PARIS,
DECEMBER 5, 2019

PRESS RELEASE

PRESS CONTACT

Tuline Laeser
tuline.laeser@cea.fr
Tel.: + 33 1 64 50 20 97

A first in France

Rapid Genome Analysis Aids Diagnosis of Neonatal ICU Patients

Teams from Dijon-Bourgogne University Hospital, Inserm and CEA have recently established the results of the whole-genome analysis of severely ill neonates, hospitalized in neonatal ICUs – the time of which was slashed from the current 18-month average to just 38 days. Thanks to this rapid analysis, the resulting diagnosis of two-thirds of the infants enrolled in the project enabled one third of them to receive faster and more appropriate treatment. The deployment of this process over the coming years will make it possible to optimize the management of these patients.

Although a number of countries use whole-genome sequencing for diagnostic purposes and while France has recently launched its 2025 Genomic Medicine Plan (PFMG2025)[1], its urgent use in a neonatal setting is not very widespread at present. Yet rapid genetic examination is a crucial factor when a diagnosis is required urgently – a common situation when it comes to rare diseases with early pediatric onset or rapid progression. Teams from Dijon-Bourgogne University Hospital, Inserm and CEA conducted a feasibility study of fast high-throughput genome sequencing before envisaging such a process for the future, in the framework of the PFMG2025.

In this pilot study, called Fastgenomics[2], some thirty children hospitalized in neonatal ICUs across eight university hospitals belonging to the AnDDI-rares network[3] underwent fast genome analysis in the previous nine months. High-throughput sequencing of the genomes of the children and their parents and a primary bioinformatics analysis were carried out on the sequencing platform of the French National Research Center for Human Genomics (CEA-CNRGH), in collaboration with the Very Large Computing Center (TGCC) of the CEA and the Computing Center of Université de Bourgogne (CCuB). The genomics data were interpreted by the TRANSLAD University Hospital Federation (FHU TRANSLAD), in close collaboration with the Inserm U1231 GAD (Genetics of Developmental Disorders) research team.

---

1 *In 2016, France launched its 2025 Plan for Genomic Medicine (PFMG2025). It aims to implement mass whole-genome sequencing for the diagnosis of rare diseases through the establishment of very high-throughput platforms, as well as pilot studies to define the prescribing conditions for such investigations.*

2 *Fastgenomics: French national pilot study prepared by the AnDDI-rares national healthcare network, FHU TRANSLAD and CEA-CNRGH, and supported by a financial donation from SANOFI-GENZYME.*

3 *AnDDI-rares: National rare diseases network dedicated to diseases with somatic and cognitive developmental abnormalities. http://anddi-rares.org*

PARIS,
DECEMBER 5, 2019

PRESS RELEASE

PRESS CONTACT

Tuline Laeser
tuline.laeser@cea.fr
Tel.: + 33 1 64 50 20 97

Mobilizing the teams meant that it was possible to obtain the analysis results within 49 days, with the most rapid turnaround being 38 days. This is particularly fast for a genetic analysis, given that despite the considerable advances made, the average time to obtain a genetic diagnosis in France continues to remain long: 1.5 years on average, and up to 5 years for 25% of patients. Rapid analysis of the genomes of these neonates made it possible to diagnose two thirds of them, with one third able to receive quicker and more appropriate treatment.

Such analysis has been made possible thanks to major advances in the high-throughput sequencing of the gene set. The new-generation high-throughput DNA sequencing technologies – which analyze a person's entire genome – have emerged in recent years as a tool of choice in the study of rare diseases. These cutting-edge technologies are used at CNRGH and have already implicated numerous genes in numerous diseases. The FHU TRANSLAD team from Dijon-Bourgogne University Hospital was one of the first in France to demonstrate the value of exome sequencing (with the exome representing 1% of the total size of the genome) in the diagnosis of severe diseases with early pediatric onset, as well as developmental abnormalities and intellectual disability.

Diagnosing rare diseases in the neonatal period

Rare diseases (affecting fewer than 1 in 2,000 people) are a major public health problem because they represent around 8,000 conditions and affect more than 3 million people in France. Given that the majority of these diseases are of pediatric onset, they are responsible for 10% of deaths before 5 years of age. Up to 80% of these diseases are considered to have a genetic origin. Establishing a diagnosis brings multiple benefits to the patients and their families: it clarifies the cause and the prognosis, enables access to treatment or clinical trials, determines risk of recurrence, cuts out needless diagnostic tests, enables the management of known complications, facilitates the acquisition of specific financial and practical support, and gives them the possibility to forge links with other families dealing with the same challenges.

