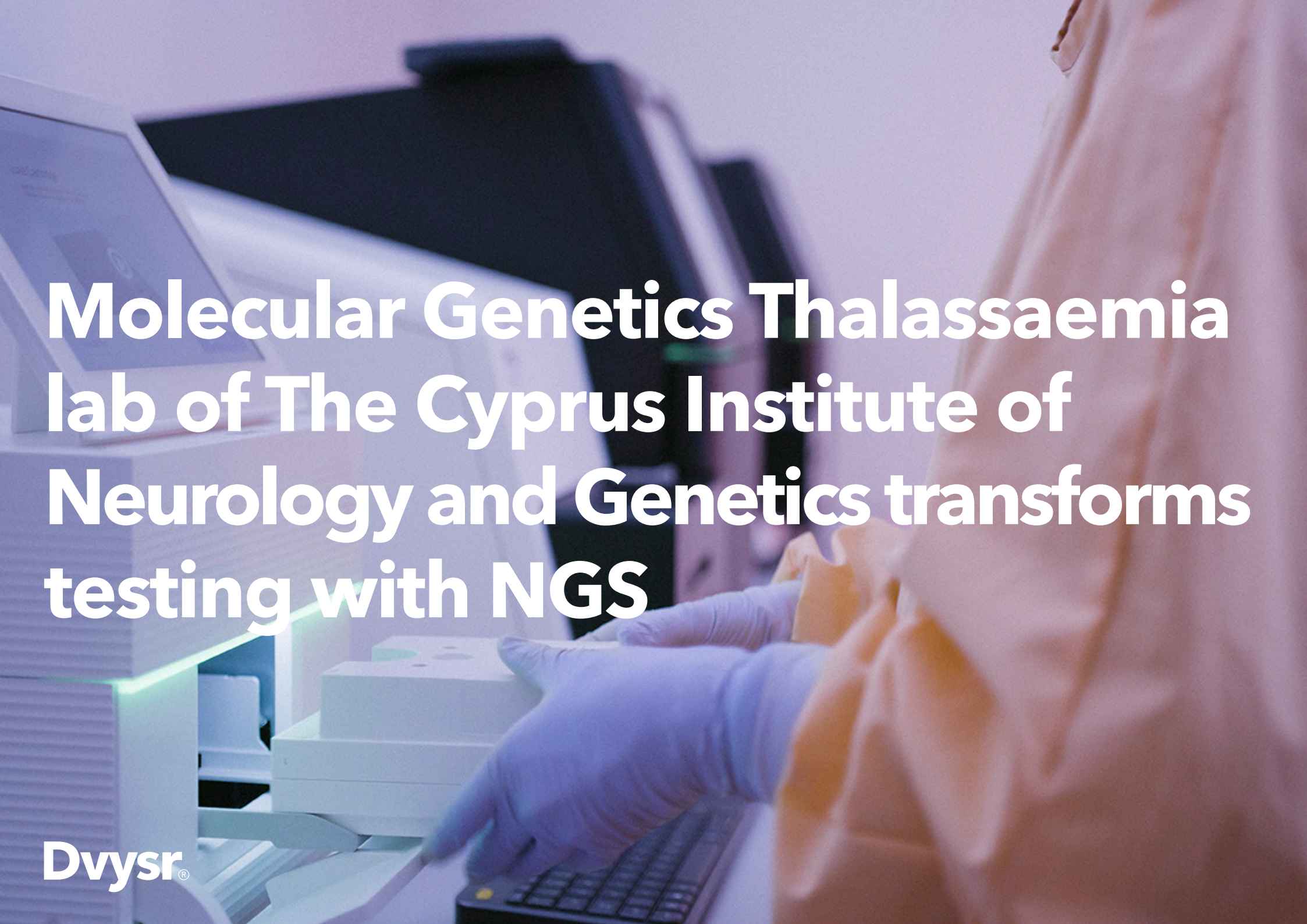

Molecular Genetics Thalassaemia lab of The Cyprus Institute of Neurology and Genetics transforms testing with NGS

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Dr. Thessalia Papasavva is the Group Supervisor of the Thalassaemia Diagnostics Research group of the Molecular Genetics Thalassaemia Department, headed by Prof Marina Kleanthous. Driven by a passion to prevent disease, Dr. Papasavva has spent more than 25 years at Cyprus Institute of Neurology and Genetics, 17 of which in this department.

In this case study Dr. Papasavva describes her laboratory's journey from traditional thalassemia testing to a state-of-the-art NGS technology and what a difference this has made in their daily work.

■■■ Thalassemia prevention in Cyprus

Thalassemia is a serious health problem in Cyprus where 12 % of the population are carriers of beta-thalassemia and about 19% are carriers of alpha-thalassemia. Due to the high incidence of beta and the severity of the disease, the state has initiated a carrier screening program to prevent the spread and reduce suffering. The program includes premarital screening of the entire population.

