PAIDHOS

First robot-assisted surgical procedures for pediatric patients with congenital cardiopathy

ISSUE 19.

Magazine discussing social and scientific matters at the SJD Barcelona Children's Hospital

SJD Sant Joan de Déu Barcelona · Children's Hospital

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The treatments offered in healthcare environments are improving day by day, achieving, if not complete cures, at least a significant improvement to patients' quality of life. This is all thanks to research, innovation, technological advances and, most importantly, the effort and dedication of healthcare professionals. The contributions of public administrations and wider society—be that foundations, associations, businesses or families—are fundamental to ensuring this continued improvement.

At the SJD Barcelona Children's Hospital, progress is happening across several areas. One of these highly impactful areas of progress is in rare pediatric disease, which will see a huge push with the launch of Únicas SJD in 2026 – a one-of-a-kind research and healthcare facility for rare diseases. It will host several research platforms for studying genetics, metabolomics and radiomics, as well as a multimodal pediatric characterisation centre. It will also offer gene therapy, cell therapy, neuromodulation and deep brain stimulation. The objective of the facility is to allow affected children to be diagnosed sooner, granting them access to more advanced, and more personalised, treatment options. It is also an example of the close involvement of wider society, with a significant donation from the Amancio Ortega Foundation and continued support from both the 'La Caixa' Foundation and the Daniel Bravo Andreu Private Foundation.

In this issue of Paidhos, we have included an article about this huge project, but we also discuss other initiatives that highlight the dynamism of a leading hospital such as ours in the ongoing improving to healthcare for patients and their families. Some examples are robot-assisted surgical procedures on patients with congenital cardiopathies, the new platform for developing and manufacturing advanced therapies, or cryopreservation of ovarian tissue to safeguard the fertility of young girls treated for cancer.

Around one year ago, we welcomed two very special patients from a rural part of Mauritania—Khadija and Cherive—who were joined at the abdomen. Thanks to our Surgery and Neonatal teams, the Spanish Air Force and our solidarity programme Cuida'm, the separation procedure was a success and both girls now lead a normal life in their home country. That is just another example of innovation, commitment and solidarity: the fundamental values of the Saint John of God.

Manel del Castillo
Managing Director at the
SJD Barcelona Children's Hospital

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Únicas SJD, a one-of-a-kind research centre for rare diseases, opening in 2026

The SJD Barcelona Children's Hospital and the Amancio Ortega Foundation have recently signed a collaboration agreement to promote research into rare diseases. The ceremony was held at the Hospital, with President of the Foundation, Flora Pérez Marcote, in attendance, as well as SJD Managing Director Manel del Castillo.

The Amancio Ortega Foundation will donate around 60 million Euros **towards the construction and kitting-out of a pioneering international research and healthcare centre for rare diseases—Únicas SJD—**that is currently under construction on land located near the hospital, granted by the Esplugues de Llobregat Council. It is expected to open its doors in early 2026.

Spanning almost 14,000 square metres over six floors, the centre will house the most advanced facilities for the research and treatment of rare diseases, including various platforms for genomic, metabolomic and radiomic studies, and also a multimodal pediatric characterisation centre. It will also offer new treatment options such as gene therapy, cell therapy, neuromodulation and deep brain stimulation.

Thanks to this centre, the SJD Barcelona Children's Hospital will expand knowledge of rare diseases through ongoing research and the application of new treatments. In 80% of cases where a person has a rare disease (around three million in Spain), the disease manifests in childhood. On average, these patients wait more than three years before they get a specific diagnosis, needing to frequently travel from their local communities to get it. This centre will allow **children with rare diseases to be diagnosed sooner, giving them access to new advanced therapies and innovative, personalised treatments.**

The centre will be part of the Únicas Network—a network launched by SJD Barcelona Children's Hospital and the Spanish Federation for Rare Diseases (FEDER)—consisting of 30 hospitals across Spain. The aim of this network is to promote the exchange of information and sharing of knowledge in precision diagnostics and new treatment options, thereby benefitting all pediatric patients, regardless of where in Spain they live.

Leading figure in rare diseases

In the last decade, the SJD Barcelona Children's Hospital has taken several steps forward in the field of rare pediatric diseases. This has been thanks to its close collaboration with public administrations and the support it receives from wider society. Donations from entities such as the 'La Caixa' Foundation and the Daniel Bravo Andreu Foundation—key players in the Catalonian health and research sector—have made possible various initiatives targeted at patients with rare diseases. This collaboration between various institutions has given rise to projects such as the SJD Pediatric Cancer Center Barcelona, a monographic centre for pediatric cancer, or La Casa de Sofía, the first facility in Spain that provides both social care and healthcare to children and adolescents with chronic illnesses.

The Únicas SJD precision medicine centre project has also benefitted from the support of other entities, such as the Leo Messi Foundation and the Stavros Niarchos Foundation. This has made it pos-

sible to develop key care platforms for patients, such as the Clinical Command Center, which is in its initial phase of operation and offers remote medicine and monitoring services.

Manel del Castillo, Managing Director of the SJD Barcelona Children's Hospital, notes: 'the contribution from the Amancio Ortega Foundation towards setting up this centre is a huge step forward for children with rare diseases, and also for the specialists who study them.' He adds: 'On behalf of all of those children, thank you for helping us take this huge step forward, in both quality and quantity, in the healthcare we provide and the research we conduct into these unique and increasingly unseen illnesses.'

Amancio Ortega Foundation

The Amancio Ortega Foundation runs projects related to education and social wellbeing, partnering with institutions that are involved in the care of vulnerable groups and people. In recent years, it has helped action several collaboration agreements, such as the Neurological Rehabilitation centre with the NIPACE in Guadalajara, the Comprehensive Pediatric Palliative Care Centre with the Porqueviven Foundation and, in the field of rare diseases, an agreement with FEDER to support research, diagnosis and the use of advanced therapies on patients.

Santiago's story

It is estimated that around three million people in Spain have a rare disease. In 80% of these cases, it appears during childhood. Oftentimes, these patients wait years—an average of four—before they get a specific diagnosis, needing to frequently travel from their local communities to get it. One example is Santiago, a nine-year-old boy living in Navarra (Spain).

At just seven-years-old, Santiago began to show symptoms of an extremely rare disease called DYT-TOR1A, a neurological disease that causes involuntary muscle contractions in the lower limbs. His symptoms got increasingly worse, until he was unable to walk at all and needed a wheelchair to get around.

After several appointments, a specialist in Navarra suspected dystonia as the cause of Santiago's symptoms, and referred him to the SJD Barcelona Children's Hospital. The patient was operated on by the Neurosurgery Team, led by Dr José Hinojosa, who implanted a deep brain stimulation device. One and a half months later, the patient was walking to his check-ups. Now, two years on since the operation, Santiago can walk, play and lead a completely normal life like any boy his age.

Santiago's story is just one example of the treatments planned for this new facility specialising in rare diseases by SJD Barcelona Children's Hospital and the Únicas Network.

