

Synthetic molecules may be less expensive alternative to therapeutic antibodies, researchers find

April 4 2008



Dr. Thomas Kodadek, chief of translational research, led researchers who have developed a simple and inexpensive method to screen small synthetic molecules and pull out a handful that might treat cancer and other diseases. Credit: UT Southwestern Medical Center

Researchers at UT Southwestern Medical Center have developed a simple and inexpensive method to screen small synthetic molecules and pull out a handful that might treat cancer and other diseases less expensively than current methods.

In one screen of more than 300,000 such molecules, called peptoids, the new technique quickly singled out five promising candidates that



mimicked an antibody already on the market for treating cancer. One of the compounds blocked the growth of human tumors in a mouse model.

Antibodies are molecules produced by the body to help ward off infection. Natural and manmade antibodies work by latching onto very specific targets such as receptors on the surface of cells.

"Many new drugs being made today are antibodies, but they are extremely expensive to make. Financially, the U.S. health care system is going to have a difficult time accommodating the next 500 drugs being antibodies," said Dr. Thomas Kodadek, chief of translational research at UT Southwestern and senior author of the study, which appears online and in an upcoming issue of the *Journal of the American Chemical Society*.

"Our results show that a peptoid can attack a harmful receptor in the body with the same precision as an antibody, but would cost much less to develop," said Dr. Kodadek.

Peptoids are designed in the laboratory to resemble chains of natural molecules called peptides. Some peptides are used as medications, such as insulin or antibodies used to treat some cancers, but because the stomach digests them, most can't be taken by mouth and must be injected.

By contrast, peptoids are resistant to the stomach enzymes that degrade natural peptides, so it is possible that they could be swallowed as a pill. Peptoids are much less expensive and easier to manufacture than antibodies, Dr. Kodadek said. They are also much smaller than antibodies, so they might be better at penetrating tumors or other disease sites, he said.

"Our technique is simple and fast, works with existing chemicals and



needs no high-tech instrumentation, except for a microscope to detect the fluorescent colors we use to sort the compounds," said Dr. D. Gomika Udugamasooriya, postdoctoral researcher in internal medicine and lead author of the study.

The new technique also has major advantages over traditional screening techniques that are commonly used to discover biologically active compounds from large collections. These screens, which require extensive automation, generally cost \$40,000 or more; the new method can be conducted for less than \$1,000.

The researchers screened about 300,000 peptoids to see which ones would interact with VEGFR2, a type of molecule on the surface of human cells. VEGFR2 is essential in creating new blood vessels through interaction with the hormone VEGF, which is normally a helpful process but is harmful to the body when the new blood vessels are nourishing a growing tumor.

A commercially produced antibody is used to treat some cancers by blocking the VEGF-VEGFR2 interaction and thus starving the tumor, but it costs a patient about \$20,000 a year, Dr. Kodadek said.

The new screening technology involves hundreds of thousands of peptoids, bound to tiny plastic beads. In the study, the cells with VEGFR2 were labeled to fluoresce red and those lacking VEGFR2 were labeled to fluoresce green. After exposing the beads to the mixture of cells, the beads were examined under a fluorescent microscope. Those bound to red cells – the ones with VEGFR2 – were collected.

This screen, which took a couple of days, isolated five peptoids out of approximately 300,000 screened, showing that the process was an effective way to quickly narrow down a search, Dr. Kodadek said.



The researchers further tested one of the five peptoids that bound most tightly to VEGFR2 and found that it blocked VEGFR2's action in cultured cells. When they gave it in low doses to mice with implanted human bone- and soft-tissue cancer, the peptoid slowed the growth of the tumors and reduced the density of blood vessels leading to them.

"This new technique of rapidly isolating biologically active peptoids offers a way to hasten the drug-discovery process and may ultimately benefit patients by providing them with new therapies at a fraction of the cost of current drugs," Dr. Kodadek said.

Source: UT Southwestern Medical Center

Citation: Synthetic molecules may be less expensive alternative to therapeutic antibodies, researchers find (2008, April 4) retrieved 3 May 2024 from <u>https://phys.org/news/2008-04-synthetic-molecules-expensive-alternative-therapeutic.html</u>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.