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Early Diagnostics for Neurodegeneration, first steps in ALS and Alzheimer's Disease Prevention

Dr. Sean James Miller
CEO

Pluripotent Diagnostics Corp. (PDx)
https://pluripotentdiagnostics.com/

Interview conducted by:
Lynn Fosse, Senior Editor
CEOCFO Magazine

CEOCFO: ***Dr. Miller, would you give us a little background on Pluripotent Diagnostics Corp, PDx?***
Dr. Miller: Absolutely! Pluripotent Diagnostics, or PDx as we like to call it, is associated with early detection of neurological disorders. In particular, we are currently heavily focused on ALS/Lou Gehrig's disease and Alzheimer's disease. We have developed computational models with artificial intelligence and high-performance computing; this is non-invasive blood draws or cotton swabs from our patients. Next, the PDx team uses all the medical imaging data from the patient such as medical imaging files, clinical data, genetics, stem cell induction and longitudinal imaging, and other multi-omics that are available.

This allows us to create a comprehensive profile for each of our patients, with which we are then able to look for early signs of neurodegenerative disorders. If we do find symptoms or signs of these disorders, then we can move into early intervention or therapy. Early diagnostics means early treatment and that is really the idea and focus right now of how we can combat some of these neurodegenerative disorders before pathology really takes over.

CEOCFO: ***What can you extract? What is the AI able to come up with that your computational approach, could not be done?***
Dr. Miller: We have partnered with major international institutions to utilize the large patient datasets in the scientific community. This data, for example over 100,000 patients, was used to establish our high sensitivity, and low false-positive detection system. It is the ability of newer technologies in biomedical and computational systems to detect anomalies in our patients that we couldn't previously detect. For instance, we have 200 TB of clinical data for our patients, and with this we have established novel architecture and pipelines to efficiently sort, filter, and uncover associations only in our disease patients and never in the healthy control.

CEOCFO: ***What might your system pick up? What type of an indicator; three more red marks here show something, two things linked together here show something else?***
Dr. Miller: At PDx, our systems are capable of detecting novel patterns and anomalies in our patients. We provide a complete comprehensive profiling for each individual that is focused on much more than single categories for disease associations. To answer your second question, absolutely, our system is training and performing better every day to find associations between numerical, text, and imaging files of our patients.

CEOCFO: ***How did you know when you had enough information and when it was right?***

Dr. Miller: With COVID, it really provided us an opportunity to discover like-minded scientists dedicated to tackling the world's most complex disorders using cutting-edge technologies across multiple fields. We actually worked twelve hour shifts every day for seven days a week for months, because we have access now to large databases for our patients of eight hundred ALS patients and up to fifteen thousand Alzheimer's disease patients. At PDx we are continually increasing those sample sizes as well. However, when we ran this genetics data first on our ALS patients we were really focused on more of a yes or no, because we are a diagnostic company, we do not want to provide such thing as a false positive to one of our clients or patients, especially for something so devastating as a neurodegenerative disorder.

Our approach was not only looking at very strong and stringent statistics. But where we performed and created our models for our ALS patients, where we only find these genetic symptoms or genetic mutations associated with just the ALS population and never in a healthy person. We compared and performed models with the support provided by some of our collaborations with NVIDIA's Inception Program for AI startups, Amazon AWS, and Oracle for Startups. We were working on an ALS model for almost a year now, but it was only about two months ago that we actually realized what we had. That is when by using a genetic mutation classifier, we were able to input raw sequences from any patient in there, because we have, at PDx, our own adaptation pipeline, base alignment, and annotation software programs.

We are really experts now in this field and what we can do is take those files and then put it into our genetic mutation classifier and identify the risk of developing ALS, and with, as I said, such a low false positive rate, that is essentially at zero-point one percent, so it is very statistically significant. Just to add some context into the idea of our diagnostics and what has been previously done in the ALS field. In 2011 the NIH/National Institute of Health, discovered that there is a gene mutation within ALS patients that is not found in healthy controls to such a degree and this consists of about five to ten percent of all ALS patients. On a genetic level, five to ten percent of all ALS patients expressed this mutation in the gene called C9orf72 (chromosome 9 open reading frame 72). In the ALS field for this whole past decade, we thought that this is definitely the golden ticket to ALS discovery on a genetic level. That is a five to ten percent. Our approach here in 2020 is now showing that we are able to identify up to sixty percent of our patients with ALS at a zero-point one percent false positive rate. Therefore, you can see that we are increasing five/tenfold increase prior to what was recently discovered about ten years ago.

"PDx's mission is patient-first, by providing an opportunity for our aging population to be screened and diagnosed with dementia before disease onset. This provides us an opportunistic window to start early patient-specific therapies to combat neurodegeneration." Dr. Sean James Miller

CEOCFO: ***What has been the interest from the medical community?***
Dr. Miller: We have some wonderful collaborations with some top tier institutions and companies right now that are really excited about what we are doing. You will see some of our press releases coming out about new team members and scientific advisors joining PDx Corporation, such as the addition of Dr. Paul Weiss (UC Presidential Chair, UCLA) to our Scientific Advisory Board. However, in addition it is that for clinicians and physicians, this is a really exciting field, especially when it comes to identifying patients early, before pathology really takes hold of the patient. This allows us for early therapeutic intervention.

If we know specifically the mechanisms of action or what the disease may be doing within our patients, then we can tailor these therapies specifically for that patient as well. Therefore, on a clinical level, I think it is really exciting that they ability to think that we could actually discover ALS before motor neurons degenerate and pathology exists in these patients and allow us to start treatment. Hopefully, that will prolong patient lifespan or even prevent or one day cure ALS. Of course, this is the same model and similar to what we are doing in the Alzheimer's disease field.

