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An Interview with Dr. John Henning

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ABSTRACT

Dr. John Henning, hop breeder and genomics researcher at the U.S. Department of Agriculture, was asked about his work in developing new hop varieties and the current state of development in understanding the hop genome and what this means for future hop variety development. Currently, breeders are being asked for more flavors and stronger flavors, with an emphasis on tropical fruit. Future work will probably look at targeting specific oils and thiols made possible by genomic sequencing and markers.

Keywords: hop, genome, sequencing, Cascade, Teamaker, *neomexicanus*

Dr. John Henning has led the USDA-ARS public hop breeding program since taking over leadership from Dr. Alfred Haunold in 1996 and is the lead scientist presiding over USDA's hop research program. He has released nine hop varieties (Newport, Sterling, BitterGold, Mt. Rainier, Triumph, Santiam, Horizon, Teamaker, and TriplePearl) and 11 germplasm lines, with two highly anticipated experimental lines nearing public release.

He is an internationally recognized hop geneticist working at the forefront of hop research covering genomics and molecular breeding. He holds a courtesy professor appointment in the Crop & Soil Science department along with affiliate appointment in Oregon State University's (OSU's) Center for Genomic Research & Bioinformatics and collaborates closely with genomics and bioinformatics faculty at OSU and elsewhere.

Dr. Henning has become a leading expert in genetic mapping involving development of marker-saturated linkage groups. Within the past 3 years he has published multiple quantitative trait locus (QTL) mapping projects covering resistance to downy mildew, powdery mildew, and dwarf hop; two hop genomes (Teamaker and Cascade) with complete annotations as well as identifying the Y-chromosome specific DNA, X-chromosome DNA, and the paired regions between X and Y called the "pseudo-autosomal" regions; and was the first to identify the genes and genomic regions controlling one of the seven R genes for resistance identified in hop. Dr. Henning and colleagues from OSU have worked recently to assemble and annotate the complete diploid-phased hop genome into the 10 presumed chromosomes for the cultivar Cascade. This work is publicly available at www.Hopbase.org.

He has cooperated in several international studies with scientists from New Zealand, Germany, Czech Republic, Slovenia, and Great Britain. Finally, he works closely with industry partners to identify and validate molecular markers for multiple traits, which are being utilized for breeding purposes.

Q *If you are introduced at a party and somebody asks you what it is you do, what's your answer?*

A Typically I ask them if they're a beer drinker, and then if so I just let them know that I'm a hop breeder and that I'm breeding for the United States Department of Agriculture. And a lot of the hops that they've drank beers from have come from that program and would continue to come from that program.

Q *Would your answer have been different 5 years ago?*

A Maybe I would have said more about genomics work 5 years ago. We've had such great success in that area. I don't necessarily bring that up. And typically when I did in the past, you'd see people's eyes glaze over and they'd start to lose interest. But you always have interest from people when you talk about beer and what goes into it.

Q *Have your goals as a breeder changed in recent years? And if so, how?*

A Yes, they have. There's a strong emphasis now—for all of the breeders, not just me, but for all breeders—to really come up with new unique flavors. And, interestingly enough, if that new and unique flavor is sufficiently desirable, but it's not as dramatic of a concern as it used to be. Yield used to be the big thing, yield and disease resistance. They're both still part of a strong program that I focus on. But I've actually had brewers ask me, hey, would you throw something away if it was such a fantastically unique aroma, but it only yields six or seven to eight bails? I probably wouldn't throw it away now if it's that good and that desired by brewers.

I should add that I will be incorporating looking at heat stress. I've had a postdoc, Renee Ericksen, who was doing research with me for a couple of years, and her full focus was on hop's reaction to heat and drought stress. So we have a lot of very good data on that. And we have a fairly good idea of what genes are getting turned on during heat and drought stress. And we also are working towards getting some funding to actually start identifying some markers that would be linked to drought stress or heat stress.

Q *Before I ask the next question, we probably need to fill in readers on the five botanical varieties of* Humulus lupulus. *Do you have an elevator explanation for brewers?*

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A The cultivated hop is *Humulus lupulus* var. *lupulus*. Other members of *Humulus* species that can mate with the cultivated hop are the closely related wild species *H. lupulus* var. *neomexicanus*, *H. lupulus* var. *lupuloides*, and *H. lupulus pubescens*. These wild species are thought to have evolved from lines carried by early human migrations from Asia. Finally, a more distantly related line would be *H. lupulus* var. *cordifolius*, the so-called "wild hop" of Japan.

Q *Because* neomexicanus *hops have survived in the American Southwest, does that mean they are better suited to a future that might include more heat incidents like the one that occurred this summer in the Northwest?*

A It probably does, but they're not the only source. In looking at the lines that I have in both single-hill plots and advanced plots, there are significant differences between families and then between crosses. I have two crosses that I was really thinking about potentially releasing fairly soon. However, one of those crosses did very poorly. The other cross has grown and flowered like there's nothing wrong. It just looked at the heat and at everything and said, hmmm, I'm fine. Even without the incorporation of *neomexicanus* we are developing heat-resistant lines.