SJD Barcelona Children's Hospital and Hospital Clínic Barcelona join forces to treat children and adolescents with congenital cardiopathy

The SJD Barcelona Children's Hospital and Hospital Clínic Barcelona have founded a congenital cardiopathy centre to offer joint, life-long care to children born with heart malformations. This partnership has allowed the pediatric age group access to minimally invasive surgical procedures that were already in use among adult patients, such as robot-assisted surgery and thoracoscopies.

Every year, around 600 babies are born in Catalonia with a congenital cardiopathy, be that a structural heart issue (in the atria or with the heart valves, for example), or in the great vessels. Around 30% of all cases concern a severe cardiopathy. Thanks to progress in the last few decades, 95% of these children reach adulthood, albeit with very specific needs.

Now, the same team of professionals will monitor and treat these patients throughout their life. 'Successful management of patients with cardiovascular disease is based on high-quality multidisciplinary care and a long-term monitoring strategy that ensures continued care throughout adulthood. As such, having a comprehensive, specialised facility with a transversal vision is key to improving the quality of healthcare for these patients', explains Daniel Pereda, Head of the Congenital Cardiopathy Centre (SJD - Clinic).

The new centre has two facilities—one at SJD Barcelona Children's Hospital, and the other at Hospital Clínic Barcelona—which together, boasts an extensive, mutually complementary service offering, as well as an integrated team of 23 staff members, including cardiovascular surgeons, cardiologists, pediatricians and anesthesiologists.

Thanks to the partnership between SJD Barcelona Children's Hospital and Hospital Clínic Barcelona, the creation of this centre has allowed the pediatric age group access to surgical techniques that, until now, were only used in adult heart surgery, such as minimally invasive thoracoscopic surgery and robot-assisted operations.

Before, children and young people with congenital cardiopathies had to undergo open heart surgery, which not only meant a significantly longer post-op and recovery period for the patient, but also had greater esthetic repercussions.

The new Congenital Cardiopathy Centre (SJD - Clínic) has already carried out seven operations between October 2023 and April 2024 on such pediatric patients. In three cases, surgeons opted for thoracoscopic surgery, which involves making small incisions to the child's chest and inserting a device with a video camera to allow visualisation of the surgical site and the instruments needed for the procedure. The first child operated on using this technique had a heart tumor requiring resection. The youngest patient operated in this way so far was just six years old.

First case of robot-assisted surgery in children

In another four cases, the surgical team opted for robot-assisted heart surgery. The first pediatric patient to undergo robot-assisted surgery was a 13-year-old girl from the Basque Country (Spain) who had an ostium primum atrial septal defect (both atria were connected) and a defective mitral valve. These malformations were causing abnormal blood circulation in the heart and the imbalance was overloading the right side of the heart. Over time, this caused heart failure.

For this patient, the disease was further worsened by very pronounced scoliosis, which made accessing the heart very difficult. That is why heart surgeons decided to use robot-assisted surgery. They made four small incisions in the patient's chest, around 8 mm in diameter each, through which they inserted a camera into the heart to visualise the surgical site and the instruments needed to perform the procedure. Doing so allowed the surgical team at the Congenital Cardiopathy Centre to close the connection between both atria, and also repair the damaged mitral valve. The operation lasted four hours and involved a dozen different professionals.

The second patient to undergo robot-assisted surgery was a 15-year-old boy who, months prior, had underwent a catheterisation to treat an atrial septal defect, and who now presented with an infection of the closure device (endocarditis).

Pereda explains that, for children, robot-assisted surgery is limited by the size and age of the patient, because surgical instruments are designed and manufactured for use on adult patients. As such, surgeons only consider this option for older children and adolescents. The main candidates for this type of surgery are those with the following conditions: atrial septal defect (when unable to be resolved via catheterisation), mitral valve defect, tricuspid valve defect, or heart tumors. It is predicted that a dozen patients will undergo minimally invasive robot-assisted surgery each year, with another 20 thoracoscopy procedures annually.

Iu Teixidó, 15 years old
One of the first pediatric patients to undergo robot-assisted heart surgery

'My brother had his heart operation a few hours after being born and he has a huge scar on his chest. I didn't want to have one like that, too.'

SJD Barcelona Children's Hospital creates a new platform for the development and manufacture of advanced therapies

Advanced Therapies are a new treatment option offering hope and new opportunities to children with rare diseases that have no effective treatment at this time. The SJD Barcelona Children's Hospital has recently launched a platform alongside Hospital Clínic Barcelona to develop and manufacture new therapies for the pediatric age group.

Some of these therapies already exist, such as CAR-T therapy, used in cases of drug-resistant acute lymphoblastic leukemia. Other areas to be developed include therapeutic strategies in the field of Pediatric Oncology, such as CAR-T combined with dendritic cells to treat diffuse midline gliomas, a tumor with a very poor prognosis. In the field of monogenic diseases, a new gene therapy is being developed for a very rare, severe form of primary immunodeficiency, MHC class II deficiency syndrome.

In recent years, the SJD Barcelona Children's Hospital has seen an increasing number of patients with complex rare diseases, and has therefore launched various initiatives to increase knowledge and develop new treatments. It was one of the first hospitals in Spain to administer CAR-T therapy to a child with leukemia. In addition, alongside Hospital Clínic Barcelona, it developed CAR-T ARI-0001 to treat acute lymphoblastic leukemia that is resistant to other treatments. Now it is taking a step even further and aims to manufacture these therapies in-house. To do so, it has launched a new research, investigation and manufacturing platform for advanced therapies.

Advanced therapies are medications obtained by manipulating genes, cells or tissues to treat a disease in a more efficient, personalised way. For example, CAR-T cell therapy uses immune cells (called T-lymphocytes) extracted from the patient and modified to express molecules known as Chimeric Antigen Receptors (CAR) on their surface. These genetically modified T-lymphocytes are then readministered to the patient, and the new receptors allow the cells to recognise and destroy cancer cells.

Advanced therapies are a new category of medication, and as such, must be manufactured in facilities meeting very precise specifications that follow a series of very strict regulations, known as Good Manufacturing Practice (GMP). This ensures the safest end product possible for the patient. Recently, the Spanish Agency of Medicines and Medical Devices (AEMPS) inspected the facilities at the new SJD Advanced Therapies Platform, awarding them with full certification. 'The positive outcome of this inspection not only confirms the quality and safety of our procedures, but it also strengthens our resolve to offer innovative, effective treatments for cancer', explains Dr Julio Castaño, Technical Director of the platform's manufacturing department.

Few centres have these facilities—known as cleanrooms—because they require a significant economic investment, specific infrastructure and equipment and a team of expert professionals. 'In our case', explains Dr Alessandra Magnani, Head of the Advanced Therapies Platform at SJD Barcelona Children's Hospital, 'it was the logical next step after opening the SJD Pediatric Cancer Center Barcelona, where we treat patients from all over the world with extremely complex cancers. It was also in line with the aim of the Únicas project for personalised medicine in the treatment of rare diseases. At the SJD Barcelona Children's Hospital, we have clinical experts in extremely complex diseases, researchers studying these diseases, and patients who suffer from them and require treatment. With these new cleanrooms, we now also have the infrastructure to develop and manufacture therapies. It was a key piece that was missing.'

