

## Genome Insider Episode 8: A Plantiful Future: Xiaohan Yang

ALISON: Hey! I'm Alison Takemura, and this is Genome Insider, a podcast of the US Department of Energy Joint Genome Institute or JGI. Let me take you back to a workshop in Boston. Like any good scientific meeting, it was a thought-provoking surprise for this scientist. Let me introduce you.

XIAOHAN: I'm Xiaohan Yang from Oak Ridge National Lab, one of the National Labs funded by DOE.

ALISON: Usually, Xiaohan is researching away in the national lab in Oak Ridge, Tennessee. But before the pandemic kept him at home, he was out in Boston for this scientific workshop. It had brought together scientists, business leaders, and policy experts to talk about addressing that huge, existential problem that we wish were already solved: the climate crisis.

The workshop had high ranking and retired officials from the DOE Office of Science, business people... Not to mention all the other scientists. A quick rundown: biologist George Church from Harvard, biochemical engineer Kristala Prather from MIT (who is also a JGI collaborator), soil scientist Keith Paustian from Colorado State University in Fort Collins, plant ecologist Stan Wullschleger from Oak Ridge National Laboratory, and atmospheric scientist Susan Solomon from MIT. She's famous for helping discover the chemical culprit responsible for the last global climate crisis, the ozone hole. So, this was a pretty special workshop. As Xiaohan puts it,

XIAOHAN: That's the only workshop... different from other scientific focus workshops I have.

ALISON: It was different, because it was so... applied. It was unabashedly about using science to reduce greenhouse gases in the atmosphere. Those gases are overheating the Earth like an oppressive down blanket. Now, of course, Xiaohan is concerned about that, but he usually thinks about research taking a lot of time, and progressing incrementally. But there were policy experts at the conference who told Xiaohan something different.

XIAOHAN. They said, "We have a different perspective. I don't worry about your details, technical details, right? But just tell me, Can this solve the problem in the real world, not just in the lab, in the greenhouse. No matter your Science or Nature publications." So we need that, because they need to put it into their policy.

ALISON: I want to underscore what Xiaohan just said: publications, even if they're in rock star journals like Science and Nature — are not the end goal. What we want are breakthroughs that work outside the lab and can be used to cut greenhouse gases on a global scale. That's why Xiaohan was at that Boston conference. His work is on biology-based climate change solutions.

ALISON: Xiaohan works on designing plants to grow faster, in poorer conditions so that they can be used for biofuels, or as a way to soak up more of the greenhouse gas carbon dioxide. To give you a little historical perspective, before industrialization, when society began to rapidly

consume fossil fuels, carbon dioxide in the atmosphere was just 280 parts per million. But now, that number has ballooned dangerously by more than 40 percent to 412 parts per million.

Xiaohan wants to design plants to help alleviate this buildup of atmospheric carbon.

XIAOHAN: We need to customize the crops. We need more design in mind. Because the plants evolve not for human. There's maybe one or two traits good for human but not necessarily really serving our purposes.

ALISON: The way Xiaohan sees it, even artificial selection isn't enough to optimize plants in some of the ways that people care about, like addressing climate change. So, one focus of Xiaohan's research is..

XIAOHAN: Use the current technology to accelerate domestication of bioenergy crops.

ALISON: For example, let's start with agave. These plants often have spear-like, succulent leaves, and they thrive in the desert. Agave is a genus that gives us sweet agave nectar, rope fibers, and tequila. Agave uses crassulacean acid metabolism, that's CAM or C-A-M, photosynthesis, And when the environment is hot and dry, CAM photosynthesis, is way more water efficient than the more common C3 photosynthesis.

Xiaohan and his Oak Ridge colleagues worked with the JGI to identify the genes involved in CAM pathways. And they asked, can we take a gene that's crucial for CAM's efficiency, and transfer it to a different plant? The answer turned out to be, Yes, indeed.

XIAOHAN: So we engineer one gene from agave, that's a desert plant, into tobacco, a C3 plant very similar to poplar and other like major crops.

ALISON: The tobacco plant might sound like an odd choice - I know it was to me when I first heard it - but it's an easy to transform model system. So, engineering the agave gene into tobacco is a stepping stone toward putting the gene into poplar trees. JGI loves the poplar tree; it's a JGI Flagship Plant and a potential biofuel feedstock that's central to DOE's bioenergy strategy. OK, so getting back to that CAM photosynthesis gene — taken from agave, and plopped into tobacco. It turned out to be helpful in lots of ways.