Q *When you talk with growers across the country, from Michigan and Vermont and New York and so on, what are their burning questions?*

A They would really like to see something that has built-in resistance. They're necessarily OK with powdery mildew, but downy mildew is their biggest concern because it's so devastating out there. But they'd also like to have something that grows well out there. Something that grows well in Washington may not grow well in other states. So I've also been trying to get a lot of my experimental lines out into the Midwest and start growing them out there and seeing how well they do out there in that location. And there are some varieties even that I'm thinking probably have more of a market there in the Midwest than they do somewhere else. There's nothing saying I wouldn't release those lines that do well out there in the Midwest as varieties specific for the Midwest or the Northeast. They don't necessarily have to do fantastic in the Pacific Northwest. It's a justifiable release.

Q *How can farmers outside the Northwest get involved to see how well experimental lines will grow in their yards, and provide you useful feedback?*

A The best way would be for farmers outside of the Northwest to work with a state extension agent or university faculty to set up plots, either at the university or on their yards, but monitored by faculty or extension. This way, more than one farmer can benefit from the resulting data, and the data can be publicly available through extension bulletins or websites.

Q *In the 1950s, 1960s, and even 1970s, when the breeding programs really got rolling in the United States, was there much thought given to breeding for regions beyond the Northwest?*

A Not that I could see. I mean, it was very focused. I'm going to say laser focused.

And it was laser focused on what was currently the important brewing community at that time, which would of course be the macro brewers and alpha level. I suppose I was the first to start shifting that focus to other regions and targets.

Q *What's the number one question you get from brewers?*

A What's the next hop of that I'll be releasing? That's always the question. The other thing they'd like to see is unique flavors, again. They're not so interested in yield. They're not so interested in disease resistance, although I should take that back. They're interested in disease resistance from their perspective. They don't want to see any pesticides in their hops, the hops that they're purchasing. They would love to have something be pest resistant so that they don't have to deal with any sort of pesticide residues. But, really, most of the growers do such a good job in timing their sprays that the pesticides don't show up in their hops anyways. Brewers really want flavor.

Q *What questions would you like to see the brewers ask more often?*

A Gosh, I would love to get more specificity in terms of what flavors or compounds they're interested in. If we as breeders have flavor targets that are a little bit more discernible, that makes it a lot easier for us. So, if someone really likes linalool, for example, let us know—or geraniol, limonene, any of these other compounds that are specific targets. We can select for that a lot easier than just saying "I want something with unique flavor," because unique flavor can mean anything.

Q *So you can target for linalool?*

A Yeah, you could. We can make our selections for linalool or things like that.

Q *Do you have markers for it?*

A I have tentative markers. For some of the essential oils we're working toward kind of pinpointing down a wide range of markers for the different compounds. That's going to take a little bit of funding from the brewers maybe, but that's necessary to really get this done. I can do an OK job on a smaller budget, but to do it right it needs a bit more money.

Q *What about thiols? It is only in the last 15 years that we've begun to understand the role they play in aromas and flavor currently in demand, often described as tropical and so on.*

A Thiols have become, in many respects, more important for development of new cultivars. These minute but powerful compounds are the cause for much of the tropical and citrus flavor so desired by brewers. Unfortunately, chemical analyses for these compounds are relatively expensive (about $200 per sample), so we typically don't analyze many samples per year. The Hop Quality Group has been aiding my breeding program in many ways over the past 6 or 7 years, and one of the ways they've helped is by identifying superior lines from breeding and then paying for analyses of these lines for specific thiols. Several breeding lines have been selected and advanced to the next stage based primarily upon these analyses.

Q *Now we were talking about the hop genome, right? When did you start your work on mapping the genome?*

A I believe I was talking about it back in 2010, even 2009. And the first funding that I got for it was in 2012, from the Hop Research Council as well as one of the private hop breeding companies. But I look back at some of that now and just think, "Wow, what I didn't know!"

Q *What has made it possible to sequence the hop genome?*

A Probably the biggest thing that's been happening is just the technological advances in sequencing itself. Early on we were able to do what's basically called short read sequencing, which would be sort of first generation, maybe second generation. I'm not sure what they call it, but short read sequencing, which is what I started off with and which is what we used to make the Teamaker genome. But then the advent of the third generation and even the fourth generation of sequencing has really allowed us to put together the genome.

Q *Where do we stand now?*

A We have sequenced all 10 chromosomes and all of the genes and their locations and as well as over one million single nucleotide polymorphism (SNP) markers, and all of that has been mapped. We now have what we call the linkage disequilibrium blocks or LD blocks. So we know which regions actually will recombine or areas of the genome that will not recombine—in other words, blocks of genes that always pass on to the next generation in the same fashion. So, if we have a gene that's within one of those linkage blocks, we know that it's always going to be present in certain configurations.

