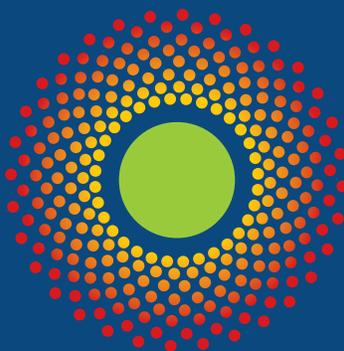


# Enroll!

Updates from the Enroll-HD  
global community



## INSIDE THIS ISSUE:

The Decision  
Sticking With It  
Behind The Scenes With Maria Ramos  
Science In Public  
Q&A with Sylvain Chouinard

AUTUMN 2016

## THE DECISION

*Astri Arnesen and Svein Olaf Olsen talk publicly about the most private decision for HD families*

For people from an HD family who don't know their gene status, the decision to get tested can be gut-wrenching. It's a private decision. And it can also be isolating. People who don't have HD in the family don't fully understand. Meanwhile other family members have their own opinions, because one person's decision to test might have implications for them too. The result is that people considering this decision can feel alone, hidden in the shadows.

In recent years the Norwegian couple Astri Arnesen and Svein Olaf Olsen have begun to publicly tell the story of how they made this decision—and its consequences for their family. At first they spoke at several HD meetings in Norway, then at the European Huntington Association (EHA) conference in Warsaw in 2015, then at CHDI's HD Therapeutics Conference in Palm Springs, California in 2016. They are making their private life public in order to counter the stigma and shame that still clings to HD, and sometimes to HD families.

In their joint presentation they openly describe all of the emotional turmoil that they have gone through as a couple and as parents. Astri's mother and grandfather both had HD, and she describes in vivid detail the ways that those illnesses—and the inability to talk about them—shaped her life as a child. She and Svein Olaf, both teachers by

*"It's not like any other disease.  
It's around me, it's family."*

**—Astri Arnesen**

profession, tell the story of how they fell in love and decided to have a family despite the knowledge that Astri was at risk. They narrate their disagreements about when and how much to tell their two daughters. In their presentation they talk about many things that are still rarely discussed in public.

During Astri's childhood her mother had terrible mood swings and anger. But it wasn't until Astri was in her 20s that the family actually talked about it. One of the ways she coped was by avoiding finding out her own gene status. "For me, the hope of not having the gene was a powerful part of my way of handling it," she says. "The hope was such a strong way for me to cope."

Even so, their family was still being affected by HD. Svein Olaf secretly became convinced that his wife was already showing symptoms of HD. When she trembled or twitched before falling asleep, or lost her temper



Svein Olaf Olsen (l) and Astri Arnesen with presenter Charles Sabine after their talk at the CHDI HD Therapeutics Conference in February 2016. You can view the Postcard from Palm Springs at [www.chdifoundation.org](http://www.chdifoundation.org).



*Olsen and Arnesen hiking in Italy last summer.*

and yelled at him, he thought: This is it. This is the first sign of HD. He convinced himself that his eldest daughter, then only a teenager, had symptoms as well.

Svein Olaf was grief-stricken, consumed with worry and despair, but hid the feelings from his wife and family. "I didn't know this," she says now. "I sensed this with the way he treated me, but I didn't understand why. He never talked about his fear." He spoke about it with only two friends, both doctors. It was intensely isolating.

Svein Olaf felt that he was losing his mind. He was afraid that, due to the psychological pressure, he might break down and run away from his wife and family, whom he dearly loved. "It's incredible," he says now. "I thought she was sick, and I was the sick guy."

Once their elder daughter turned 18, she decided she wanted to learn her own genetic status. She made a promise to her mother that she would keep the result a secret so that Astri could avoid learning her own status by implication. But Astri knew she could not allow her daughter to accept such a burden alone. She was 47, and she realized that if she did in fact have the HD gene she should start to prepare.

*"There's a lot of relief in feeling that you're part of something bigger."*

**—Astri Arnesen**

When Astri decided to take the genetic test, she was suddenly terrified for the first time since childhood. She would finally confront the truth.

