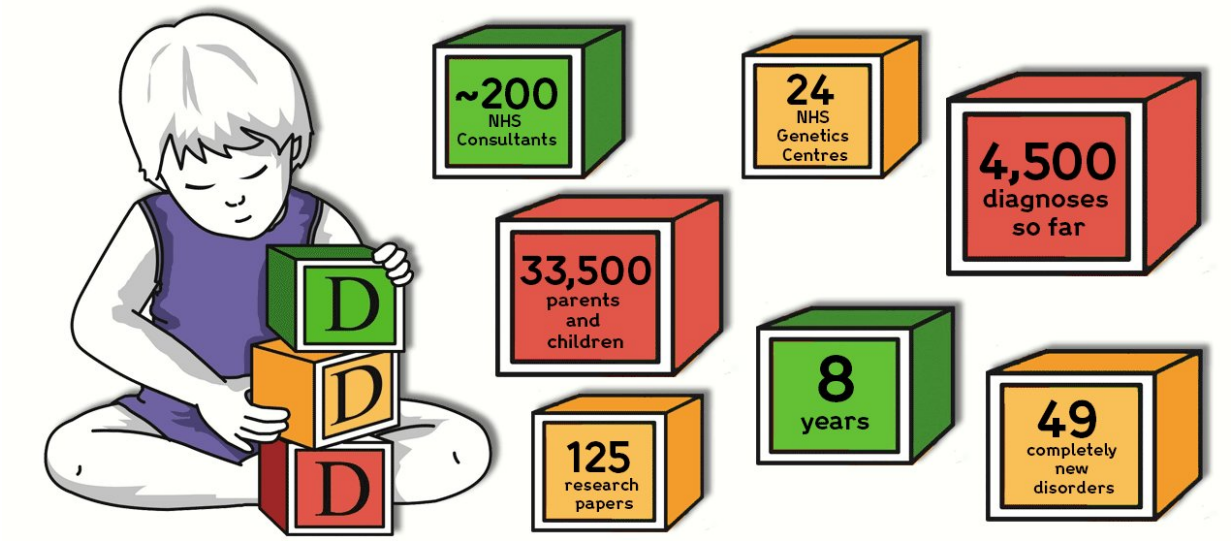
Milestone reached in major developmental disorders project

October 16 2018



Credit: Wellcome Trust Sanger Institute

The Deciphering Developmental Disorders (DDD) project aims to provide diagnoses for the families of around 13,600 children with severe undiagnosed developmental disorders. Launched eight years ago this month at the Wellcome Sanger Institute, the project has just completed the first phase of analysing the gene sequences of every participant in the study. The project has provided genetic diagnoses to approximately one third of the families involved so far and now moves into its next phase.

With 125 scientific papers published on the study to date, this project is helping researchers and families understand the genetic causes of the disorders. This helps the family access services and can inform their child's treatment.

Every year, thousands of babies are born in the UK who do not develop normally because of their particular genetic makeup. These developmental disorders are often obvious shortly after birth, and can lead to conditions such as intellectual disability, epilepsy, autism or heart defects.

Each individual disorder can be extremely rare, which makes it very difficult to diagnose what has happened. The DDD study was set up in October 2010 to find diagnoses for these children with as yet unknown developmental disorders, and to understand the causes of these conditions.

Working closely with consultant NHS clinicians in all 24 Regional Genetic Centres across the UK and Ireland, the DDD researchers have sequenced the DNA of the 33,500 parents and children involved in the study. To date, the project has found diagnoses for over 4,500 children, and the researchers are continuing to search for genetic causes for the remaining families in the study where these developmental disorders are not yet understood.

"Over the last eight years, we have shown the power of combining clinical and genomic information to diagnose rare developmental diseases. There are about 200 consultant clinicians responsible for patients in the DDD and this informal UK-wide network of expert clinicians is vital to the success of the project. We have provided diagnoses for thousands of the families involved in the study and over the next five years we hope to provide many more answers to the remaining families," says Dr. Matthew Hurles, leader of the DDD

project from the Wellcome Sanger Institute

Diagnoses are extremely important for people as they allow families with the same genetic conditions to meet up and access support, and can help inform treatment for the child. They also allow families to understand the risk for any further children they may have.

"Correct diagnoses for families with rare developmental disorders are really important for helping them understand the disorder and for guiding future care. It is crucial that people have access to clinicians with expertise in rare disease, who can ensure the genetic results really do explain the child's clinical problems and provide information and support to their families," says Dr. Helen Firth, Consultant Clinical Geneticist at Cambridge University Hospitals Trust, and Honorary faculty at the Wellcome Sanger Institute.

Of the hundreds of different disorders diagnosed, many of which were only seen in a single child within the study, the DDD has defined 49 completely novel disorders, and the anonymised results have been published in 125 academic papers. These publications allow other researchers to build on the results and will help propel further discoveries.

From the start, DDD has considered the ethical implications arising from genome sequencing. Questions about the best way to ask for consent, and whether participants should be informed of additional findings, were carefully considered. Bringing together the views of the public, patients, participants, clinical geneticists and researchers has shaped the debate in the UK and internationally. It has also set a strong precedent for similar projects.

The DDD study was the inspiration for the NHS 100,000 genomes project and the future NHS genomics service, which will provide genetic

answers for many more people in the future.

"As a result of the DDD project thousands of children with rare neurodevelopmental disorders now have a diagnosis, and their families can use this to inform their decisions about further children and to guide and target appropriate medical care. Collaborators meetings informed and educated the clinicians, and the scientists were able to understand the enormous impact their work had for the families in the research. This collaborative approach establishes a model for genomic medicine that can guide the new NHS England genomic service," says Dr. Jane Hurst, President of the UK Clinical Genetic Society and lead for the DDD project at Great Ormond Street Hospital.

Provided by Wellcome Trust Sanger Institute