OPINION, **Q&A**

Questions for Will Spooren: Paving a path to autism drugs

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Any new drug treatment for autism faces huge hurdles on the road to the clinic. The disorder has such diverse symptoms that researchers disagree on what benefits a drug needs to show in order to be approved. Researchers also lack a well-characterized population of people in whom to test

medications.

In 2012, a group of neuroscientists launched a large collaborative effort called the **European Autism Interventions — A Multicentre Study for Developing New Medications (EU-AIMS)**. The goal of the five-year project is to provide a framework for drug discovery and clinical trials in autism. More than three years into the initiative, it's boasting several accomplishments.

To support future trials, the project leaders have built a network of 88 clinics and research institutions in 37 countries that collectively see roughly 15,000 new people with autism each year. The leaders are also backing studies aimed at developing tools to make trials more efficient and conclusive.

One study, which follows about 500 children aged 5 months to 3 years who have an older sibling with autism, is revealing sensory **biomarkers** that foreshadow autism symptoms. A second study is tracking a group of people with autism over time, painting a detailed picture of their symptoms, patterns of brain activity and quality of life. Another team has developed stem cell lines from the hair of people with autism.

Funding for the project — 30 million euros (roughly $34 million) — comes from the **Innovative Medicines Initiative** (IMI), a public-private endeavor that broadly aims to boost drug-discovery research in Europe. Half of the IMI's funds come from the European Union and the other half, in the form of personnel and resources, from the **European Federation of Pharmaceutical Industries and Associations**. The U.S.-based research and advocacy organization **Autism Speaks** contributed $1 million and provided the genome sequencing for the project's two major studies.

We spoke to Will Spooren, head of behavioral pharmacology and preclinical imaging at **F. Hoffmann-La Roche** in Basel, Switzerland, about the project's progress and next steps.

***Spectrum:* What is your role in EU-AIMS?**

Will Spooren: I'm the coordinator; I set up the initiative with the help of people from other companies. The other leader is **Declan Murphy** at King's College London, who leads the academic group. Together we make sure the project is running as has been defined.

S: What was the inspiration for EU-AIMS?

WS: There was a ***Nature Medicine* conference** that we organized in Switzerland in 2009 where we brought leaders in neurodevelopmental disorders. We realized that if we want to move forward, the whole infrastructure for doing drug discovery is lacking in Europe. It's about establishing clinical sites; it's about establishing clinical endpoints; it's about establishing a regulatory framework. It's something that we cannot do alone. It needs to be done in a concerted effort with a

host of other players. We said, “How are we going to do it?” An IMI project came to our mind.

S: What are the key successes of the project?

WS: One is that we’ve been able to recruit people with autism for trials. That’s not a given. Sometimes it’s very difficult to recruit these individuals, particularly those who have a low intelligence quotient (IQ). That’s where the medical need is and what we’ve been able to do very well.

One other success is our clinical trial network. It covers newly diagnosed individuals from about 37 countries, who speak about 30 different languages from 30 different cultures across Europe.

We are also building a regulatory framework for drug discovery by asking the **European Medicines Agency**, the equivalent of the U.S. Food and Drug Administration, for advice about the right way to diagnose and treat clinical trial participants. We were the first consortium to visit the agency about this topic.

S: What are some other successes?

WS: In our **high-risk sibling study**, we showed that a sibling at risk for autism has a **more pronounced pupillary response** than a sibling not at risk. When the child looks at a dot on a television and a light shines in their eye, we measure how fast the pupil constricts. The constriction is faster and more pronounced in the siblings at higher risk.

That has huge potential as a diagnostic criterion. Maybe it changes with treatment. I feel it needs to be replicated, but it’s an interesting finding.

Another big success is the protocol for using hair cells. This was developed in **Jack Price’s** lab at the Institute of Psychiatry at King’s College London. We were collecting material from people with autism. We started using a skin punch and isolated fibroblasts, but it was difficult to collect samples. We then went to blood, but it still involves a needle. So we thought, “What can we do with a keratinocyte? It’s just pulling out a hair. How hurtful is that?”

It turned out to be a difficult protocol. In the beginning, we suffered from infections in the dish, because hair is not as sterile as skin from a skin punch.

S: What are your future plans?

WS: This project will end in two years, so we are now thinking beyond. We have a couple of things we need to do. One is we have these individuals who will be, at the end of the project, deeply studied, deeply characterized. We have an observational study of about 500 people between the ages 6 and 30 years. These are going to be incredibly important individuals for us because a study

like this has never been done. This depth of the characterization has never been done.

We want to create a new IMI-funded project and see if we can extend that work. We want to see what changes in the lives of these people. What kind of support does an individual with autism need at age 10, 20 or 40? We are discussing individuals with **Asperger syndrome**. Where are they in society? What are they doing? Are they happy? Are they sad? Do they need medication?

We want to use the clinical network we are setting up in Europe as a clinical trial network and a network for basic research.

We'd also like to do comparisons across cultures. Within that, we hope to see trial-ready cohorts that might be helpful to a researcher who, for example, wants to study gastrointestinal-related things in autism. A specific food a person eats or a specific interest they have could also be used to stratify people into different groups for testing drugs or studying behavior.