On the day she went to get her results, Astri and Svein Olaf flew together to Bergen, in Norway. On their journey, Svein Olaf's sense of doom was so strong that he actually hoped the plane would crash rather than deliver them to their fate.

Astri's test was negative. She did not have the mutated HD gene, and so neither did their children.

It was a great relief. But both say it took two or three years to come to terms with the knowledge. It affected them in surprising ways.

Astri says although she did not feel guilty, as some people do, it was nonetheless very difficult to tell her siblings. One brother recently died from HD; her older sister is in a nursing home with symptoms. Her siblings were happy for her, although one of her sisters, who has Asperger's Syndrome, felt sad to hear the news. She was sad, she said, because Astri was no longer part of something that all the siblings had shared—the sense of being at risk, and not knowing their actual genetic status. "We were no longer in the same boat,"

says Astri. "I could feel the sorrow too."

### *The Huntingtonians*

When they give their talk, Astri maintains her calm even as she recounts painful events

in her life: her father's growing estrangement from the family as her mother became increasingly ill; her younger brother's death. Svein Olaf, by contrast, chokes up repeatedly. They are willing to expose themselves in this way, and relive some of the most difficult moments in their lives, because they feel it is helpful for others to hear.

After so many years of silence, Svein Olaf now talks about HD a lot—publicly, to friends, even to new acquaintances. "It's fantastic to be able to do that," he says.

If you don't know your gene status, and don't want to know, you can join Enroll-HD without finding out. You won't be told what your gene status is, and it won't even be revealed to the site staff who do the questionnaires and other exams for Enroll-HD. Your doctor, and the other medical staff at the clinic, won't know either.

HD is still part of Astri's identity, she says. "I will never lose that. It's not like any other disease, in which you get cured and it's gone away," she says. "It's around me, it's family."

Astri and Svein Olaf describe themselves as "huntingtonian," meaning that they are and always will be part of the HD world. "The community is very strong," says Astri. "We call it our second family."

Astri was president of the Norwegian HD Association for almost 10 years, and is now vice-president of the EHA, an umbrella association of HD family groups in Europe. Svein Olaf is a board member-at-large. The EHA supports local organizations by helping arrange meetings and other practical support, and helps start new associations in places like Bulgaria, Slovenia and Cyprus.

For Astri, the hope that once sustained her through years of uncertainty and difficulty has changed. Her new hope: That research will soon provide more help for people with HD. For that reason, she and Svein Olaf want to spread the word about what research does, how it works, and some of the recent advances. "I'm not a missionary," she says. "I just want to make people aware of the possibilities, and make more informed choices about what's right for them."

One goal is building stronger connections and more trust between researchers and the larger HD community. That means getting the word out about Enroll-HD and preparing people to join this study and others that will launch in the next few years.

## STICKING WITH IT

*As Enroll-HD goes into its fifth year, retaining participants becomes the goal*

**F**or Enroll-HD, signing up new volunteers is only the start. The most valuable information gathered by the study will come from collecting data on the same people followed over a long period of time, to track and compare changes that take place over years.

For that reason, retention—helping people stick with the study—is just as important as signing them up to begin with.

It also means working with clinical staff to help them cultivate trusting relationships with HD families.

Svein Olaf and Astri want to encourage clinicians to listen to patients' concerns, and also to explain the value of participating in research. Although progress may sometimes seem to be slow, discoveries often emerge suddenly and unexpectedly. Research is the only way that the situation for HD will improve, and the time frame is unpredictable—but participating is the only way to speed that process up.

*"To participate can make a difference, this is what we want to tell people."*

**—Svein Olaf Olsen**

They both emphasize that participating in research is an individual choice. But both also think that it can dispel fear. "There's a lot of relief in feeling that you're part of something bigger," says Astri. "To participate can make a difference, this is what we want to tell people," agrees Svein Olaf. "You can make a difference for those who come after you." At their talk at CHDI's HD Therapeutics Conference, Astri concluded by thanking the scientists in the room as a source of new hope for her and other HD families.