The new SJD Advanced Therapies Platform is part of the joint platform with Hospital Clínic, coordinated by Dr Manuel Juan. It is also part of: the Catalan Advanced Therapies Network, promoted by Biocat; the Spanish state consortiums CERTERA and TERAV, promoted by the ISCIII; and a European consortium for the production of CAR-T cells for pediatric oncohematology.

Unlike other platforms, advanced therapies for the pediatric age group are both developed and manufactured in the same space. 'Concentrating the research, development and manufacturing of advanced therapies into the one place is a cru-

cial aspect of our transversal approach. Not only does it allow us to directly use research findings in clinical applications, but also to monitor patient progress after they have been given our therapies and continually improve the treatments we offer. If we know the full manufacturing history of a therapy—instead of it arriving already made from an external lab—we can optimise the production conditions, discern the reasons for different results between patients, and ultimately, offer them more effective, personalised treatments', explains Magnani.

The new SJD Advanced Therapies Platform will span 1,280 square metres and boast an advanced therapy manufacturing area with four bespoke cleanrooms to produce various advanced therapies (cell therapy, tissue engineering and gene therapy). Staff from several fields will work together in this facility, including Oncology, Oncohematology, Neuromuscular Disease, Primary Immunodeficiency and other Hematological diseases.

Regarding production, cleanroom staff have already begun to manufacture CAR-T ARI-0001, and alongside Hospital Clínic, research has already started on developing a new gene therapy to treat a very rare, severe form of primary immunodeficiency, MHC class II deficiency syndrome. Children with this disease are unprotected against common pathogens that would normally be harmless, making them susceptible to disease from a very early age. If left untreated, this immunodeficiency can be lethal during the first ten to twenty years of life.

'What we do know is that this immunodeficiency is due to genetic defects that alter the expression of the MHC molecule. That means it is harder for lymphocyte cells to mature, thereby limiting the body's immune response to infection. We treat patients with this disease at our hospital, who are monitored by Dr Laia Alsina, Head of the SJD Clinical Immunology Department. Until now, the only treatment for affected patients was an allogenic bone marrow transplant. But that is not the optimal treatment, especially if the patient does not have an HLA compatible donor, based on the genetic correction of the patient's own hematopoietic stem cells', explains Magnani.

'We are working closely with Hospital Clínic and CIEMAT in Madrid on several genetic correction techniques—the height of innovation—to identify the best method to correct this disease. We believe that finding a treatment and therapeutic approach for this disease can open doors to finding treatments for other diseases with similar processes', she concludes.

The new facilities will also be open to other centres and teams interested in developing advanced therapies because, according to Magnani, 'our facilities have huge production potential above and beyond our current needs.'

The SJD Advanced Therapies Platform has been made possible thanks to a donation from Rosalía Gispert and the Amancio Ortega Foundation.

'Creating the Advanced Therapies Platform was the logical step. Our hospital has clinical experts in extremely complex diseases, researchers studying these diseases, and patients who suffer from them and require treatment. Now, with these new cleanrooms, we also have the infrastructure to develop and manufacture therapies and offer new hope for treatment to our patients.'

Alessandra Magnani

First gene therapy for a patient under four years old with Duchenne muscular dystrophy

Researchers from the Neuromuscular Diseases Department at the SJD Barcelona Children's Hospital have, for the first time ever, used gene therapy on a child under the age of four with Duchenne muscular dystrophy, as part of an international clinical trial. The trial is currently active and open to these patients, with six different hospitals from around the world already involved. The team, led by Andrés Nascimento, has been the first in the world to include a patient under the age of four in the trial for this type of genetic treatment. At present, one other patient has received the treatment at the SJD Barcelona Children's Hospital. In addition, there are another eight children in hospitals across Europe receiving the treatment.

Duchenne muscular dystrophy is an uncommon genetic condition within the rare diseases category. It is linked to the X chromosome and causes progressive muscle weakness. Children are diagnosed with this disease in their first years of life, with their muscles progressively weakening over time. Around three or four years old is when this disease begins to have a more obvious impact, with children eventually losing their ability to walk at around 12 or 14 years old. At present, there is no treatment that offers a cure or a way to improve symptoms of the disease. As such, it is very difficult to fight. The only therapies that exist are those which seek to delay the disease's progression, though they are still unable to completely stabilise symptoms.

Gene therapy, when it is applied as early as possible, is the most promising treatment option to combat this genetic muscular deterioration disease. Until now, only patients over the age of four had been treated, with very positive results. This led to the U.S. Food and Drug Administration approving this treatment for use on four- or five-year-old patients. An important aspect of this disease is that it is progressive. The more time that passes, the more muscle tissue is lost and replaced with fat and fibrosis. That is why it is important to provide treatment before muscle damage becomes irreversible.

'Our team has been the first to include a child this young in this new clinical trial—known as Envol. The patients are tolerating the treatment well, with no side effects, which has allowed us to open a new cohort of four children between two and three years old', explains Andrés Nascimento, Head of the Neuromuscular Diseases Unit at the SJD Barcelona Children's Hospital, and member of the Applied Research Group in Neuromuscular Diseases at the SJD Research Institute. Nascimento adds: 'the treatment was given several weeks ago and the patient has remained stable, with no side-effects. We hope to be able to confirm positive results as time goes on. We have high hopes, as this gene therapy is being applied to healthier muscle tissue that has not started to significantly deteriorate yet'.

Duchenne muscular dystrophy is a rare, genetic condition that causes progressive muscle weakness from a very early age, eventually leading to losing the ability to walk, as well as breathing and heart issues.

Until now, only patients older than four years old were treated.

Dr Andrés Nascimento's team (second from the left, lower part of the image).

First gene therapy for Duchenne muscular dystrophy

The rise of gene therapy is a huge step forward for patients with Duchenne muscular dystrophy. One of the challenges of this therapy is the size of the dystrophin gene, which is very large and cannot be introduced through normal adeno-associated viral vectors (modified adenovirus), which would carry the new gene to existing cells to incorporate it into them.

A few years ago, a group of patients were identified who had reached an advanced adult age, experienced muscle pain, had higher muscle enzymes, certain mobility issues and motor difficulties, but who were still able to walk. These individuals had alterations in their dystrophin gene, resulting in smaller but functional version of the protein, known as microdystrophins. This finding suggested that the presence of microdystrophin—albeit in a lesser quantity or size—could provide some level of protection against severe symptoms of Duchenne muscular dystrophy. Based on these findings, scientists began to explore the possibilities of using microdystrophin as a treatment option for patients with the disease.