We hope to have this genome published by the end of this year, certainly submitted before then. But I've already used that genome for developing maps for powdery mildew, downy mildew, plant height, and for genome-wide association studies for traits such as essential oils, alpha acid, beta acid, and a number of other important compounds or traits. And I know where the major regions of influence in the genome are for all of these traits.

Q *What's the difference between mapping a plant genome and, say, the yeast genome or the human genome? Is it true plants are more complicated?*

A Yes, and certainly hop. Hop is very complicated because it looks like there's been three evolutionary episodes of replication. If you look at the hemp genome, it's only about 700–800 megabases long, so it's fairly simple. Then amplify that three times and add in things called transposons and retrotransposons. These latter non-gene regions have a tendency to tandemly replicate through the generations, which results in expansion of the genome size on top of the whole genome getting replicated. These transposons and retrotransposons used to be called "nonsense DNA."

We now know that's not true, but this would be just replicated regions of the genome that are caused by transposons. And so we have all of this sort of replication going on there. Then you have a plant that's outcrossing, so it's not an inbred cross. So you constantly have heterozygosity going on because of that outcrossing. Plants that are inbred, those are relatively easy to sequence, to work with, because there's not a lot of variability there—inbreeding gets rid of the variability. When you start talking about something that's very heterozygous, has a lot of repeated DNA, and then has whole sections of the genome repeated—that's when you start talking about some real difficulties. And that's why the hop genome was such a difficult one to actually do.

Q *What needs to be done next in terms of the sequencing?*

A Now we need to start sequencing other hop genomes, not just one. My group is in the process of sequencing two male hop genomes—one of which is completed and the second one is soon to be finished. That's something that definitely needs to be done, to sequence the hop male genome, because there's the whole Y chromosome, but we don't have specifics about the whole chromosome—only the part that pairs with the X chromosome. Sequencing a female, we have just the X chromosome. So sequencing more genomes, males, but then sequencing a lot of the other female varieties that are out there. There's a lot of variability, and Cascade may not be representative of everything out there. There's a lot of work that needs to be done still.

Q *If we look back across the family trees of the hundreds of hop varieties available, an astonishing number have Brewer's Gold or Fuggle somewhere on their trees. Should breeders have taken more advantage of the diversity in the genetic makeup of American wild hops?*

A Yes. It should have been done. One of the problems when using the wild hops, and I did quite a bit of work in this early on, is you can make your cross with a wild hop, but your offspring are so far from what you are targeting for a variety that it's a really long-term process. So it probably doesn't make a lot of sense for a plant breeding company to be focusing on that. But I do know that they are making crosses with wild genotypes. And that's what we call our "back 40" programs. That is, the field is out in the back 40, and all of us breeders are doing that.

But if you think about it, half of your genome, once you make a cross with a wild line, half of your genome is now wild type, and how do you breed something from it that's going to be high yield or has good storage stability, or reasonable alpha levels? You can go down the list. Some wild-type traits aren't necessarily desirable.

Q *Your lab is not set up to identify if feral hops are actually a known variety, or perhaps the offspring of one. What alternatives are there for discovering the possible heritage of hops found growing in the wild?*

A One can potentially identify a hop based upon its chemical composition including bittering acid levels and relative levels of essential oil compounds. A more accurate method is the use of molecular markers. A colleague of mine in USDA, Dr. Nahla Bassil, and I recently submitted a paper that describes two molecular methods to identify an unknown hop line. Once this is published, any genetics laboratory can use these methods to identify an unknown hop line or provide insight into the genetic ancestry of a feral hop.

Q *Are you still excited to go to work most days?*

A I am. And I've got the best of both worlds. I get to be out in the field just doing regular farm work. Then I get to sit down and do high-level complex genomics studies, and then writing and evaluations at the same time. But as I age in my career, I think I get more excited about varieties that are releasing than I do about which papers get published. When I was a lot younger, papers were the big thing, and if you've been in USDA, you know why, because it's publish or perish. As I mature in my career, and I understand what's of more importance and what's a better legacy, people remember who released a variety. They're not going to remember who wrote a paper.

Q *Meanwhile, the community of breeders is much larger than when you started.*

A Yes, and there are more all the time. They're starting a hop breeding program in New York, which has gotten funding and it's taking off. Minnesota would like to start their own breeding project as well. Josh Havill is sort of spearheading that in that area. Nebraska also has a breeding program going. These are the public ones, and then, of course, you have the private companies. I'm trying to help out as much as I can for New York and Minnesota and Nebraska, trying to provide germplasm for them to get things moving forward.

Q *Which of the many hop varieties that you have released are you most proud of? And do you think some of the experimental varieties that have only numbers now have the potential to be even more memorable?*

A I'm very proud of Triumph. However, my soon to be released "074" (her name will be revealed in an upcoming release) will potentially have a greater impact based upon its amazing aroma and flavoring potential, high yields, and drought/heat tolerance coupled with high adaptability across all of the United States, from the Northwest to Vermont.

It appears you have just answered most brewers' favorite question! Thanks, John.