And both have a new kind of optimism. "Hopefully, I'll be in my bed at night when I'm 90, and I'll look back and think: 'This is so fantastic that we found this cure or this silencing drug,'" says Svein Olaf. "And I would smile, if I were a part of it."

**11,324**  
**PEOPLE**  
**CURRENTLY**  
**SIGNED UP**  
**FOR ENROLL-HD**  
**IN 14 NATIONS**  
AS OF SEPTEMBER 1, 2016

"In Enroll-HD we want to collect good data to get a good portrait of HD," says neurologist Tiago Mestre, assistant professor at the University of Ottawa and medical director of Enroll-HD. "For that we need to know how things change over time." Enroll-HD is also intended to be a platform to enable further research and clinical trials of drugs—studies that require good data collection and consistent participation. (For more about this, read the article "Enroll-HD as a Platform" at [www.enroll-hd.org](http://www.enroll-hd.org).)

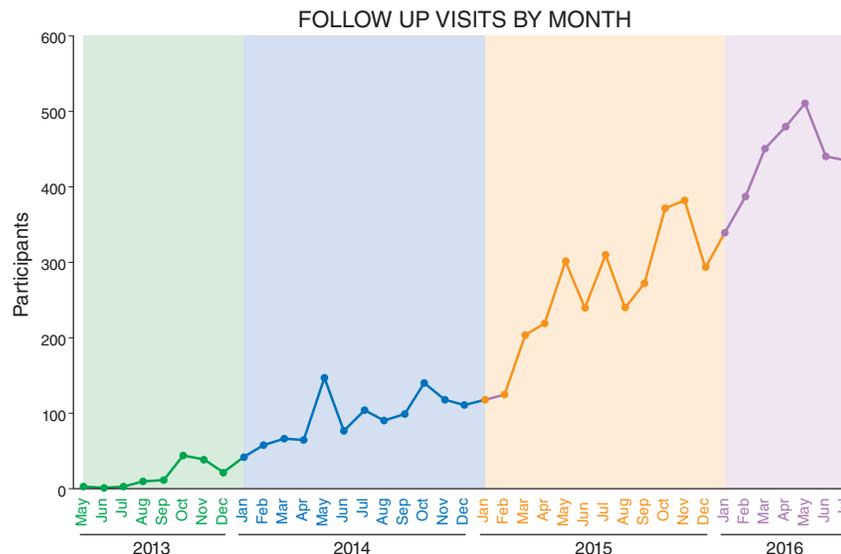
Researchers want to be able to track people's motor performance and cognitive abilities, for example. And they want to

understand how sleep or diet affect quality of life and how the disease progresses over time. The only way to get that information is if people come back repeatedly.

There are a lot of reasons people might not come back. They might lose interest in the study, or they might move, or they might become too ill, either with HD symptoms or another condition. A study site might have inconvenient appointment times, or might not do enough follow up to remind participants when the time approaches.

Now that Enroll-HD has been up and running for four years, thousands of people have returned for their third and fourth study visit. Retention is running at about 80 percent overall so far, which is pretty good for a study like this. So far, there's no obvious trends, says James Moyer, project manager at Quintiles, the contract research organization that helps coordinate Enroll-HD: bigger sites do just as well as smaller ones, and most countries are comparable.

Over time, it's natural for some people to drop out. But it's essential that this doesn't happen too often. "If you don't retain the patients, you'll be losing information," says Mestre. If many of the people who drop out leave for the same reason, it can weaken the whole study. For example, if many Enroll-HD participants whose symptoms get worse very quickly drop out, then the study will be biased. That is to say, it won't be representative of the overall population. And it won't capture what's different about those people from others whose symptoms progress more slowly. All that information may be crucial to future studies, such as clinical trials.



Return visits began rising in the second year of Enroll-HD (blue); now roughly 500 people come back each month.

