Scientists find new genes for cancer, other diseases in plants, yeast and worms

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From deep within the genomes of organisms as diverse as plants, worms and yeast, scientists have uncovered new genes responsible for causing human diseases such as cancer and deafness.

The University of Texas at Austin scientists exploited the fact that all life on Earth shares common ancestry, and therefore shares sets of genes.

They found genes in yeast, for example, that humans use to make veins and arteries, even though yeasts have no blood vessels at all. Yeasts use those same genes to fix their cell walls in response to stress.

"Basically, we figured out a way to discover the genetic basis for disease by looking at organisms other than humans and finding disease equivalents," says Edward Marcotte, professor of chemistry and biochemistry.

To find the new genes, Marcotte and his graduate students developed a computer algorithm that first sifts through vast sets of existing genomic data for worms, mice, yeast, plants and humans. The algorithm pairs up sets of genes that overlap between these organisms and humans.

In doing so, it highlights genes that are known to work together to do one thing in the non-human organism, but the function of which are not yet known in humans. The scientists can then test those new genes in the lab to determine their function.

"The basic essence of the method is that there are ancient modules of genes that have been reused in different contexts over time," says Marcotte. "So the yeast uses a particular module with a particular set of inputs and outputs to do one task. Humans use this same module with different inputs and outputs to do another."

In the case of blood vessel formation, or angiogenesis, the scientists found 62 genes that yeast use to fix their cell walls that matched with a few genes known to be responsible for vein and artery formation in humans.

Developmental biologist John Wallingford and his graduate students then tested the human equivalents of the 62 yeast genes in developing frog embryos in the lab. This confirmed that eight of those 62 genes help build blood vessels in animals. Several of these genes were also confirmed in humans.

The newly found human angiogenesis genes are great candidates for drugs, says Marcotte.

"Tumors fool your body into feeding them by initiating blood vessel growth, and that's the reason we're interested in angiogenesis," says Marcotte. "So, genes for angiogenesis are common targets for chemotherapy. Some of the most effective chemotherapies block angiogenesis."

The scientists also found a set of genes in nematode worms involved in human breast cancer. Surprisingly, it is the same set of genes in the worms responsible for determining how many male offspring a parent worm births.

In plants, they found a gene that is involved with a genetic disorder called Waardenburg syndrome, which causes a significant fraction of

cases of human deafness. (Strangely, plants use the gene as part of their system for sensing gravity, called gravitropism.)

The researchers are teasing out genes for a variety of human disorders, from mental retardation and birth defects to cataracts. Their goal is to find new genetic targets for therapy.

"By exploiting evolution and looking at lower organisms that don't even have the organs we're looking for—blood vessels or even heads—but share some of the underlying molecular processes, we're able to discover genes relevant to human diseases," says Marcotte.

Marcotte admits it may seem odd to look for human disease genes in something like a plant or yeast, but that the information is proving to be extremely useful, if not surprising.

"When we found the genes in plants responsible for Waardenberg syndrome in humans," he says, "we were screaming in the halls."

Marcotte, Wallingford and colleagues published their research in *PNAS* (*Proceedings of the National Academy of Sciences*).

Provided by University of Texas at Austin