratory Investigation*.

More information: Karin M Hardiman et al. Intra-tumor genetic heterogeneity in rectal cancer, *Laboratory Investigation* (2015). DOI: 10.1038/labinvest.2015.131

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