From there, all the preclinical trials took off, with Sarepta—the laboratory behind this gene therapy—launching phases one and two, which showed that the therapy was safe and effective. This allowed for the development and eventual launch of phase three of the trial (Embark) for patients aged four to eight. In the clinical trial, the adeno-associated virus (vector), with the ability to inject new genetic material into muscle cells, does so with microdystrophin. The first children in this age group to be treated tolerated the treatment well, seeing significant improvements to their motor function.

Early treatment leads to better effectiveness

This same group of specialists took part in phase three of the Embark study, managing to recruit 12 patients aged four to eight. These data will be reviewed by the European Medicines Agency (EMA) in the hope that the therapy will be approved. A few weeks ago, the Envol clinical trial began for children under the age of four. The trial hopes to recruit an initial cohort of ten patients between the age of three and four, as per safety results for this group. Even younger patients will be allowed to take part at a later stage, such as those age two to three, or even months-old children—who, in fact, have not even been born yet—in order to determine the safety and efficacy of early treatment.

Six hospitals are taking part in this international trial, from the United Kingdom, Italy, the Netherlands, France, Belgium and Spain. The SJD Barcelona Children's Hospital is responsible for two patients, and judging by the number of patients and families on the waiting list, we are confident that we will be able to recruit around four more participants. Once again, just like with the Embark study, our facility will have the most study patients.

'Our aim is to always try to offer every possible treatment option to our patients. However, not everyone is a suitable candidate. There are several very specific clinical and genetic criteria that must be met. One of the most significant limiting factors in receiving this treatment is that patients must not have any antibodies against the vector (modified adenovirus) used to administer the dystrophin microgene', highlights Andrés Nascimento.

Pioneering procedure to repair two malformations causing severe respiratory failure in a baby

For the first time ever in Spain, a team of surgeons at the SJD Barcelona Children's Hospital treated two malformations in an infant patient in one sitting: Tetralogy of Fallot, a congenital cardiopathy that restricts blood flow to the lungs, and a narrowing of the trachea which caused respiratory failure.

Professionals treating the mother during her pregnancy detected a heart malformation in the fetus during a routine prenatal ultrasound check-up. The infant was diagnosed with tracheal stenosis a few days after birth. His trachea was very narrow along its entire length, causing respiratory failure and continuous stridor (an abnormal breathing sound), which worsened over time.

Specialists at the Heart Unit and ENT Department at the SJD Barcelona Children's Hospital who were treating the child decided to wait until he gained some weight before operating, and suggested repairing both malformations in a single procedure to minimise risks. 'We knew that, if we only operated on one of the malformations, the child would not tolerate the post-op period', recalls Stefano Congiu, Head of Heart Surgery at SJD.

This is the first time in Spain that the two malformations were operated in one single procedure. 'It's a one-of-a-kind case. There are very few cases like this worldwide. We found nothing on it in scientific literature. Normally, affected children have one malformation or the other, but it is very uncommon to have both at the same time', Congiu continues.

The operation took place when the infant was eight months old. In the first few hours of the procedure, aided by extracorporeal circulation, heart surgeons closed the abnormal opening between the two ventricles using a pericardial patch, repairing the defect. They then proceeded to widen the outflow of the right ventricle towards the lungs to allow for normal circulation and blood oxygenation. To finish this stage, they used an ECG to verify that the Tetralogy of Fallot had been corrected before proceeding to the tracheal surgery.

Then, with the child still attached to extracorporeal circulation, ENT surgeons cut a section from the middle of the trachea, bringing both cut ends together over one another to widen the windpipe. 'The procedure meant that the patient's breathing improved and there was no further stridor', notes Oliver Haag, Head of the ENT Department at SJD.

After the procedure, lasting five hours and involving 20 different professionals, the infant was transferred to the ICU. One month later, he was discharged.


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An innovative genetic screening by SJD and CNAG successfully finds a diagnosis for 23 children with a neuromuscular disease

Neuromuscular diseases affect between eight and 16 million people around the world, which corresponds to 0.1 to 0.2% of the world population. This small proportion, alongside varying symptoms presented by patients, makes it very difficult to reach a diagnosis. This leads to the 'odyssey' that many families who are affected by a rare disease have to embark upon, waiting years before finally getting a diagnosis. Seeing as 80% of rare diseases are genetic in origin, scientists are focusing on finding the cause of these diseases in our genes.

That is what a group of researchers from the SJD Research Institute (IRSJD) and the National Centre for Genomic Analysis (CNAG) have been doing, using an innovative new genetic screening method. They have helped 23 children with neuromuscular diseases finally reach a diagnosis, putting an end to years of waiting—over eight years, in some cases.

The results, published in the European Journal of Human Genetics, are from a study involving 58 pediatric patients at the SJD Barcelona Children's Hospital. Each patient was affected by some type of neuromuscular disease, presenting with muscle weakness and/or loss of muscle mass, and none of them had a prior genetic diagnosis despite having undergone exome sequencing studies – a genetic screening technique that studies the part of DNA that codes for proteins, where the mutations associated with these diseases are usually found. The reanalysis of undiagnosed patients' data—an increasingly common practice in the field of rare diseases—is vital because of the ever-changing nature of scientific knowledge and the discovery of new genes associated with uncommon diseases. This practice usually helps to provide molecular diagnoses in approximately 15% of cases, while new genetic screening methods have managed to increase this figure to up to 40%.

Whole genome sequencing and the integration of other omics techniques have been key at reaching a diagnosis.

This concept is reiterated by Dr Leslie Matalonga, author of the study and Head of Clinical Genomics at CNAG: 'The methods we have used in this study (whole genome sequencing and the integration of other omics techniques) are crucial for establishing a diagnosis for undiagnosed patients. Nowadays, however, their implementation is costly for healthcare systems, and in most cases, they are carried out during research projects. At CNAG, we are also working on developing tools and methods to maximise the automation of these processes, and facilitate their future integration into routine hospital practice, consequently reducing diagnosis times.'

For affected families, getting a definitive diagnosis is an essential step towards treatment that can help them improve their quality of life and, in some cases, even stop the disease from progressing. Furthermore, it gives them more information about how the disease does progress, and the potential for passing the disease to future children.

Daniel Natera and Berta Estévez from SJD with one of the diagnosed patients and their mother.

New genetic screening approach

In the last 14 years, the number of genes found to be associated with the development of neuromuscular diseases has doubled. Thanks to next-generation sequencing, almost 700 genes have been discovered in recent years. Although it is a huge step forward, more than half of families affected by a neuromuscular disease still do not know the origin of their condition. The innovative approach, developed by research teams at the IRSJD and CNAG, is specifically designed to help these families. The new genetic screening method combines the benefits of several omics techniques, allowing for the combination of more clinical and genetic data, thereby increasing the possibility of reaching new diagnoses for pediatric patients.

The analysis begins with an exhaustive phenotyping of the patient, performed by the medical team at the SJD Barcelona Children's Hospital. 'This work includes a standardised summary of symptoms and results from a broad range of tests, such as MRI scans, neurophysiological data or lab data', says Dr Daniel Natera, Pediatric Neurologist at the SJD Neuromuscular Unit.