### A good start

It's up to the clinical site team to make sure that people keep coming back, and they all have different tactics.

Setting expectations for participants early on is important so that people know what's required of them, and are aware of the fact that there's no end date for a study like Enroll-HD—people are encouraged to stick with the study as long as possible. "It starts with the message that sites give to patients when they enroll in the study," says Moyer. "That's critical—setting the expectation that this is a long-term study. Having that long-term buy-in and commitment is important."

*"If you don't retain the patients, you'll be losing information."*

**—Tiago Mestre,  
medical director of Enroll-HD**

Getting the first visit off to a good start by establishing a rapport—not just focusing on collecting data—might be the single most important thing site staff can do, says Paul McCann, study coordinator at the University of Alberta in Edmonton. "If the first visit goes swimmingly and you hit it off, they'll come back," he says. At the Edmonton site they aim to be as flexible and understanding as possible, and make sure that participants are comfortable. "We always say: let us know if you need a break, a glass of water," he says. "These are human beings, not a 9-digit ID number."

Along the same lines, it doesn't work to try to convince people who aren't ready to participate in research. People need time to come to terms with the diagnosis, says Laura Paermentier, clinical research coordinator of the New Zealand Brain Research Institute (NZBRI) in Christchurch, on the South Island of New Zealand.

Personal relationships and a broader sense of belonging to the HD community are also a major draw. "Sites often have a longstanding history with the participants, they've been doing clinical care for 20 years, knew the father and grandfather, and are now treating the current generation," says Moyer.

At the NZBRI, the Enroll-HD team is just two people—Paermentier and neurologist Tim Anderson. Participants seem to like the "consistency of care," says Paermentier; they like the

fact that the same staff is there from year to year. “There is always something positive to say, regardless of the stage of the disease,” she says. “We take interest in people’s lives, we get to know their hobbies, their peculiarities, their dogs, etc.” But the right balance is important: Being overly familiar or too personal can also be unpleasant for participants.

McCann says that the principal investigator at the Edmonton site, Oksana Suchowersky, makes sure that participants know they can also talk about health concerns when they come in for a study visit. “It’s not unusual for people to leave the research visit with a referral to physiotherapy or a prescription,” he says. “It’s a two-way street: You’re helping us with research, so we’ll help the best we can.” The team there also goes to fundraisers, walks and runs. “Not because we feel we have to, but because we want to,” he says. But people who see that the team supports HD outside of work may also be more willing to come in for research studies.

### *Stay in the loop*

On a more practical level, logistical flexibility can also make a big difference. Because HD is a rare disease, study sites may be few and far between in nations with smaller populations. In those cases, participants may need to drive for hours to reach a study site. At CHUM in Montreal and at the Hereditary Neurological Disease Center in Kansas, Enroll-HD appointments are frequently held on the weekend. It’s easier for participants—although it may not be convenient for the medical staff.

“Accept that life happens and that there are more important things than a visit window,” says Paermentier. In their experience, people who drop out of the study usually do so for logistical reasons: they’ve moved, or can no longer take time off work, or the travel is too difficult, or their disease has advanced to the point where making a clinic visit is too arduous.

McCann has found that scheduling appointments far in advance is also a good idea. He calls a few months ahead of

time, to make the trip as convenient as possible—then follows up in the weeks and days before the visit.

Keeping participants in the loop with regular communication is also a good way to retain interest, suggests Mestre. That might include updates about how the study is going, what the future holds, and updates about clinical trials. The Christchurch team sends out a newsletter twice a year, which includes updates, personal stories and hopeful messages. “It comes down to good communication, and also good dynamics between the participants and the team, in the sense that the patient feels engaged,” adds Mestre.

Retention will become even more important in years to come as more and more people from Enroll-HD are offered the chance to be in a clinical trial of a new drug or other treatment. For ethical reasons, early-stage trials usually involve the smallest number of people that can still provide meaningful results. That’s done just in case there are unanticipated side effects. “Because it’s an experimental intervention, we don’t want to include more than are strictly necessary,” says Mestre. However, if many people drop out of a small study there won’t be enough data at the end to get a clear answer.

