MedicalXpress

From genomic data to new cancer drug

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New discoveries about follicular lymphoma, a currently intractable form of cancer, highlight the power of functional genomics in cancer gene discovery. A report in the Oct 28th issue of *Cell* demonstrates how genetic insights can be translated directly into therapies.

The findings are but one example of what has now become possible given the avalanche of data on cancer genomes.

"With access to tumor genomic data, suddenly we can do this; we know what has changed, and the question now is to define which changes are really important," says Hans-Guido Wendel of Memorial Sloan-Kettering Cancer Center, and senior author of this study. "With that information, we can start to develop new therapies."

Wendel's group has developed a way to target and shrinks tumors when delivered to mice with an incurable form of lymphoma. Loss of the anti-cancer protein known as EPHA7 (ephrin receptor A7) is an important driver of the disease, the new evidence shows.

"We went all the way from genomic data to a potential new drug," said Wendel. "EPHA7 was not on anyone's radar screen for lymphoma. Now it is."

Wendel's team focused their attention on a portion of chromosome 6 that is commonly lost in human patients and is related to poor outcomes. But such large-scale changes can only tell you so much. "Tumors often acquire complex genomic aberrations including gains and losses of large

sections or even entire chromosomes," the researchers said. "Identifying the target gene or genes from such complex genomic changes remains a significant challenge."

They used a method called RNA interference to silence genes in that stretch of the genome. That effort led them to EPHA7, a tumor suppressor protein that is shed from the surface of lymphocytes.

It is important that EPHA7 is a soluble factor, Wendel explained. "You can purify it, put it in a bottle, and see if it can be administered as a drug."

When the researchers injected EPHA7 into mice with human tumors, those tumors shrunk. They found that a particularly effective way to deliver EPHA7 to cancer cells is to fuse it with an antibody that specifically targets lymphomas.

The researchers say EPHA7 has immediate therapeutic potential, although they intend to pursue smaller versions of the protein that might be easier to make. There is also reason to think EPHA7 may ultimately have promise for the treatment of other forms of cancer as it binds a protein with links to breast and ovarian cancer.

Provided by Cell Press