CEOCFO: ***At some point might everyone of a certain of age be tested? Who should be using this and at what stage of life?***
Dr. Miller: Especially the population that has ALS/Lou Gehrig's disease in the family; what we would consider familial ALS. Having someone else within your family with ALS, you would want to get yourself sequenced or run through PDx's pipeline, where you essentially just take a cotton swab, you swan the inside of your mouth, you put into the tube that we have, you ship it to us and then we are able to sequence and then provide those results within thirty days. Then of course, we are waiting for FDA approval to really be able to push this forward. Once that appears then we are able to

actually start doing that for each person. That is one audience, which is the people who have an association within their family.

The other approach is also really the general public and even in the future, testing of babies and such before birth to identify if there is a risk of developing neurodegeneration and at what risk or sensitivity. The idea is that because it is inexpensive for us to run this test; it is a cotton swab, followed by DNA isolations, sequencing and then our computer models determine likelihood of development. Therefore, the general public should look into this, because it is more of a health public issue and it does not need to be a financial issue, as I said, we can actually do it very inexpensively.

We are finalizing our new subscription model, that will allow us to perform annual screenings for all clients and patients. Stay tuned.

CEOCFO: ***What do you and your team understand about working through some of the FDA requirements?***
Dr. Miller: One exciting part was the FDA submission part; we are working on our in vitro diagnostics or IVD submissions within the realm of rare disorders. The FDA and government are actually accelerating acceptances to IVDs for rare disorders because of how devastating they are, but also how rare they are as well, and usually complex. Therefore, we definitely have a segment where we are going with accelerated applications, but furthermore, our study came from a United States of America clinical trial. It is very clean and it is approved at a federal level already, so we are hoping that helps us push through.

We also have two scientific manuscripts. One has been accepted and one is in review and we are hoping that scientific peer review process with other scientists in the field, will also further validate and show strong evidence that the FDA should push forward with this. I think our statistical models are showing that we are at zero-point one percent false positive rate and this is incredible compared to prior FDA approved diagnostic tools.

Then finally, PDx has onboarded and signed a contract with an FDA regulatory consulting firm. My background is neurology and neurobiology, and with much of our staff here, most of our team has PhDs, but many of them are in fields like neurogenetics or data science. We come with a very technical background right now, so that is why we are aware of the challenges with the FDA and that is why we hired a very exceptional regulatory team to take this on with us.

CEOCFO: ***So many believe that they can do it themselves but end up being very disappointed!***
Dr. Miller: This is a reason, why we went to a FDA regulatory firm is because I think that my time is better to really push forward with our scientific direction and for PDx to get out to the community and for us to really reach out to this audience and especially our patients. We want to do this as efficiently and as quickly as we can. In order to do that, we have to realize, like you said, that we are not experts in everything. That is why we pulled them on, because we do want this FDA approval. We are serious about this and we have some really cutting-edge science!

CEOCFO: ***What, if anything, might people miss about PDx that they need to understand?***
Dr. Miller: We are not just focused on ALS and Alzheimer's disease, although we are very neurological and neurodegenerative focused right now. We are talking to potential collaborations in the fields of multiple sclerosis and Parkinson's disease as well. In the Alzheimer's project, we already have fifteen thousand patients.

CEOCFO: ***You mentioned funding from various sources. Do you have enough to get to where you need to be? Are you seeking investors or more partnerships?***
Dr. Miller: We are seeking seed or Series A funding right now. We do have meetings and discussions ongoing with a few VC firms right now and we are really pushing hard. We are able to, from private investments; cover even our FDA submissions and international patent, which is very expensive. Our patents and our lawyers are all covered. Therefore, we are okay on that level, but we are pushing for serious investments, so that we can really expand PDx by pulling on more scientists and just push this forward as quick as we can, to really start helping our global community.

CEOCFO: ***What do you find the response is from investors? Do they understand what you have and how important it is?***
Dr. Miller: I believe so! I think we have had a lot of excitement directed around PDx, especially in the recent months since we came out with our ALS genetic mutation classifier. Those who understand the background and the importance of

neurodegenerative disorders and how detrimental they are to the public do understand. For instance, in 2020 Alzheimer's disease is going to cost one trillion dollars. Therefore, we are able to jump in that.

In their approach, of course, many of these VC's are interested potentially what their money outcome is going to be and it looks great on that level. Our science is incredible! We want to continue to push forward and get to our patients these diagnostics so we can really start working on early therapeutics.

CEOCFO: ***Why look at PDx, Pluripotent Diagnostics Corp?***
Dr. Miller: We are the first ever to file for an international submission for a patent for ALS genetic screening. We are the first to create this genetic mutation classifier. We are the first to show over tenfold increase on the detection of picking up an ALS patient based off of sequencing and some other parameters in our model. We can do it inexpensively and we have an exceptional team of scientists and advisors in various fields that come from very respected universities.

I think our scientific advisory board has some of the world's most incredible scientists. We have also been working with business development experts as well. The approach with PDx is not only do we come out with some very exciting science in the ALS field. In addition, we have just an excellent, excellent team of scientists and that team is really what drives PDx faster and stronger than some of these companies right now.

PDx's mission is patient-first, by providing an opportunity for our aging population to be screened and diagnosed with dementia before disease onset. This provides us an opportunistic window to start early patient-specific therapies to combat neurodegeneration.