It’s also possible that in future researchers will begin to focus on some therapeutically important aspect of HD that is overlooked today, and having a decade’s worth of high-quality data already collected and organized could be crucial to such a discovery.

Sometimes participants’ symptoms advance to the point that visits to the Enroll-HD site become too difficult. McCann mentioned one couple who drive more than 9 hours for clinic visits. It would be too disruptive to make the trip

this year, the husband told McCann. But he hadn’t yet told his wife, because he knew she’d be disappointed. She looks forward to the visit, he said.

*“We’re interested in the data, but the well being and respect of one human to another is more important.”*

**—Paul McCann,  
University of Alberta**

*“Having long-term buy-in and commitment is important.”*

**—James Moyer, Quintiles**

That’s the kind of relationship that many sites have with some of their participants—a respectful partnership that leads to friendship. “We’re interested in the data, but the wellbeing and respect of one human to another is more important,” says McCann. “There has to be compassion, understanding, and give and take. HD is a demanding disease.”





## BEHIND THE SCENES WITH... **MARIA RAMOS-ARROYO**

**M**aria Ramos-Arroyo has been part of HD research from the beginning of her career. A member of the team that originally discovered the location of the gene from samples from Venezuelan people, she would later be the Spanish representative on the steering committee for REGISTRY, the study that preceded Enroll-HD in Europe. She is now head of the medical genetics department at the Complejo Hospitalario de Navarra in Pamplona, Spain.

### **How did you begin studying HD?**

I started working on HD a long, long time ago, as a postdoctoral fellow. I finished my medical degree in 1979 and then wanted to do genetics. Spain did not have that specialty. So I went to the United States, and I happened to go to Indianapolis where the big Venezuelan-United States study was starting. I was really delighted.

From 1984 until, I think, 2003 I went to Venezuela every year. We used to go as a team, between 11 and 15 people: geneticists, psychiatrists, neurologists. We collected data from the families and we lived with them for 13 to 15 days a year.

It was a fantastic experience. I got to know people there who we visited every year. And I also got to know fantastic people who were part of my team. We lived day and night together in the same hotel and worked for hours and hours and hours, from early morning until late at night.

I got to know people and see all the kids growing, but also becoming ill and dying from the disease. The living conditions of the families there in Venezuela were so different from how we were living at that time. It was a lesson for life. It was a big experience for me from the scientific point of view, but also the human.

### **What is the significance of what the team discovered in Venezuela?**

The HD gene was the first dominant gene discovered by linkage. That was a really big issue at that time.

The thing is, when we found the gene we thought we'd have the knowledge to find the cure for HD and other diseases. We expected that if we knew what the gene was we'd be able to find a treatment, something to give back to patients and alleviate symptoms. Unfortunately, with HD and other

genetic diseases, treatments have not been as easy as we initially expected.

### **Why has that been so difficult?**

We know what the gene is. We know what the protein is. But that protein is in all tissues in our body. We don't know why that protein is doing something wrong in tissues like the brain, and not in other tissues like muscle, for instance.

Concerning treatment, how do we get the normal protein to only those tissues where the protein is doing damage? [That] is very difficult for HD and many other genetic diseases.



*Maria Ramos-Arroyo was part of the team that first pinpointed the position of the HD gene in the genome.*

### **How have things changed since then?**

When I first came back to Spain nobody knew much about HD. I remember trying to find a job, going to hospitals, saying: I know something about HD, would they be interested in research on it? They said 'What? What is that?' The disease was not really known.

Finally I got a position here in Pamplona to set up a genetic clinic. I started my own HD clinic here and started to collaborate with neurologists, collecting the families in my region.

There are 45 families in my area. Not all maintain frequent contact with me but they know we're here. That's the most important thing—that there's someone in the clinic who cares for them, and is willing to treat them.