After this detailed assessment of patients' symptoms, it is complemented by two omics techniques for the genetic screening. First, trio genome sequencing, which involves obtaining a complete DNA sequence (every gene) from the patient and their biological parents using Next-Generation Sequencing (NGS), thereby allowing for the identification of genetic variants and mutations. Then, for specific cases, a transcriptome sequence is done (RNA; gene expression) using a muscle biopsy from the patient. This identifies abnormalities in the composition of RNA molecules (transcripts) or in their expression.

Dr Anna Esteve, Head of the Functional Genomics team at CNAG and author of the study, explains: 'At CNAG, we sequenced RNA samples from our patients using state-of-the-art genome technology. We then processed and analysed the data, which helped us examine the active genes within the muscles. This technique allows us to detect abnormal or incorrect gene expression or structure, crucial clues in helping us locate the genetic mutations responsible for the development of neuromuscular diseases.'

A key platform for the interpretation of results

All of the results are processed using the RD-Connect GPAP platform (Genome-Phenome Analysis Platform), a collaborative genetic analysis platform developed and based at CNAG under the framework of various European projects (RD-Connect, EJPRD and ELIXIR) for the diagnosis of rare diseases. This tool not only compares information from patients, but also includes data from more than 30,000 individuals with rare diseases (patients and family members).

This means that researchers at IRSJD and CNAG have a comprehensive record of all available information ready for interpretation. This interpretation process—involving a combination of phenotype, genome and transcriptome data—plays a key role in establishing a molecular cause. For example, abnormalities in RNA may point to a specific cause or gene in particular, or alternatively, transcriptome data can help explain the predicted effects of a certain genetic variant identified in the genome. In cases of findings concerning variants of uncertain significance in candidate genes, the SJD Translational Diagnostics and Therapeutics Programme can increase the diagnosis rate thanks to functional biology, cellular and molecular studies.

According to IRSJD researcher Berta Estévez, 'having a multidisciplinary team was essential for reaching such a high diagnosis rate, as we were able to combine clinical knowledge with genetic knowledge.' She continues, 'knowing the symptoms is like knowing the disease's first and last name. Knowing the genetic cause, however, is like knowing the disease's address.'

The 'Eureka!' moment happened 23 times, one for every time researchers found the cause of a child's disease. This allowed the SJD medical team to render a genetic diagnosis and begin to consider potential treatments for each individual patient.

This new analytical approach is part of the Solve-RD project, funded by the European Commission to promote research into rare diseases. The RD-Connect GPAP has played an important role in Solve-RD, as it was used to compile and process all phenotype and genome data in the project.

Leading experts in rare diseases

The SJD Barcelona Children's Hospital is a reference centre in Spain for its diagnosis and treatment of rare diseases, which, in 80% of cases, are diagnosed in childhood. It is currently promoting the Únicas Network, which consists of 30 hospitals across Spain, whose goal is to improve healthcare for these patients. Charitable support has been a key factor in the progress that has been made at SJD in the study, diagnosis and treatment of rare diseases. As such, we must recognise the support received from the 'La Caixa' Foundation and from the Daniel Bravo Andreu Private Foundation.

Khadija and Cherive, the conjoined twins who underwent surgery last year to separate them, now live a normal life in their home country

Twins Khadija and Cherive were born on 8 October 2023 in Mauritania, joined at the upper abdomen and sharing one umbilical cord between them. As it was impossible to separate them in their home country, Mauritanian health authorities turned to the SJD Barcelona Children's Hospital by means of the international cooperation agreement between the Mauritanian Department of Health and the Catalan hospital.

One week after they were born, the medical team at the SJD Barcelona Children's Hospital received photos from Mauritania, deciding that the separation was possible and could be performed at the Barcelona facility. Khadija and Cherive would then travel to the SJD Barcelona Children's Hospital for treatment thanks to the Hospital's charitable programme, Cuida'm. This initiative uses private donations to fund treatment for children with severe (but curable) diseases who live in low-income countries and cannot be treated there.

The campaign to bring Khadija and Cherive over was launched immediately. On the 25th of October, the girls were transported to Barcelona in a Spanish Air Force aircraft, and cared for at all times by a neonatal team from the SJD Barcelona Children's Hospital. 'We were prepared to give the girls as much support as possible, but it wasn't necessary. They were as good as gold. The medical teams in Mauritania had them well looked after', recalls Ana Alarcón, one of the neonatal pediatricians who accompanied the twins during their journey.

The girls landed in Barcelona on the morning of 26 October, and were transferred to the SJD Barcelona Children's Hospital by pediatric EMS ambulance. Professionals got to work immediately, carrying out various radiodiagnostic tests to confirm the degree to which the twins were conjoined, finding out which organs were shared, and if there were bone and/or blood connections between both girls. Testing confirmed that the twins were omphalopagus, meaning they were joined at near the bellybutton and had two separate livers, but there was a six centimetre area of shared tissue.

It is estimated that conjoined twins make up one in every 250,000 twin births across the world. Many are stillborn or do not survive their first few months of life due to the severity of their connection (such as the organs they share). The percentage of omphalopagus twins—joined at the bellybutton, and who can share a liver and/or parts of the digestive tract—makes up 20% of all conjoined twins.

Khadija and Cherive are now growing into normal, healthy girls

Khadija and Cherive, a few months after the operation

Simulation of the procedure

For very complex surgical procedures carried out at the SJD Barcelona Children's Hospital, or for those requiring the involvement of many different professional teams (such as with separating conjoined twins), the Hospital often chooses to simulate the operation beforehand. This allows the surgical team to plan the surgery in detail and practice their technique before the actual operation. With this in mind, teams on the Simulation Programme and in the 3D Unit at the Hospital created a to-scale virtual 3D replica of the twins, which allowed the surgical team to decide which approach would be best for the operation and practice it.

One week before the real operation, the simulation took place. The aim was to reproduce not only the surgical procedure that was to take place, but also the physical space. 'This operation had an added complication. While we started with just one operation on the one patient (being the conjoined twins to be separated), after they were separated we would then have two patients and two distinct operations. We had to have two operating tables in the one theatre to properly finish the procedure on both girls separately, to reconstruct their abdominal wall and close the wound', explains Xavier Tarrado, Head of Pediatric Surgery at the SJD Barcelona Children's Hospital.

José Quintillá, Head of the Hospital's Simulation Programme, explains that, among several other clinical aspects, the virtual trial run allowed the surgical team to figure out the best way to position the twins on the operating table, how to intubate them and the best surgical approach. It also allowed them to decide how to lay out the various surgical tools and how they should move around the theatre so as not to get in the way of their colleagues.

'It was extremely useful. Thanks to the simulation, the surgical team felt like we had already performed this operation before. We knew exactly how to tackle the procedure, and this meant we completed it much faster and in a much safer way', says Tarrado.

