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Sequencing of 500 genomes brings personalized medicine closer

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The genomes of 500 people with a range of diseases – including cancer, immunological disorders, and rare inherited diseases – are to be sequenced in full detail thanks to a new collaboration between the University of Oxford and Illumina, a leading manufacturer of sequencing systems.

The project has been designed to explore how whole-genome sequencing might be used in informing the diagnosis and treatment decisions for individual patients in years to come.

"It is a really exciting opportunity to explore the potential for moving next-generation sequencing into the clinic," says Professor Peter Donnelly, director of the Wellcome Trust Center for Human Genetics at the University of Oxford. "Overall, we will study over a hundred different conditions – we want to cast the net as wide as possible in order to learn the areas in which sequencing can make a real impact.

"The initiative represents a crucial step as we move towards a new healthcare paradigm in which genetic information from next-generation sequencing is likely to become much more widely used in routine medical practice."

As the cost of sequencing the entire human genome – all 3 billion letters in our DNA codes – comes down, it is becoming possible to see a time when it becomes more routine. But although a number of individual's genomes around the world have now been sequenced in complete detail, the scale of this project and the focus on clinical care rather than pure research puts it at the forefront of developments in the field. "It is a very large study by any standards," says Professor Donnelly.

The project will focus on conditions involving mutations that would be difficult or impossible to discover by standard genetic tests. The data generated by Illumina's technology will be analyzed by researchers at Oxford with the aim of identifying genetic changes that can help in diagnosing disease, informing potential treatment options, and offering genetic counselling for the individual patients.

"This collaboration represents a remarkable and very important step toward using whole-genome sequencing for translational medicine – where a patient's individual genetic information can be used to make key healthcare decisions," said David Bentley, vice president and chief scientist at Illumina. "We are excited to be working with Oxford on this effort. This collaboration also will help Illumina advance its technology

to better meet the specific needs of clinical environments."

The collaboration will see 400 genomes sequenced at the Wellcome Trust Centre for Human Genetics in Oxford using Illumina systems. The other 100 genomes will be sequenced at Illumina's UK site in Chesterford, Essex.

Sequencing aids diagnosis for 4-year-old girl

One example of the potential of whole-genome sequencing has already been seen at Oxford.

Sequencing the genomes of one family revealed a genetic mutation in a four-year old girl that appears to have occurred spontaneously and caused a serious condition.

The girl had craniosynostosis, a serious disorder affecting 1 in 2,500 children which results in the premature fusion of the bony plates of the skull, hindering expansion of the skull and restricting brain growth, explains Dr. Steve Twigg, who carried out the work with Professor Andrew Wilkie at the Weatherall Institute for Molecular Medicine, Oxford University.

The condition requires surgery to solve the potentially life-threatening problems caused by raised intracranial pressure and difficulties with breathing.

"Because the parents were unaffected we assumed that any mutation would have arisen spontaneously," says Dr. Twigg. "We therefore carried out whole genome sequencing of both parents and the child, looking for changes in the child that were not present in the parents.

"We identified a single base change in a gene on the X chromosome.

This is almost certainly the mutation responsible for the child's craniosynostosis," he adds, but stresses that further work is required to absolutely confirm this.

In this case, whole genome sequencing provided the family with an explanation for their daughter's condition and allowed genetic counselling to be given. The parents could be told the risk of the condition would be low for any further children they might have, but advice for the daughter when she comes to thinking about having children would be very important.

The identification of the genetic cause of this condition in this case could potentially provide answers for other families too, should this mutation be found in other children.

"If more patients with mutations in the same gene are found then this might have implications for the surgical strategy and patient care in other cases," says Dr. Twigg.

Provided by Oxford University