### What research questions were you asking then?

We were trying to correlate the number of repeats of the mutation that causes HD with the age of onset of the disease or the symptoms. Because sometimes people show motor symptoms but also have psychiatric symptoms, or behavioral problems.

We also tried to see if we could find another gene that could modulate the age of onset. Also some epidemiological studies, trying to see how frequent the disease is in Spain. The prevalence is 0.5 per 10,000 people, which is relatively low. But although it's a rare disease, it's not as rare as we thought it was.



Ramos (second from left) visiting Lagunetas, a small village on Venezuela's Lake Maracaibo, in 1989.

### How did you get involved in REGISTRY, the European observational study that came before Enroll-HD?

In the beginning I didn't join. I didn't find it very interesting in terms of research. I've told Bernhard [Landwehrmeyer, the principal investigator of REGISTRY and also Enroll-HD] this before!

A few years later I started to see the aim of REGISTRY: That they tried to follow patients along their lives, in a prospective study.

[It seemed like] a possibility for patients to get more care, and for us to be closer to them. At that point patients didn't come to the clinic very often, because we didn't have much to offer. REGISTRY was like a joint effort to get something together. In 2006 I joined and started collecting participants for the study. I also was asked to be the member of the steering committee, representing Spain.

From the scientific point of view, REGISTRY is a very important and interesting study. But there's another side of the study that is very important for patients.

One of the things REGISTRY really did for Spain was get other neurologists interested in HD. It's now a well-known disease among my colleagues. Families are more willing

to accept the disease and be informed about diagnosis or possible treatment. Mostly they ask for help to give the best care to family members. That is something REGISTRY did.

*"HD has been one of the most important things that happened to me, from the personal and professional aspect. It gave me good friends, and the possibility of helping my community."*

**—Maria Ramos-Arroyo**

### What kinds of things can we learn from these studies?

We are now investigating the possible clinical manifestations in carriers with 27 to 35 CAG repeats, known as intermediate alleles. At present, these alleles are not considered to be associated with symptoms of the disease. However, in the last five

to six years, there have been individual reports as well as data from large studies, like COHORT and PHAROS, which suggest that a person with an intermediate allele might develop some neurological symptoms similar to those we see in HD patients, but at an older age. Recently, we have also analyzed data from REGISTRY with similar, but not absolutely conclusive, results. We need additional large prospective population-based studies to confirm or rule out these preliminary findings, as it may have important implications for genetic counseling. With REGISTRY and Enroll-HD we can gather data from a large number of patients followed for many years, which is crucial for picking up subtle clinical manifestations caused by the HD gene.

I'm sure that these studies will give us the possibility to conduct robust investigations with enough power to reach a definitive answer.

### What do you expect will be different with Enroll-HD?

REGISTRY was kind of a family study. All the researchers knew each other, we had an annual meeting. It was very familiar, very cozy. We also shared our research with family members, because they would go to the meetings with us.

Enroll-HD enlarges the study. It may be that because it's bigger it might be impersonal. But it needs to be done. It will be

more powerful. And numbers in HD really count: We need numbers, we need data. We need to collaborate, to go all at once, with the same goals and tools and purposes. I think that's the way to do it.

### You've been involved in HD research for so long—what insights do you have about it?

HD has been one of the most important things that happened to me, from both the personal and professional aspect. It has been not only the main part of my research, but part of my personal life. It gave me good friends, and the possibility of helping my community. That is the summary.



## SCIENCE IN PUBLIC

*Researcher Rachel Harding, who studies the structure of huntingtin, the protein that causes HD, is also experimenting with open science*

Medical research can be intensely competitive—and, as a result, surprisingly secretive. Researchers can be reluctant to share data or describe what they're doing because they're afraid their ideas might be taken and they'll be scooped. In science, there's no second prize: Whoever makes a discovery first gets the credit. Although scientists agree in theory that collaboration and data-sharing is more effective, many don't do it.

So when Rachel Harding, a postdoctoral fellow at the Structural Genomics Consortium (SGC) in Toronto, suggested making all of her HD research public while it was still in progress, some told her she was taking a foolish risk. "A lot of traditional academic scientists believe it's mental," she says. "Why would you do that? Everyone could steal all your data."

