Bringing pharmacogenomics to the masses

HudsonAlpha Health Alliance outreach program facilitates adoption of clinical genomics testing

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Devin Absher, PhD has studied the genetics of complex human traits and diseases for over 20 years and was a pioneer in genome-wide and epigenome-wide association studies. He continues pursuing his passion for human genetics as a faculty member and Director of Genomic Health at HudsonAlpha, a nonprofit biotechnology institute in Huntsville, Alabama. We spoke with Dr. Absher about the mission of HudsonAlpha, his clinical work in pharmacogenetics (PGx), and how a recently validated lab developed test (LDT) improved his lab's workflow.

Q: What is the mission of HudsonAlpha Institute for Biotechnology?

Devin Absher (DA): HudsonAlpha was founded with three mission areas originally. Research is the primary mission area, with 16 faculty that run robust federally funded research in both human and plant science. This research team serves and collaborates with academic medical centers, including the University of Alabama at Birmingham (UAB).

We also have an educational mission. Our educational program is designed to elevate scientific literacy, both in our state and around the country, specifically around genetic and genomic literacy. There are a lot of programs for everything from high school students and middle school students, all the way to clinicians and the general public. We have programs that develop modules for teachers to help them with their science classes. We have training and summer camps, where students and educators come here to learn about genetics and genomics. We also help clinicians with information about genetics and genomics and how it might impact their practice in medicine.

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Our third mission is economic development. We are a nonprofit situated on a campus that's also the home to 46 biotech companies—typically small biotech companies. By having this community of genetics-focused industry here in Alabama, we are trying to diversify the economy and bring biotech to the state. It's an ecosystem that facilitates interactions between the for-profit companies and the nonprofit, HudsonAlpha.

Q: How has the mission of HudsonAlpha expanded?

DA: Six years ago, HudsonAlpha added a fourth mission area, what we call Genomic Health. This mission area focuses on driving the adoption of genomics in clinical care and how to bring the expertise that we have to clinicians, to health systems, and even to large employers who are doing a lot of genetic screening as a wellness benefit for their employees. We are looking at just about any environment where genetic testing is being deployed, but where there's not enough expertise to do so effectively.

One of the ways Genomic Health facilitates the adoption of genetics is through an entity called the Health Alliance, which assists our partners in the establishment of genomic medicine programs. We also have a clinic on our campus, the Smith Family Clinic for Genomic Medicine. This is a focused referral clinic for rare genetic disorders, where patients can be diagnosed. Then we have a CLIA/CAP* -certified lab, the Clinical Services Lab, that makes genomics-based lab tests available to our clinical partners. Services include whole-genome sequencing, PGx, and precision oncology tests. As Director of Genomic Health, I oversee all of our clinical efforts—the clinical lab, the clinic, and the Health Alliance—and forging mutually beneficial partnerships between HudsonAlpha and health systems that need our help and expertise.

Q: How does the Health Alliance support health systems?

DA: The Health Alliance bundles all the things that we do at HudsonAlpha, including the education and engagement components for patients and physicians, to prepare health systems to deploy a precision medicine program. Our program integrates not just the lab tests, but all of the clinical support components around it. This includes access to the medical expertise we have, medical geneticists and genetic counselors; access to the clinical lab, which provides the lab tests and interpretation of genetic data for clinical purposes; it's an end-to-end service that the Health Alliance

* CLIA, Clinical Laboratory Improvement Amendments; CAP, College of American Pathologists

provides to a health system to give them all the tools they need to make genomic medicine successful.

It's very common for health system administrators to say, “we really want to get involved in precision medicine, so we're going to make a test available.” But without all of the support pieces around it, they'll often get very low uptake. Their patients will not consent for these tests, or their physicians won't order the tests. The Health Alliance brings a project management perspective to the process. It's not just a lab test, it's a project that involves lots of pieces that are customizable for the needs of that particular health system, and their needs vary widely. Some of them may have pharmacists who can interpret these results and write up clinical notes, for example. And other places may not have that expertise in house. Some of them may have genetic counselors and some may not. The Health Alliance has all the various components of expertise that are necessary to make programs like these successful and to fill in any gaps.

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Q: Where does the Health Alliance focus its outreach efforts?