In the end, the patients had their operation on 8 November. It lasted five hours and involved around 20 different professionals: from anesthesiologists, surgeons, neonatologists, nurses and assistants, to engineers, bioengineers and imaging technicians, among others.

After the operation, Khadija and Cherive were transferred to the Neonatal Intensive Care Unit and recovered quickly. Five days later, they were transferred to the hospital ward, and soon after, discharged. A surgeon from Mauritania, who came to Barcelona to observe the procedure, is monitoring the girls in their home country.

'Since returning to Mauritania, we have been closely monitoring them with the team at the Nouakchott Hospital. Khadija and Cherive are in good health, and are growing into normal, healthy girls', explains Ana Alarcón. She adds, 'they have become a symbol of hope and progress in their country, so much so that, last April, they were involved in the launch day for the polio vaccination campaign alongside the Mauritanian Minister of Health.'

Partnership between SJD and Mauritania

Khadija and Cherive's treatment was only possible thanks to the charitable programme Cuida'm, run by the SJD Barcelona Children's Hospital. This programme, which is donation-funded, allows children with severe (but curable) diseases who live in low-income countries to come to the SJD Barcelona Children's Hospital and get the treatment they need, which they cannot access in their home country. The goal is for them to return home healthy and with a better quality of life.

Cuida'm is part of the international cooperation initiative run by the SJD Barcelona Children's Hospital, which also offers digital consulting and training services for primary pediatric caregivers in countries like Mauritania.

Leading figures in ovary tissue preservation to safeguard the future fertility of young girls treated for cancer

The SJD Barcelona Children's Hospital treats the highest number of pediatric cancer cases in Spain, with 400 new patients every year. Since 2000, it has offered a leading ovarian tissue cryopreservation programme for girls and women who, due to a disease or past treatment (oftentimes cancer, though there can be others), have compromised fertility.

In the last few decades, the SJD Barcelona Children's Hospital has become one of the facilities with the highest number of frozen ovarian tissue samples in Spain. Between 2000 and 2024, in partnership with the Blood and Tissue Bank of Catalonia (BST), SJD has extracted and cryopreserved a total of 313 ovarian tissue samples. Of these samples, 46% (143) are from patients diagnosed with pediatric cancer or cancer during infancy or adolescence.

So far, staff at the SJD fertility preservation programme have reimplanted tissue from 22 women wanting to have children. Eight of them were successful: three spontaneously and another four through in-vitro fertilisation techniques. One of these women joined the fertility preservation programme after being diagnosed with pediatric cancer—namely, an osteosarcoma—as a teenager.

Cryopreservation of ovarian tissue in cases of pediatric cancer

'When a woman is diagnosed with a tumor that may threaten her fertility, the first option is to extract eggs and freeze them. However, in young girls, preservation of egg cells is not possible because they have not yet started puberty. In these cases, the only option is to extract and preserve the ovary tissue itself, which is what we do. The youngest patient was only 22 months old when we extracted her tissue', explains Dr Cristina Salvador, Co-Coordinator of the fertility preservation programme at the SJD Barcelona Children's Hospital alongside Dr Santiago González.

When the patient is a teenager and has already started menstruating, staff can choose to freeze egg cells if and when it is possible. 'However, the amount of time we have available is crucial. To extract egg cells, the patient must undergo ovarian stimulation. That means a two-week buffer period that, sometimes, we just do not have, as Oncologists have to start treatment immediately. That is why we sometimes have to rule out egg freezing in these cases and go for ovarian tissue preservation instead', adds Salvador.

The extraction of ovarian tissue is done in theatre via a laparoscopy, while simultaneously doing any other procedures that the patient needs. Once extracted, the tissue is sent to the BST, where it is stored until the patient reaches adulthood and wants to have children, but is unable to do so. That is when the tissue would be reimplanted, which is also done via a laparoscopic procedure.

The process of extracting ovarian tissue is coordinated with the BST to ensure it is stored as fast as possible. Upon arrival at the facility, the tissue undergoes a special, controlled freezing process. The temperature goes as low as -196°C, preserving as many cells as possible. The cryopreserved tissue is stored in tanks of liquid nitrogen until they are needed for reimplantation. Then they undergo a controlled defrosting process so they arrive in theatre in optimal condition.

Since the year 2000, the SJD Barcelona Children's Hospital has diagnosed 143 young girls with a tumor that requires treatment that could affect their future fertility

Cristina Salvador and Santiago González.

Pregnancy rate of 34%

'Cryopreservation of ovarian tissue and its subsequent transplantation is a technique that yields very positive results. It has a pregnancy rate of 34%. At present, we cannot be clinically certain that the reimplanted tissue will result in viable pregnancy, so, four months post-implantation, we normally perform in-vitro fertilisation and watch for signs of tissue activity. We have also seen cases where the patient got pregnant naturally', notes Salvador.

The SJD Barcelona Children's Hospital has been a leading player in the field of ovarian tissue transplantation to preserve fertility. It has been cryopreserving ovarian tissue since the year 2000. In 2012, for the first time ever in Spain, it helped a woman without ovaries become a mother. The patient had her ovaries removed after finding benign tumor growths. Staff on the fertility preservation programme extracted and preserved a small sample of healthy ovary tissue in 2003, which was reimplanted in 2011. After one cycle of in-vitro fertilisation, the patient fell pregnant and gave birth nine months later.

'Thanks to the fertility preservation program, I was able to become a mother'

Anna was only 18 years old when she was diagnosed with pediatric cancer—namely, an osteosarcoma—and the staff treating her suggested extracting ovarian tissue to reimplant later down the line should she ever wish to have children and be unable to fall pregnant. 'I said yes just in case, because I didn't know whether I wanted to have children or not back then. I hadn't even thought about it, to be honest', she recalls, with her child Biel in her arms.

Anna overcame the cancer, and a decade later, she got married. 'That's when I knew that I wanted to be a mother. My husband and I began trying, but nothing happened. We tried and failed for two years, until I decided to get in touch with the SJD Barcelona Children's Hospital to see if anything could be done', she recounts.

After several attempts at artificial insemination and an in-vitro fertilisation procedure, staff treating Anna suggested reimplanting the ovarian tissue she had extracted 14 years prior. The transplant took place on 23 March 2022, and then just three months later, on 20 June 2022, Anna took a pregnancy test, confirming she was three weeks pregnant. Biel came into the world on 26 February 2023.

'Thanks to the fertility preservation programme at the SJD Barcelona Children's Hospital, I've been able to become a mother. I am so thankful for the staff who decided to study whether cryopreservation of ovary tissue could help girls and women in the same situation I was in. Back then, I didn't realise the weight of what they were suggesting, but now, with age, I've realised just how much I wanted to be a mother. It would have been much more difficult to bring my dreams to life another way', she explains.

Interview

'Our goal is to turn everything our group researches into a phase one clinical trial.'

