

New technique catalogs lymphoma-linked genetic variations

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(Medical Xpress)—As anyone familiar with the X-Men knows, mutants can be either very good or very bad—or somewhere in between. The same appears true within cancer cells, which may harbor hundreds of mutations that set them apart from other cells in the body; the scientific challenge has been to figure out which mutations are culprits and which are innocent bystanders. Now, researchers at Johns Hopkins Medicine have devised a novel approach to sorting them out: they generated random mutations in a gene associated with lymphoma, tested the proteins produced by the genes to see how they performed, and generated a catalog of mutants with cancer-causing potential.

"Our goal was to correlate various mutations with potential to promote lymphoma," says Joel Pomerantz, Ph.D., an associate professor in the Johns Hopkins School of Medicine's Institute for Cell Engineering. For the study, to be reported in a January 2013 issue of [Molecular and Cellular Biology](#), Pomerantz and his research team focused on the protein CARD11. CARD11 plays a key role in signaling the presence of infection, which leads infection-fighting [white blood cells](#) to grow and divide. Certain mutations can turn CARD11 permanently "on," causing out-of-control cell division that results in cancers called lymphomas, which strike about 75,000 Americans each year.

To find out which [genetic mutations](#) would increase CARD11's activity, Pomerantz and his team made copies of the CARD11 gene in a way that made [random mutations](#) likely. They then used the faulty copies to make mutant proteins, and tested the ability of those proteins to trigger the

signaling reaction that is CARD11's specialty. This let the researchers figure out which mutations increased the protein's activity, and by how much—information that can be compared to emerging data about CARD11 mutations found in human lymphomas. "We found that several of the overactive mutations we'd identified have already been found in patients," Pomerantz says.

Noting that CARD11 is part of the NF- κ B signaling pathway, a target of some cancer therapies, Pomerantz says the new cataloging technique could lead to more personalized treatment. "We imagine eventually being able to correlate response to a particular therapy with a particular mutation," he says. For now, Pomerantz and his team are delving deeper into what gives the bad CARD11 mutants their special powers, looking for mechanisms to explain how certain changes increase the protein's activity.

More information: Paper: [mcb.asm.org/content/early/2012 ... CB.00850-12.abstract](https://mcb.asm.org/content/early/2012/12/27/00850-12.abstract)

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