DA: It’s natural for large academic medical centers to be the home of genomic medicine and precision medicine. But there are a large number of patients who never go to an academic medical center for their care. Many places in our health care system don’t have expertise in genomics. We’re talking about community health systems, regional health systems, rural health systems, or employers who might be running a wellness program. The Health Alliance is really designed to help facilitate the rest of the health systems’ adoption of genomics in their care models.

There’s a need out there that we can fulfill. Our strategy is to find the health systems that really need help. If you just look at the state of Alabama, for example, there are parts of this state with really poor access to health care. And that’s true in rural parts of lots of states in the US. Obviously, the lack of access to genetic testing is going to continue to drive a divergence of access as the more urban and wealthier areas adopt precision medicine, and the more rural areas do not. You’re going to see even greater discrepancies in health care outcomes. As an independent nonprofit, we make an ideal partner for those places.

Q: Do you serve communities outside of Alabama?

DA: It continues to expand. We currently have a project with a Native American tribe in Oklahoma, the Muscogee Creek Nation, which is a really interesting group, a tribe that has really wanted to take the lead in precision medicine. They're interested in having their citizens get access to genetic testing. We're helping them

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build genomic medicine activities within their health system and providing support to do that, all while ensuring that they have the appropriate autonomy and control of their own data.

One of the things that I think distinguishes HudsonAlpha's approach to this from other for-profit companies is that we have a patient-centric approach that gives patients, and health systems, control and autonomy around their data. We are not here to monetize that data. We are here to lower the barrier of entry for health systems that need the help.

Q: How are you using PGx and what impact do you hope to make with that?

DA: Whenever we've talked to health systems, or to employers who are interested in some sort of genetics program, pharmacogenetics is often the first step that they take into that space. It's highly relevant to a large number of patients or study participants because of the number of medications that people take and because of the frequency of the variants that influence the metabolism of those medications. For many health systems wanting to get involved in precision medicine, it's just a natural first step to start with PGx. We think that that is a gateway to more utilization of genomics in care. Once they've started in PGx, there's often an awareness of how other genetic tests can benefit their patient population.

Q: How do your Health Alliance partners use PGx testing?

DA: It depends on the program and the health system, or the employer, and what their goals are. Sometimes these tests are offered generally to every patient or participant in a program, regardless of whether they're even taking medications. Obviously, it could inform medication choices down the road. The benefits may come to the patient 5 or 10 years later, but it still has value. Other programs are trying to have an immediate impact, so they will enroll participants that are on specific medications, or who are on multiple medications, in hopes that these tests will inform choices for their physicians about what medications are appropriate, or inappropriate for them.

On the employer side, there are economic advantages. Some retiree unions have done large-scale pharmacogenetic testing in their populations and they've shown that they actually save money in their prescription drug costs by getting people onto drugs that are most appropriate for them.

Q: What tools have you been using for your PGx testing?

DA: Prior to our lab's recently developed solution, we were using a less comprehensive genotyping array. We supplemented that older array with TaqMan assays to cover variants in certain genes, specifically copy number calls for *CYP2D6*, that the platform didn't really assess well. What's shifted recently is that the Clinical Services Lab has validated a new array with enhanced PGx markers to help make that a more comprehensive test. It has a lot more content that is relevant for PGx. It also has a lot of redundancy built in to ensure success for clinical tests and it eliminates the need for some of the ancillary assays we were doing previously. So, we think it's a good choice for a PGx test.

Since it also has a lot of genome-wide markers, the comprehensive array we are using can serve a lot of different purposes beyond just PGx. It gives you the ability to do other genetic association studies, impute polygenic risk scores, and even screen some of the other clinically relevant content covered by the array, including rare variants and genes recommended by the American College of Medical Genetics for screening of adult, actionable diseases—cardiomyopathies, heritable cancers, and other diseases.

There are other things the platform brings that a straight PGx test doesn't. I think that's also a reason why we chose it. Particularly, in the populations that we serve, including non-European populations, the diversity of the markers on the array for imputation, or for direct typing of clinically relevant variants for those populations, is another advantage.

Q: What inspired you to evaluate the comprehensive PGx array upon which you built your LDT?

DA: The array provides a lot of different content for different clinical contexts. It covers everything from a PGx perspective that carries strong clinical evidence behind it. Everything that you would want on a clinical pharmacogenetics report, you can derive from this array. On top of that, you get side benefits of much more genetic data that is useful in a diverse population.