Ángel Montero Carcaboso

Head of the Pediatric Cancer Treatment Group at the SJD Pediatric Cancer Center Barcelona

Ángel Montero Carcaboso joined the SJD Barcelona Children's Hospital in 2010 after working at the Saint Jude Children's Research Hospital, a pediatric oncology centre in the USA, already primed with a vision to launch a pioneering line of research in the field of pediatric cancer. Montero joined a group of ten people founded by Jaume Mora and Carmen de Torres. That year, the group raised around 200,000 Euros in donations for research. The team now boasts 50 professionals and counts on 2 million Euros in donations to fund five large-scale lines of research.

Ángel Montero: It was the right place at the right time. My goal is to use technology to improve drug delivery to tumors, and create safer, more effective treatments.

Pediatric Cancer Treatment Laboratory sounds like it deals with a broad range of projects. What research projects are going on right now?

We have several projects in progress. We have contributed towards the development of advanced therapies based on oncolytic viruses, collaborating with leading international figures in the field. These viruses are very promising for new cancer treatments. We have a project right now that improves the delivery of medication to the brain, which can help drugs be more effective against brain tumors. Generally speaking, all of my projects look at how drugs are delivered, and how they can be improved to target specific characteristics of each tumor. It would be a way to create increasingly personalised targeted therapies. We are also focusing on new laboratory models that faithfully reproduce the diseases we want to study. This field of study was very new in Europe when it started at SJD, and we have contributed towards establishing models for diffuse midline gliomas, pediatric sarcomas and neuroblastomas. These models we have had a hand in developing are now part of routine usage at several international facilities.

Fifteen years ago, the bottleneck in pediatric cancer research was that we did not have enough samples and models. Today, that problem has been solved,

and the pediatric cancers that we knew nothing about before are now hot topics of study in the field of Oncology.

What do we learn from disease models that we cannot learn by other means? Why are they so useful?

The disease models created from biopsies help us reproduce the unique aspects of each subgroup of patient, as well as have a kind of avatar that faithfully replicates each disease. Most importantly, these individualised models allow us to identify biomarkers which could predict whether a treatment is going to be effective or not. To reach similar conclusions in a solely clinical environment, we would need a number of patients that is not always available in the pediatric setting.

'My goal is to use technology to improve drug delivery to tumors, and create safer, more effective treatments.'

How are they different to adult disease models?

There are indeed differences, which makes it even more important to have models specifically for pediatric cancers. Adult tumors are very different to tumors in children and young adults: type of cancer, type of cancerous cell, the mutations they contain, fusion genes (which are very common in pediatric cancer), response to treatment, etc. That is what makes it important to have pediatric-specific models.

One of the first applications of these models was to assess the prognosis of sarcomas.

Yes, and we have been creating various other models for different types of cancer. When we got the first models for sarcomas and neuroblastomas, we saw that in cases where the child's tumor had been successfully grafted into rats, the child's disease normally relapsed. So then we started asking ourselves whether this could be used as a prognostic factor. After ten years of study and an enormous number of samples, we were able to conclude that, positive grafting was indeed a negative prognostic factor. Although this seemed obvious, we had to prove it scientifically, and this let us come to a solid conclusion.

How does this progress in pediatric cancer research translate into concrete improvements to treatment for patients?

That is what motivates us to come to the lab every day. Our main goal is to turn everything our group researches into a phase one clinical trial. In each and every one of our projects, no matter what disease it concerns, we work towards finding enough evidence to approve a phase one clinical trial. We want all of our findings to turn into something applicable.

You combine your work as a researcher with your penchant for innovation. Recently you founded the startup Gate2Brain, a spin-off developed by both the Institute for Research in Biomedicine (IRB) and the SJD Barcelona Children's Hospital, which aims to develop new drugs that better cross the blood-brain barrier. How is the development of these products going?

Startups are an essential vehicle for bringing our new technology to our patients in the form of a phase one clinical trial. Protecting the intellectual property of each institution is important, but more important still is licensing it to someone who can make the most of it. Most institutions cannot make the most of the resulting data, but startups have full-time dedicated staff to do so, such as Meritxell Teixidó at Gate2Brain. It is important that institutions get involved with startups, while also giving them the autonomy they need to function properly.

With a phase one clinical trial in sight, how long before it can make the jump to clinical practice?

Around two years. The project has some good data backing it and a great scientific team. Gate2Brain has won some highly competitive grants within the European Community. We still need to finalise the preclinical phase and conduct several toxicity tests in independent laboratories. Another factor needed to get to phase one would be to attract investors who can help create the conditions necessary for a comprehensive development environment.

The main task at hand at Gate2Brain is using peptides as delivery vehicles for drugs to enter the brain and treat brain cancer, be they drugs developed by the sponsor or by other entities. How do you expect peptides to change the treatment of brain tumors in the pediatric age group?

We have a preliminary study drug candidate for use in treating glioma-type brain cancers. However, the cutting-edge peptide technology platform licensed by Gate2Brain is applicable to other active molecules, even if they are for other brain diseases, not just for cancer treatment.

Does that mean that these peptides are only for use in the pediatric age group, or can they be used on adults, too?

This technology does not focus on the tumor itself, but rather getting the medication to the tumor, meaning it can be used with all kinds of drugs and on all kinds of patients, with no age restriction. The preclinical results at the SJD Barcelona Children's Hospital allowed us to request two patents that cover the use of the technology in adult-specific diseases as well. This will help us attract more investors to the project.

Let's go back to one of the other lines of research we had mentioned, which holds a great deal of weight in the laboratory – research into oncolytic viruses.

In this regard, we are working with Theriva, the company that created the VCN-01 oncolytic adenovirus to treat pancreatic cancer. The virus destroys cancerous cells if and when they have a target mutation in a group of genes known as the 'retinoblastoma pathway'. It is a very common pathway in cancer cases and it has this name because it was discovered with retinoblastomas (cancer of the retina in children). It is not exclusive to this type of cancer, however. The majority of tumors have some kind of abnormality in some part of this pathway, meaning that the virus can recognise these cells and replicate itself inside them. In fact, it can only replicate itself within this aberrant pathway, and not in normal cells.

This led us to assessing the use of VCN-01 in retinoblastoma cases, as this tumor involves a mutation in this pathway. That is how we started using this therapy, which, moreover, was ideal for rapid application in clinical practice because it was already produced on a clinical scale and was in use in adult clinical trials.

With your research into retinoblastomas, you won the 2019 Vanguardia Science Award. How has the research progressed in the last five years?

We are currently analysing data from phase one of the study, which recently ended. On a preclinical level, we are still working on improving adenovirus-based treatments and applying them to other tumors when combined with drugs in the Camptothecin family. These drugs act as potent stimulators of viral activity in preclinical models.

As such, in the field of oncolytic adenovirus research, there has been a shift in thought. It was initially thought that these viruses acted primarily through oncolysis, destroying cancerous cells. However, we now know that they also stimulate the immune system, exposing the tumor and leaving it vulnerable to the body's immune cells.

In the middle of this labyrinth of research, how have state-of-the-art techniques like genetic sequencing affected your research into pediatric cancer?

