

Tree of life: Poplar studies yield human cancer insights

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Callus forms on a segment of poplar leaf, an essential step in bioengineering new plants with desired characteristics such as higher yields of biomass. Credit: Oak Ridge National Laboratory

While studying the genes in poplar trees that control callus formation, scientists at Oak Ridge National Laboratory have uncovered genetic

networks at the root of tumor formation in several human cancers.

The research team found, with some surprise, that [plants](#) and humans share the same [genes](#) that trigger or suppress the uncontrolled growth of clusters of cells—forming callus in poplar and tumors in humans. The genes originated billions of years ago when plants and animals shared a common ancestor.

"We'd never thought about such genes being conserved," said ORNL plant biologist Wellington Muchero. "But what we are seeing is this really surprising conservation of function between plants and humans."

The research findings, detailed in *PLOS One*, have applications in engineering better plants for bioenergy production as well as identifying new targets for cancer treatment.

A boon for bioenergy

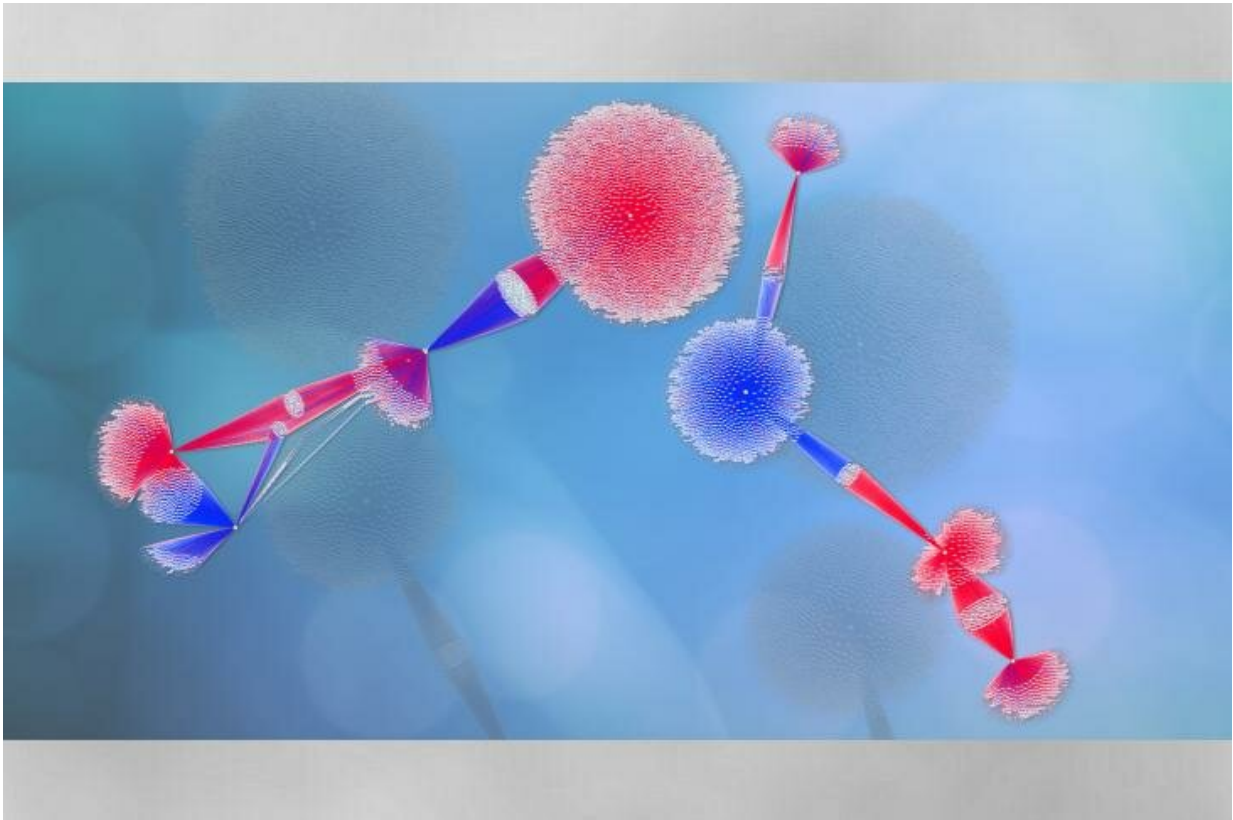
Populus or [poplar trees](#) show great promise as a bioenergy crop. Scientists at the Center for Bioenergy Innovation at ORNL are studying genetic variations in these woody perennials that can increase drought- and disease-resistance and yield more biomass to convert into biofuels and bioproducts.

The researchers' toolbox includes gene editors like CRISPR/CAS-9, a powerful [database](#) of genomic information from 882 poplar varieties, high-performance computing capabilities, and expertise stretching across multiple institutions. The bottleneck for enhancing key characteristics in poplar, according to Muchero, is callus formation.

Some plants grow callus easily. Others grow none at all. The research team used leaves cut from poplars of different genotypes to determine which genetic variations result in callus formation. Their analysis

identified genes that trigger rapid cell division and genes that restrict it.

"Callus formation is an important step in creating new genetically engineered plants," said Muchero. "Without the ability to form callus, you are at a dead end. You can introduce your gene, but you cannot grow the plant."



This visualization shows the genes (yellow squares) associated with callus formation in poplar. These genes have equivalents in humans that control the formation of tumors. The network of genes shown in red is expressed along with the callus-associated genes. The genes in blue are suppressed when the hub genes are active. Credit: Dan Jacobson, Oak Ridge National Laboratory

"Rapid regeneration of plants is one of the goals we are working towards," said Jerry Tuskan, ORNL corporate fellow and director of CBI. "We are studying cell proliferation as a means of increasing transformation efficiency."

What is healthy for poplar—active callus inducers paired with inactive callus suppressors—can be a recipe for cancer in humans.

Targeting new cancer treatments

All eight of the key genes for poplar callus formation have equivalents in humans. These same genes are associated with specific diseases, including chronic myeloid leukemia, breast cancer, and stomach cancer. While these cancer-causing hub genes are well known, it was only by examining them in [poplar](#) that scientists could see the connections between the hub genes and the array of associated genes that play a role in their regulation.

"We were able to build these networks of how these genes were related to each other and the intermediate signals that were co-occurring," said Tuskan. "With this library of co-expressed genes, pharmaceutical companies could begin identifying new targets for therapy."

A new drug could inhibit an associated enzyme from functioning, for instance, and switch off or block the genetic pathway that triggers a tumor to form. Poplar trees can help root out the best targets for drug development.

New platform for testing

Since poplars have never been domesticated, individuals vary widely in their genetic makeup. Scientists can often identify the genetic variant

that results in a specific phenotype or characteristic by examining a few hundred trees. In comparison, it would take hundreds of thousands of individuals to make a similar finding in humans, who are 99.9 percent identical in their DNA.

Stresses that cannot be applied to humans or laboratory rats can be used in controlled plant experiments to verify that a gene results in a phenotype under varied conditions. This richer understanding of how these [genetic networks](#) function could complement results from traditional mice studies to increase the efficacy of new drugs going to clinical trials.

"While we at CBI are focused on new knowledge and technologies for biofuels and bioproducts, it is very rewarding to know our work has broader applications to improve human health," said Tuskan.

More information: Gerald A. Tuskan et al. Defining the genetic components of callus formation: A GWAS approach, *PLOS ONE* (2018). [DOI: 10.1371/journal.pone.0202519](https://doi.org/10.1371/journal.pone.0202519)

Provided by Oak Ridge National Laboratory

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