The cost of this test is low enough that it can be used for screening purposes and the cost is reasonable enough for a lot of people to pay out of pocket. Health systems or employers will pay for it because there are some immediate benefits to the patients and for the potential economics of it. There is also increasing reimbursement for PGx testing.

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Q: How does your lab validate this assay for complex genetic targets, like copy number variation?

DA: All of the assays that our clinical lab runs go through a technical and a clinical validation using known clinical samples as a comparator. This validates that the assay is accurately calling the variants in those genes. We have a whole end-to-end validation from using either blood or saliva, all the way through the lab work and reporting, to ensure that the results are accurate and consistent with clinical expectations. It's very much like most other clinical lab tests in terms of how it's validated for those specific variants.

Q: How has using a single comprehensive PGx workflow benefited your lab?

DA: From a clinical lab perspective, it definitely helps to have one process, rather than multiple processes, to manage for the same patient. That really makes the validation easier and, in theory, produces more consistent and accurate data.

The effect on operating costs remains to be seen. In theory, the time and effort needed by people in the lab to process one workflow, instead of two or more, obviously is a potential benefit. The data pipeline makes it easier to process all of the data in the same way, rather than having multiple platforms doing different parts with potentially different QC metrics and things to track.

Q: How is your adoption of the comprehensive PGx array benefiting patients?

DA: First, the ability to genotype everything and provide both PGx and other clinical information from the same platform—whether you identify a cardiomyopathy or a cancer risk variant—can be helpful to those patients that are part of a screening program. Second, the PGx array content is pretty comprehensive in terms of the genes and the gene/drug combinations that it can inform. There's just a larger number of patients that are going to be impacted by this.

There's no doubt that there are patients out there taking medications that they're not metabolizing, and they're receiving little to no benefit from taking those. And, there are some who are taking medications with side effects that could be avoided if they knew their genetic profile. That's true in the cardiometabolic space and it's true in antidepressants. There's potentially a lot of benefits, some of which are short term and some of which are longer term.

Q: How is HudsonAlpha helping with genetic information control and electronic health records (EHR)?

DA: We're building a HIPAA† -compliant platform called Genome Gateway that is designed to be a permanent patient portal independent of one's health system. This will allow patients to get their genetic test results in an educational context so they can get just-in-time education around a test result. They can potentially secure and store that data and share it with other physicians. Then the clinicians who order the test will be able to do so through the same portal and interact with that data. We are building the pipeline to push that into the EHR in a way that makes it actionable for that particular health system and physicians within it.

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Q: In your opinion, what barriers do you see to clinical adoption of PGx testing?

DA: To me it's not a technological barrier. It's not a process barrier. It's more of an educational barrier. It's preparing physicians for utilizing genetic test data in their everyday practice, understanding what tests like this can tell them, and what they can't. One of the things we feel HudsonAlpha can be is an honest broker. Since we are a nonprofit, it's not our mission to sell tests that we don't think have true clinical utility. Just getting the clinicians to be comfortable with this—to provide them with the necessary clinical decision support and consult as part of the test—we think is the biggest barrier. Also, educating patients by informing them about what tests like this can and cannot say about their health care. That's even more important on the genetic side of disease risk where risk is really hard to understand. Most patients don't know how to act on that information, and they need a lot of help. This is why genetic counseling is so valuable. But the more we can do to educate and inform people before they get these tests, the more their expectations are set appropriately, and we can avoid the over interpretation that sometimes happens in genomic medicine.

Q: How would you like to see pharmacogenetics impact healthcare in the future?

DA: Ideally, we would like to be in a place where everybody has genetic data accessible in their medical record in a way that can inform their care today and in the future. That means portability of data, security of data, the ability to reinterpret that with new scien-

† HIPAA, Health Insurance Portability and Accountability Act of 1996

tific knowledge, and the infrastructure that can facilitate all of those things. Our health system is not currently built to house genomic data in an EHR, or in a physician's office. That's where Hudson-Alpha can play a role and be a gateway to that genomic content in a clinically validated way, providing both data and resources—educational and clinical content resources—to the health systems. To me, the future is when everything becomes seamless, and a patient's genomic data is something that they carry with them throughout their life.

Learn more

Benefits of pharmacogenomics, illumina.com/areas-of-interest/pharmacogenomics.html

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