Obtaining a diagnosis is a major challenge in diseases with early pediatric onset and rapid progression, and whose genetic causes are highly heterogenous, such as epilepsy, metabolic diseases, cardiac diseases, musculoskeletal diseases and other polymalformative syndromes. The 3rd French National Plan for Rare Diseases (PNMR3) envisages reducing diagnostic delay to one year, given that it is responsible for *"the potential worsening of the condition of patients, the delayed possibility for genetic counseling and the wastage of medical resources (due to multiple diagnostic consultations)*
".

PARIS,
DECEMBER 5, 2019

PRESS RELEASE

When it comes to severe neonatal diseases, obtaining rapid diagnosis is particularly important. Diagnosis, when accurate, makes it possible to modify how the patient is managed, whether in terms of treatment adaptation (such as in metabolic diseases or epilepsy), referral to specialists, dietary adjustments, additional examinations, reassessment of any need for surgery, or the consideration of these results when discussing the continuation of care.

About

The French National Research Center for Human Genomics (CNRGH)

The CNRGH, a department of the François Jacob Institute of the French Commission for Atomic Energy and Alternative Energies (CEA) offers the scientific community cutting-edge expertise and capacities for the production, storage and analysis of data needed to conduct ambitious collaborative projects selected on the basis of criteria of scientific excellence in the field of medical genomics. Since its creation, it has evaluated and integrated the best technological advances in genomics to maintain its international competitiveness, notably with the implementation of a set of integrated platforms, including a production platform for the performance of pangenomic studies on numerous samples (genotyping of polymorphisms on very high density chips, whole exome and genome sequencing, as well as transcriptome and epigenome sequencing).

The CNRGH contributes to national and European programs with respect to the development of technologies and for the study of diseases. It is involved in ambitious projects, including the elucidation of the genetic causes of rare diseases, study of the genetic bases of autism, the genetic causes of the toxicity of breast cancer therapies, and also the production of "patrimonial" data on the French population in order to supply the scientific community with the reference data needed to identify the genetic and genomic variations underlying diseases. The CNRGH production infrastructures are widely used by the scientific community in France and in Europe. Its teams have implemented, after scientific evaluation, more than 700 research projects derived from around 300 French laboratories and more than 60 foreign laboratories. For those activities, the CNRGH has contributed, since its creation, to more than 750 publications in internationally reputed scientific journals. More recently, it has become a key player in the deployment of genomics in the medical world, particularly with the attribution of a laboratory of excellence (LabEx GenMed) and the joint steering of the Reference, Innovation and Expertise Center (CREFIX) of the French Genomics Medicine plan (FMG2025).

The TRANSLAD University Hospital Federation (FHU TRANSLAD): an expert in the transfer of pangenomic high-throughput sequencing technologies in the diagnosis of rare diseases

PRESS CONTACT

Tuline Laeser
tuline.laeser@cea.fr
Tel.: + 33 1 64 50 20 97

PARIS,
DECEMBER 5, 2019

PRESS RELEASE

PRESS CONTACT

Tuline Laeser
tuline.laeser@cea.fr
Tel.: + 33 1 64 50 20 97

In 2013, the University Hospitals of Dijon-Bourgogne and Besançon, the French National Blood Service (EFS) for Bourgogne Franche-Comté, the Georges-François Leclerc Cancer Center in Dijon and the universities of Bourgogne and Franche-Comté, in close collaboration with AVIESAN, certified FHU TRANSLAD (www.translad.org), coordinated by Prof. Laurence Faivre from the Dijon-Bourgogne University Hospital Genetics Center. This FHU is devoted to healthcare, education and research in the field of developmental diseases. Its multidisciplinary team is comprised of geneticists, biologists, bioinformaticians, dermatologists, pediatricians, internal medicine practitioners, organ specialists, psychiatrists, psychologists specializing in cognition, health economists, philosophers and ethicists, who are developing
five areas of focus: the multidisciplinary management of patients and therapeutic trials; genetic diagnosis at the cutting edge of genomic innovation; training in genetics, appropriate to the new sequencing technologies; healthcare organization that is more effective and respectful of ethical challenges; and clinical, molecular, neurocognitive and pathophysiological research.

As such, from 2013, FHU TRANSLAD saw the major benefit of pangenomic high-throughput sequencing for the diagnosis of patients with rare diseases. The Inserm JRU 1231 GAD (Genetics of Developmental Disorders) research team (http://www.gad-bfc.org) was one of the first in France to develop high-throughput exome sequencing in patients with rare diseases thanks to major support from the Bourgogne Franche-Comté region, ERDF, Université Bourgogne and Dijon Bourgogne University Hospital. Since 2014, FHU TRANSLAD has performed exome analysis in over 1,600 patients, making it possible to establish causal diagnoses for more than one third of them. Fortified by this experience and its renowned expertise in bioinformatics analysis and the interpretation of genomics data, FHU TRANSLAD is now working on the transfer of genome analysis to diagnostics.