CING's Molecular Genetics of Thalassaemia Department is dedicated to the prevention of thalassemia and provides prenatal molecular diagnosis for β-thalassemia, α-thalassemia and other haemoglobinopathies as well as molecular diagnosis for carriers and patients.

Thalassemia testing at CING

CING is part of the National Thalassemia prevention program where the genetic analysis and prenatal diagnosis is performed. The Thalassemia Screening Laboratory is responsible for identifying thalassemia carriers through hematological testing using capillary electrophoresis. Once the carriers are identified they are passed over to CING for third level testing through molecular genetic analysis of the samples.

Molecular testing for thalassemia usually involves a patchwork of methods to check for all possible variants, which was also the case at CING. They made use of all the conventional molecular techniques such as PCR, real-time PCR, MLPA, Sanger sequencing and Mini sequencing.

Every population has a set of variants that are more prevalent than others and in Cyprus there are seven beta thalassemia pathogenic variants that make up about 99% of all beta thalassemia cases. One of these variants is responsible for about 80%. CING's strategy was to test at the beginning for the most

common variants. If they didn't find it, they moved on to test for a different variant. This process was repeated until a variant was found. Thus, they had to conduct a series of tests before they reached the final analysis. This procedure was implemented for beta thalassemia genetic analysis as well as for alpha thalassemia.

"The main problem with running a series of subsequent tests is not the lab work itself for each test, but the delay caused for the patient before they get their diagnosis. This delay is mainly due to the significant administrative process involved, repeated in full for every re-run. The physician would order a specific test, we would open a case, run the test, deliver an analysis and close the case. In the case of non-detection the physician would order a different test, a new case would be opened and so on until a variant was detected. This procedure can sometimes result in lengthy turn-around time, where in some cases, the patient would have to wait for months for their diagnosis."

This type of specific testing, targeted to the variant, is not only a lengthy and labor-intensive process, but it also comes with a higher risk of variant non-detection and increased error risk. Not to mention the waiting and anxiety it causes the patient.

1 tube

Single-tube NGS method for SNV, indel and CNV detection in HBA1, HBA2 and HBB.

45 min

With ready-to-use reagents, less than 45 minutes hands-on time and customised data interpretation software, it is a good match for laboratories of any size.

■■■ Evaluating NGS - the first attempt

Dr. Papassava is responsible for staying on top of scientific advancements and finding and implementing the most efficient testing technologies for CING's Molecular Genetics Thalassemia department. She decided early on that CING should take advantage of NGS to simplify thalassemia testing, but initially the goal was to create a customized panel. They collaborated with another company for almost two years without achieving the desired results and eventually abandoned this attempt.

Implementing Devyser Thalassemia NGS

With the disappointing experience of custom panel design fresh in mind, Dr. Papasavva was now only interested in a validated and ready-to-use commercial IVD product. She wanted her lab to focus their time and resources on their core business of thalassemia testing, not panel design.

Dr. Papasavva found Devyser Thalassemia NGS through an online search and conducted an initial pre-qualification based on the information available online. Together with Professor Marina Kleanthous, Head of the Molecular Genetics Thalassemia department, Dr. Papasavva concluded that Devyser's NGS product covered most of their needs including detection of both β-thalassemia and α-thalassemia.

After the initial pre-qualification Dr. Papasavva reached out to Devyser who came to demo the product in their lab.

"We tried the product, had great results and decided to implement it in our laboratory" Dr. Papasavva concludes."

Results: one patient - one reaction

"Thalassemia testing has changed completely with the introduction of Devyser Thalassemia NGS into our laboratory" says Dr. Papasavva.

"Today we can analyse all whole genes for alpha and beta thalassemia, and even more, in a single assay. This means that we have the results, a comprehensive analysis and a complete picture of the sample at the end of the run. It is very efficient compared to the traditional thalassemia testing we previously conducted and saves time on three levels - for the physician, for the lab and most importantly for the patient."