She and her boss, CEO Aled Edwards, aren't daunted by the skeptics. They calculate that the potential benefits are bigger than the risks. "We're big believers in open-access data, working in collaboration rather than competition," she says. "So we decided it'd be fun, and a new experiment for us, to see how the scientific community and wider community react to this more radical open data publishing approach." SGC is cooperatively funded by governments, pharmaceutical industry, large foundations

and smaller disease-focused foundations (including CHDI). All the work it produces is not patented but shared openly to speed up the process of science.

Harding and Edwards anticipate that the open science experiment will encourage new collaborations, and also improve the flow of information so that other

research teams learn from her experiments immediately, rather than waiting a year or more for her to publish her findings in a research journal. That will prevent the unnecessary duplication of efforts that are sometimes an unfortunate consequence of research secrecy. Harding and Edwards also hope that it will display the scientific process to people who may not know much about it, especially patients and their families.



Postdoctoral fellow Rachel Harding

*"The more time we waste repeating each other's experiments, the more time we're losing."*

**—Rachel Harding,  
Structural Genomics Consortium**

### The shape of HD

Harding's major goal is to figure out the structure of huntingtin (HTT), the protein produced from the HD gene. This protein, present in every cell in the body, is still something of a mystery; researchers have a limited understanding of what the normal, non-mutated version of the protein does, and they don't know exactly how it causes damage when it's mutated in HD.

In modern biomedicine, researchers often look to understand what a protein does by mapping out its 3-dimensional structure. "If you understand what something looks like, you can work out what it's doing," says Harding. "Given that we have a conflicting hodgepodge of data about what huntingtin is doing in cells, actually knowing what the molecule looks like would hopefully provide insight into designing next phase experiments that could lead to therapeutics." It's a massive effort that requires access to extremely expensive instruments—and it means collecting and manipulating enormous amounts of data.

Many such experiments are done by teams working independently. If they don't succeed—and most don't—the results may never be published, meaning that other groups won't know that the approach has already been tried and didn't work. In addition, many nationally-funded efforts all focus on the same questions, yet don't share information. "We don't know a lot, and yet we keep studying the same things over and over again," says Edwards.

That's one reason that inspired Harding and Edwards to go public. "We want to find out more about huntingtin as quickly as we can," she says. "The more time we waste repeating each other's experiments, the more time we're losing."

As she's been working through all the steps for her experiments, she regularly blogs to describe her experiments and uploads the protocols she's perfecting, as well as data from her experiments. She invites anyone to comment on her posts or email her about the work.

In the last few months she's been tinkering with a method to use insect cells to make certain parts of the huntingtin protein. This step is necessary because it will permit her to make large quantities of the protein fragments in the lab. Once she gets this method fine-tuned, she will purify the protein fragments—another tricky step that involves testing out many different methods. Only then can she begin the structural studies.

### *Bumps and warts*

Science is inherently prone to failure, since the whole point of research is to discover what we don't already know. False starts, do-overs, and confusion are common, but most

researchers don't advertise that fact. By blogging about it as it happens, Harding reveals all the highs and lows.

Edwards says he is proud that she is willing to take the risk, and is confident that she will be able to handle any potential downside. "She's the right person—incredibly confident, talented, and gregarious," he says. "She's taken a career risk—somebody could scoop her, and she will make mistakes," missteps that anyone following her posts might see.

Some senior scientists have in fact contacted her about the work with critiques as well as comment. But Harding hasn't been intimidated; instead, she's found it useful. People from HD families have also contacted her. "It's really nice," she says. "It's really motivational to hear people's stories, and why they're interested in any research."

The risk of having her hard-won data simply stolen by other teams is mitigated by the way she makes it public. It's published under a "Creative Commons" license, meaning that anyone who uses it is required to credit her.

