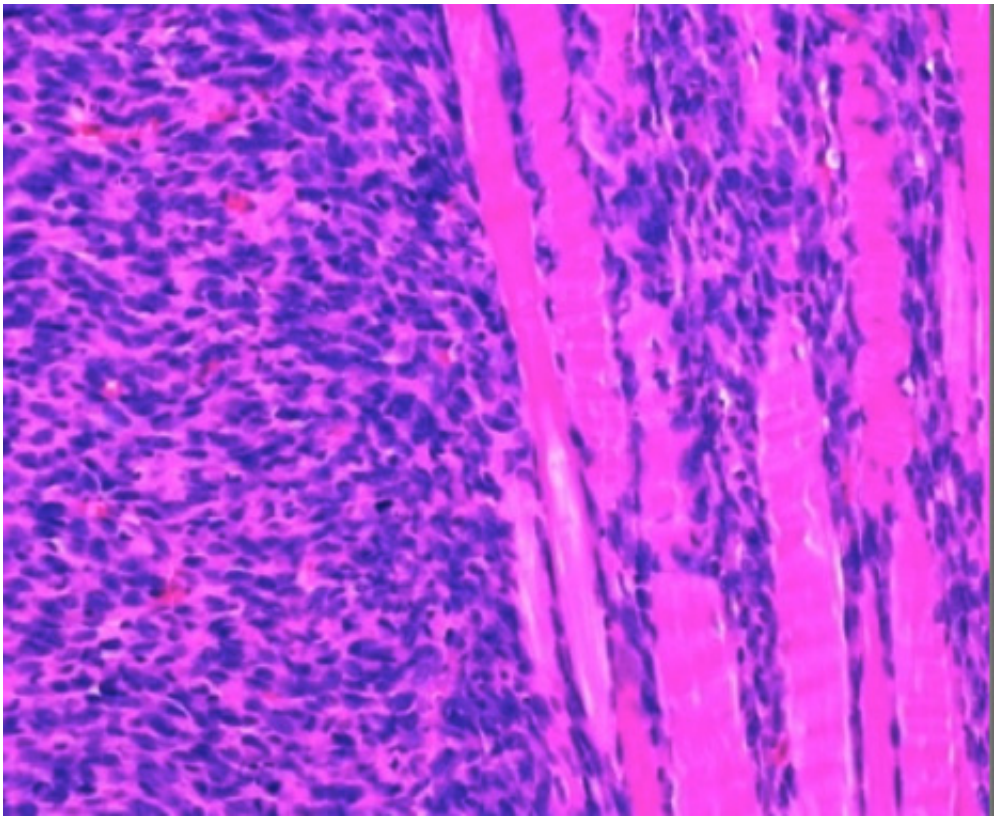
Researchers use cells to expand nature's repertoire

December 17 2013, by Bill Hathaway



Created by artificial proteins, tumor cells on left invade muscle cells in pink. Credit: DiMaio lab/Yale

Using a cell's own internal machinery, Yale researchers have produced proteins not found in nature that can cause cancer in mice, they report Dec. 16 in the *Proceedings of the National Academy of Sciences*.

The study not only sheds light on the way cancers may form, but also illustrates a new and efficient method to produce novel proteins that can be used for a variety of research, industrial, and medical purposes.

"This is a new class of biologically active proteins, which we found by simply expressing random amino acid sequences in cells and letting the cells find the active ones for us," said Dr. Daniel DiMaio, the Waldemar Von Zedtwitz Professor of Genetics, deputy director of the Yale Cancer Center, and senior author of the study.

Cell proteins are shaped by evolution from combinations of the 20 amino acids that make up the genetic alphabet, usually in chains of hundreds of amino acids. The Yale team was led by DiMaio and Yale College undergraduate Kelly M. Chacon, who conducted the experiment as part of her senior thesis. They wanted to know if they could create short, biologically active proteins that never existed in cells or had been discarded by the process of natural selection. They screened hundreds of thousands of artificial proteins consisting of random sequences of only 29 amino acids and identified four novel sequences that produced new proteins active in cell membranes. These tiny proteins do not appear to have ever occurred naturally and when introduced into mice, formed tumors—proving they were biologically active.

DiMaio notes that the random nature of natural selection may have led organisms to discard potentially useful protein structures that can be identified using this screening technique. These new forms of proteins can be used for a host of purposes, such as enhancing therapeutic responses or developing new molecules to create new biomaterials or disposal of waste.

"We will gain new insights into how proteins work and make novel products that we have not even considered yet," DiMaio said. "In addition, we may need to rethink our definition of genes, because cells

may naturally express these sorts of small proteins, which have been overlooked."

More information: De novo selection of oncogenes, www.pnas.org/cgi/doi/10.1073/pnas.1315298111

Provided by Yale University

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