Poplar (*Populus trichocarpa* and *P. deltoides*) grow in the Advanced Plant Phenotyping Laboratory (APPL) at Oak Ridge National Laboratory in Tennessee. Poplar is an important biofuel feedstock, and *Populus trichocarpa* is the first tree species to have its genome sequenced — a feat accomplished by the JGI. (Image courtesy of Oak Ridge National Laboratory, U.S. Dept. of Energy)

XIAOHAN: So, it increase both drought tolerance and salt tolerance and also increase the biomass yield. So, not only increased the growth above ground and also can increase the biomass below ground. That may be good for carbon sequestration to address the climate

change.

ALISON: In a second project, Xiaohan's team tried transferring another agave gene directly into poplar. But, unlike that first gene, this was a "mystery gene"; they didn't know what its function was. But when they put it in poplar, the plants had a new ability.

XIAOHAN: To our surprise, we found recently, they can delay dormancy. So, that means you can extend the growth period.

ALISON: That could be useful for poplar, which goes dormant when the number of daylight hours falls in the winter.

XIAOHAN: For climate change, gets warmer and warmer, but day length not going to change, right? If we utilize this new knowledge, and grow in like Florida, they can grow longer before go into dormant? Consequently, that way, you increase biomass.

So, it's kind of a new discovery. We get the knowledge from outside of our target species, from the plants that normally grow in desert.

ALISON: Building off their insights with single genes, Xiaohan and his team are now combining multiple genes into a genetic circuit. This approach has two functional elements - one: the coding genes that carry out biological functions and, two, the regulatory elements, which ensure that the genes get expressed at the right time, in the right location.

XIAOHAN: So right location I mean is, like, focus gene expression in leaf tissue. Not affect other tissues.

ALISON: That means that this approach could help minimize concerns about genetically modified crops. The introduced gene wouldn't get expressed in something you'd eat, like fruit, for example. Now, Xiaohan and his team are getting some positive results that open up new possibilities for where their synthetic plants could grow.

XIAOHAN: We have some prelim data showing the potential to increase growth, and increase water-use efficiency and also we have the technology to increase tolerance to drought and salt stress, so then we can expand the growing area, like the marginal lands.

Xiaohan (far left) stands with his CAM Biodesign team (left to right): Kaitlin J. Palla, Rongbin Hu, Degao Liu, and, in the ORNL greenhouse. Drought-tolerant succulent *Kalanchoe fedtschenkoi* plants capable of crassulacean acid metabolism, or CAM, photosynthesis are in the foreground. The JGI generated the genome sequence, as well as the gene expression atlas of *K. fedtschenkoi*. The agave genome is also being sequenced by the JGI. (Image courtesy of Oak Ridge National Laboratory, U.S. Dept. of Energy)

ALISON: But that's not all that Xiaohan is up to. He's thinking about something even bigger:

Designing a plant by selecting each gene in its genome. Why? Because no plant comes with everything you might want. For example, with food plants:

XIAOHAN: No single source of vegetables, fruits will meet our nutritional requirements - vitamins, or calcium, other like nutrient elements, right?

ALISON: Non-food crops are the same. The poplar tree grows fast — which makes it great for biofuel —

XIAOHAN: — but then their lignin content is not optimized for biofuel conversion, right?

ALISON: Lignin is a carbon-based compound that's really hard to break down — thus it's hard to use for biofuel. But lignin does make for an appealing way to sequester carbon. because microbes have a harder time eating lignin. So, Xiaohan is thinking let's engineer some strains of poplar to have less lignin, so they can be better biofuel feedstocks. And let's engineer other strains of poplar to produce more lignin, so they can better lock away carbon. Xiaohan thinks that's totally feasible — as long as we can meet the needs of the plant.

XIAOHAN: The poplar have to be happy themselves in the local environment right, then can serve the purpose as a feedstock for bioenergy or for the benefit of ecosystem service to reduce CO2 in the atmosphere.

ALISON: Xiaohan thinks plant scientists will be more effective at achieving these kinds of goals when writing a plant genome becomes possible. That might take decades to achieve, but Xiaohan doesn't think it's too out there. I mean, humans came up with something as complex yet functional as the iPhone, didn't we? Xiaohan thinks plants..

XIAOHAN: should be equivalent or more complex than iPhone.

My dream — I'm not sure in my career I can achieve that — is really design something just like an iPhone... iPhone-like plants to really customize plants for the benefit of human society.

ALISON: Xiaohan has a vision. He sees some plants being designed for medicine and nutrition, and other plants being designed for biomaterials, carbon fixation, and ecosystem services. Maybe they'll be designed to have extensive roots that prevent erosion or provide food for symbiotic microbes. To start to design a plant, Xiaohan aims to create a genetically minimal plant. To give you a sense of scale, we humans have an estimated 20,000 protein-coding genes. Plants can have a whopping 30,000 protein-coding genes.