*"We want more people to take this up, but scientists don't do anything unless you give them hard evidence."*

**—Rachel Harding,  
Structural Genomics Consortium**

Edwards and Harding treat her open-lab project as an experiment of its own, to see if this approach can accelerate discovery or produce better results. They are tracking several outcomes: Whether other scientists use her data and tools and acknowledge her contribution to the papers they write, and whether the approach sparks an unusually high number of new collaborations with other scientists in academia and industry. They plan to compare these statistics against a project conducted with a more traditional approach, in order to measure whether the open-access model significantly increases collaboration or accelerates research. If it does, Edwards wants every project that is funded by a disease-related nonprofit foundation to be open in a similar way.

"At the end of the day, what we want to do is compare this project to another project where we used conventional methods," she says. "We want more people to take this up, but scientists don't do anything unless you give them hard evidence." Researchers are basically conservative: They want proof that something works before they are willing to make changes. Harding and Edwards hope that her open-lab project will begin to provide some of this evidence. If they demonstrate that the approach was effective, they're betting some open-minded groups might take it up as well.



## RESEARCH UPDATE

Q&A with Sylvain Chouinard

**C**houinard is a neurologist and co-director of the André Barbeau Movement Disorders Unit at Montreal's major university hospital, the Centre hospitalier de l'Université de Montréal (CHUM), one of the largest sites for Enroll-HD.



Sylvain Chouinard

### Your clinic has recruited a huge number of people for Enroll-HD. How do you do it?

We're following 500 to 600 patients with HD. That's why we're so good at recruiting patients for Enroll—we have a lot of patients! We go to Quebec City twice a year, and there are big families there too.

*"It's rare that people don't want to participate, especially in Enroll-HD, since it's not a drug they need to take, and it's only once a year."*

**—Sylvain Chouinard**

We also do it differently, probably, than other clinics. We like to do weekends, where we'll see 40 or 50 patients. We find that it's very efficient. For the patients and families who are working during the week, it's much more convenient. The Quebec division of the Huntington Society of Canada will come, and the genetic counselor too. It's all volunteer. It's nice. It's like a big family reunion.

### You also have a family day—how does that work?

There's always an update on research. I'll discuss Enroll-HD, and some of the other research. We pick a subject that will interest the families. In the past, we discussed end-of-life wishes or problems with swallowing. At the end of the session we ask what people want to hear, and we organize the next one according to the wishes of the families. We do that also in Quebec City.

### Tell us about your clinic for First Nations people, in remote northeastern Quebec.

About 10 percent of the Innu community there is at risk of HD. We go up there once or twice a year, for three days. It's a social

worker, the director of the Huntington Society, two nurses, another doctor, and the genetic counselor. All the community knows we're there to see patients, and they're all coming for the study as well. We see patients but we also try to educate people about the disease.

It's amazing. It's changed our life. We're part of their family there. We appreciate them, they appreciate us. They're more advanced than many places: They're going to start a community center for HD, and a respite home. They're very well organized, because of the way the community is there. We're trying to reach out to more remote communities—we'll probably go farther north next year. There's a remote region where there are 40-50 people affected, and we're trying to reach them as well.

### When you invite people to join Enroll-HD, how do you explain it?

It's usually not a big issue. We just explain what the purpose is of the research, to better understand the disease. It's rare that people don't want to participate, especially in Enroll-HD, since it's not a drug they need to take, and it's only once a year. We also make sure that we educate people, give them more information about the research and what it means. They all want the same thing: when are we going to find the cure?

### And how do you answer that?

We're getting there, slowly! With this new trial, the gene silencing [therapy now being tested by Ionis Pharmaceuticals], that's quite amazing. I would never have thought it would be possible 20 years ago. We're making a lot of progress.

**Enroll!** is a publication of CHDI Foundation, Inc., a non-profit biomedical research organization that is exclusively dedicated to rapidly and collaboratively developing therapies that slow the progression of Huntington's disease (HD). As part of that mission, CHDI Foundation sponsors and manages Enroll-HD. More information can be found at: [www.chdifoundation.org](http://www.chdifoundation.org)

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