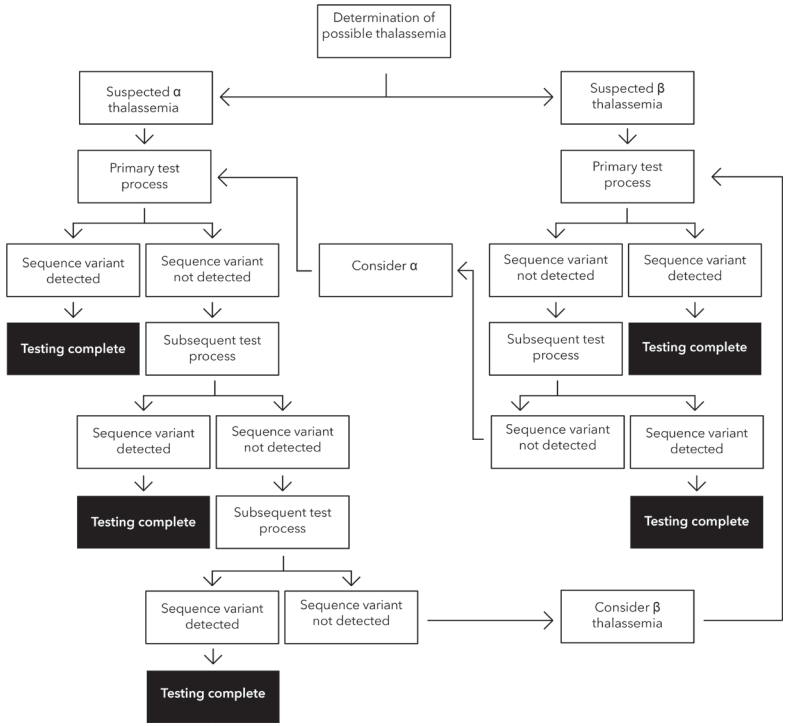
Thalassemia testing has changed completely with the introduction of Devyser Thalassemia NGS into our laboratory.

Dr. Thessalia Papasavva, CING's Molecular Genetics, Thalassemia Department

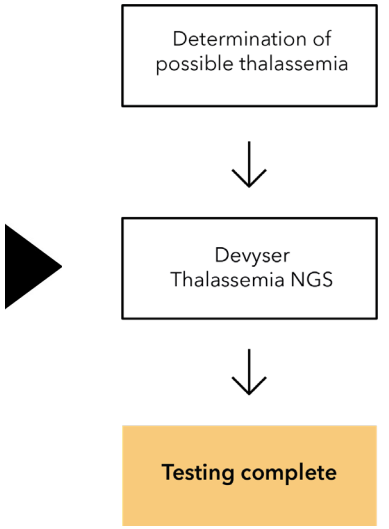
CING's key benefits of using Devyser Thalassemia NGS

- Instead of running on average three tests per patient, we now only run one and get a comprehensive analysis
- We can save on average 4 weeks for a patient waiting for their diagnosis
- The product is efficient and produces high-quality results
- The workflow is fast and simple; with just one tube we can test most of the thalassemias almost 100%
- Because we now get the full picture in a single run we can detect more variants, including some we might have previously missed if testing had been terminated with the detection of the first variant
- The software is user-friendly and has been developed and adapted to our needs through our communication with Devyser, including an integration with the ITHANET database.

Legacy workflows to determine possible alpha- and beta-thalassemia can take weeks



Testing with the streamlined NGS workflow of Devyser Thalassemia can be completed



The most important thing that I value about Devyser is the personal communication that we have! I value the human touch, the way that people respond to our needs. I always get prompt replies addressing any problems I raise. Devyser has a bespoke approach to each issue which is unique. As an example, we suggested an integration in the software to the ITHANET database, which has now been implemented. It is obvious to me that Devyser values our feedback and uses it to develop to meet our needs. This makes me feel secure.

Dr. Thessalia Papasavva, CING's Molecular Genetics, Thalassemia Department

■■■ About the Cyprus Institute of Neurology and Genetics (CING)

The Cyprus Institute of Neurology & Genetics (CING) is a private, non-profit, bi-communal, medical, research and academic center. Established in 1990 it is based in Nicosia, Cyprus. CING is dedicated to lessening the suffering of patients and their families and preventing diseases through patient care, research and educational programs on neurological and genetic conditions such as muscular dystrophy, multiple sclerosis, epilepsy, chromosomal abnormalities and all other aspects of molecular biology and genetics such as thalassemia, molecular virology, mental retardation, cardiovascular disease, stroke, cystic fibrosis and neurogenetics.

The Molecular Genetics of Thalassaemia Department offers specialized diagnostic services for haemoglobinopathies, prenatal diagnosis and non-invasive prenatal diagnosis (NIPD) during pregnancy as well as pre-implantation genetic testing. Specifically, the department provides: prenatal molecular diagnosis for β-thalassemia, α-thalassemia and other haemoglobinopathies, molecular diagnosis for carriers and patients. Pre-implantation genetic diagnosis (PGT) for β-thalassemia (including identification of compatible donor siblings by HLA typing where needed), α-thalassemia and any other monogenic disorders.

About Dr. Thessalia Papasavva

Dr. Papasavva holds a BSc degree in Microbiology from the University of Arizona, MSc degree in Applied Molecular Biology and Biotechnology from University College London and PhD degree in Medical Genetics from the National Kapodistrian University of Athens Medical School. She has more than 25 years of experience in the field of Molecular Genetics.

Dr. Papasavva manages the diagnostic part of CING's Molecular Genetics Thalassemia Department and leads a research group specializing in cell free fetal DNA and NGS methodologies. She also serves as a faculty associate at the school of The Cyprus Institute of Neurology and Genetics.

Read more about the product:

devyser.com/product-categories/thalassemias

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