XIAOHAN: Do you think that all of the 30,000 genes are necessary? Maybe not, right?

ALISON: For example, in the more efficient CAM version of photosynthesis, one gene in the pathway has five copies. And only one of those is highly expressed.

XIAOHAN: But then we'll have a second copy: much lower expression. May have some function there, right? The other three copies, no expression. So what's .. the, the function of those three copies? Why we need that?

ALISON: Xiaohan thinks, you might be able to get by with just the one highly expressed gene copy in a 'minimal plant'. To that end, let's look at *Arabidopsis thaliana*, a demure, flowering plant that researchers love to use as a model system.

XIAOHAN: Let's guess, 5,000 genes... is essential for *Arabidopsis*.

ALISON: Xiaohan hopes to use genome synthesis technology to..

XIAOHAN: ..put those 5,000 genes together in a single chromosome, right.

ALISON: OK,OK so, that's not going to happen tomorrow.

XIAOHAN: It's very challenging.

ALISON: But — and bear with me as we get a little nerdier about it — genome writing feels possible to Xiaohan, because of advances in using synthetic biology CRISPR/Cas9 technology for gene editing. This technology is so incredible, it's discovery just earned the Nobel Prize.

So, the Cas9 enzyme makes gene editing much easier than it was even a decade ago. And now, scientists have developed so-called second generation genome editing technology. They can take the original gene editing enzyme Cas9 and modify it. For example, scientists can hitch Cas9 to a second enzyme, like reverse transcriptase.

XIAOHAN: The big advantage for second generation genome editing is significantly reduce the rate of off-target mutations. So, I think technology is evolving. The technology will be more and more precise.

ALISON: So we've gotten a glimpse of the nanoscale — genome writing for plants. Now, let's zoom out. A few years ago, an article in *Science* magazine showed that just planting trees at an ecosystem scale could have a huge impact on mitigating climate change. Xiaohan and his team are also starting to think about their plants on an ecosystem scale. And for that, they're reaching out to colleagues.

XIAOHAN: We need another set of expertise. They do like ecological level modeling. We have people even at Oak Ridge who are doing that. Even with Berkeley Lab, we had a workshop, just before Christmas.

ALISON: i.e. A workshop about how to utilize plant biology to combat the climate crisis. Part of the equation that's been missing for plant research scientists like Xiaohan, has been the technology to thoroughly assess their modified plants.

XIAOHAN: My intent is to create a drought-resistant crop right? How are you going to evaluate that? So far, our lab, in the whole Oak Ridge plant biology group, we don't have the right expertise to do the whole self-assessment in a standard way.

ALISON: But companies are stepping in to fill this void. Xiaohan saw one present at a recent conference.

XIAOHAN: They, they have some like a phenotyping facility, very fancy, lots of cameras, they do machine learning based on imaging, right. It's not direct measurements, but I was very impressed by their claim. They have a lot of probes, just like go to hospital, that monitor your heartbeat and some other numbers.

ALISON: Probes above ground and below collect plant vital signs. They gather data on a plant's physiology, including how quickly water is evaporating from its leaves and how fast its roots are uptaking water from the soil. These measurements help keep enthusiastic scientists grounded in data. Because, a scientist might say,

XIAOHAN: "My genetic modified plants are great."

ALISON: But...

XIAOHAN: What's the evidence, right?

ALISON: Xiaohan wants to help the whole world through his research on plants. And one huge problem we're facing is how native forests and grasslands are being replaced by industrial agriculture. That's a practice that also releases greenhouse gases.

XIAOHAN: Food for us... very invasive actually in terms of like environment. If we increase the efficiency of the ideal crops, then we can leave a lot of land area untouched for ecosystem service. My dream, like an ideal world, ideal society will not be invasive species. Nature will be a friend of ours.

ALISON: Xiaohan believes that making better plants — plants that can grow on drier, more arid land, produce biomass more efficiently, and store carbon more permanently — could make a more sustainable world. Are plants cool, or what?

ALISON: This episode was directed and produced by me, Alison Takemura, with editorial and technical assistance from Massie Ballon, David Gilbert, and JGI's Communication intern, Ashleigh Papp.

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A huge thanks to Oak Ridge National Lab's Xiaohan Yang for sharing his research and vision of the future. And if you haven't heard it, check out Oak Ridge National Lab's podcast, The Sound of Science. Hosts Jenny and Morgan do a wonderful job of humanizing ORNL's science stories, which span plutonium-fueled space travel to a geneticist's passion for chocolate.

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