They play a crucial role. For uncurable diseases in children—such as diffuse midline gliomas, for example—fifteen years ago we did not even know what caused them. Now we are almost 100% certain that these patients have the same genetic mutation, consisting of a single amino acid change in the same protein every time. Progress like this is thanks to the oncologists and pathologists taking tumor samples from patients over the years, despite not knowing exactly what change it could bring about in the future. This was the vision of Jaume Mora, for example, our Scientific Director, and Guillermo Chantada, our Outreach Director. Both of them, working 10,000 km apart and still not having met in person, simultaneously built up a collection of pediatric cancer samples that have proven invaluable to research. Thanks to these resources and modern technology, we are now able to rapidly categorise different types of tumors, make faster decisions about treatments and prognosis, detect therapeutic targets and also recommend targeted treatments. Now, in a relatively short timeframe, Cinzia Lavarino's Molecular Oncology laboratory can categorise the tumor of any child that walks through the doors of our hospital, and we will have all of the information we need to select the best treatment option. On that note, I want to highlight that setting up equipment to take samples and analyse them would not have been possible without the generosity of families.

'Families are the heart and soul of a huge portion of the research done at our hospital.'

Speaking of families... What role have parent and patient associations played in your research and developing treatments?

They are the heart and soul of a huge portion of the research done at SJD. Families give from a place of pure generosity to help bring our projects to life, especially when donating affected tissues from their children. Something that will never cease to surprise me is that, despite having gone through the worst parts of the disease, many families wish to stay in touch with our hospital. Perhaps the most normal reaction would be to forget about us. But yet, many families bring ideas to the table, interact among themselves, organise fundraisers and continue to play a role in research activity. Right now, more than half of our lab's budget comes from donations made by families.

If you could send a message to the families of these young patients diagnosed with cancer, who are constantly supporting research at SJD, what would you say?

Aside from openly thanking them, I would say that every one of them is of value. Regardless of whether they are 'brave' or paralysed by fear, their children are SJD's top priority, and we will always keep working hard for them. For us, the most important day of the year is the day where we meet with all of the families, when we can explain our research projects and the results we have obtained. We tell them about both our successes and our failures. A patient of ours said something to me at the last family day which really stuck with me: 'You've made me laugh. I'll come back next year.' That means there is something about our project that draws them in. What gives us the absolute most pleasure is being able to tell them that one of our projects has moved to a phase one clinical trial.

What do you think the future of Pediatric Oncology holds in the next twenty years?

I imagine that immunotherapy will be much more advanced, not just for leukemia, like now, but also for solid tumors. In twenty years' time, I hope we will have discovered why solid cancers go almost undetected by the immune system. There is something in them that makes them invisible, and that is why they are so hard to treat with immunotherapy, even with treatments as potent and well-known as CAR-T.

I also think that, in twenty years, we will have new medications for brain tumors, whose activity will not be restricted by the blood-brain barrier because we will have developed an effective delivery technology to cross it.

I also hope that selective therapies will play a leading role, with treatments that carry targeted radiopharmaceuticals directly to the tumor.

'In the next twenty years, I hope that selective therapies will play a leading role, with treatments that carry targeted radiopharmaceuticals directly to the tumor.'

Hearing you speak with so much passion, it makes us wonder whether you always dreamt of a career in research when you started your studies in pharmacy or whether it was something you decided along the way.

It was partly something I decided along the way. I came into pharmacy with the same mindset as almost all young people, with no clear idea whether I wanted a career in this specific field. What I did know for certain was that pharmacy combined chemistry, biology and medicine, which were keen interests of mine. I was lucky enough to learn from mentors like José Luis Pedraz, Guillermo Chantada and Clinton Stewart, who strengthened my interest in research. I sometimes get the chance to speak to students about their professional career, and I tell them that there are many different paths to get to the same destination. The route you end up taking in your career is set by your post-graduate specialisation and the teachers you have.

Speaking of students, you briefly mentioned junior students in your team. As well as being the research group lead, do you also mentor any of the young researchers?

Yes, it is very important to me. My mission at SJD is two-fold. On the one hand, I am responsible for research projects, making sure they are successful. On the other hand, I also have a clear academic responsibility to educate new doctors. Both pillars are of equal importance. My academic goal is for doctors learning in the lab to be able to develop their career plan in the best way possible, using SJD as a springboard into further education at other prestigious institutions. At times it can be frustrating, as we have to start from scratch training new staff, but it is also refreshing for me as a mentor. We also welcome international students who choose to study here during their education, so our goal is to respond to their expectations and continue working with them, with a view to future partnership and collaboration. That way we also ensure that their expertise and knowledge, in one way or another, can still benefit our project at SJD.

'Every project we launch is collaborative, many on an international scale.'

Are partnerships an important aspect of working in pediatric cancer?

Absolutely every project we launch is collaborative, many on an international scale. In science, sharing knowledge is of vital importance, even more so in pediatric cancer. It allows us to constantly add to our collective knowledge and resources, and draw the most conclusions in our research as fast as possible.

We have very solid international relationships, especially in the development of new treatments. For example, sonodynamics, an ambitious new project we are working on alongside Alejandro Sosnik, at the Israel Institute of Technology Technion. Communication and collaboration with international centres is constant. For instance, we recently sent samples to North Carolina in the USA and to Heidelberg in Germany.

To finish up, what do you think has been the biggest frustration in your career to date, and your proudest moment?

Sometimes I have felt frustrated, with or without reason to be, when I saw research projects I considered to be finished and assumed would have a huge impact that did not get the reception I had hoped for. Perhaps this is because we live in a kind of bubble, and we naively think we are going to be the next big thing, but then the competitive society we live in gives us a reality check and smacks us back down to Earth, which is not a bad thing, really. This small moment of frustration is nothing in comparison to the happiness we feel knowing that the families we mentioned earlier are the ones who are most thankful for our progress, no matter how small a step forward it may be, always encouraging us to keep going. They understand the significance of every step forward and they celebrate each one. Families are our driving force, our source of energy, and truly make it all worthwhile.■

"Child Life team turn a traumatic experience into something far from it"

Some children and young people feel fear and anxiety when they have to undergo a medical procedure or surgery. For patients with functional diversity or developmental issues, these sensations can be exacerbated by their disease or condition. Staff at Child Life schedule a´n appointment with the child before any procedures to help improve their experience and avoid circumstances that could cause anxiety.

Some children with functional diversity or developmental issues, such as patients with autism, find social interaction and expressing their needs difficult: they exhibit repetitive behaviours; are highly sensitive to sounds, lights and textures; have problems communicating with their environment and/or understanding it, at times. All of these factors can make a visit to hospital, or even a routine medical procedure like an injection, a traumatic experience for the child if no measures are taken to alleviate it.

That is why the SJD Barcelona Children's Hospital launched the Child Life programme, with the aim of improving the experience of all patients at the hospital, especially those patients who, because of the nature of their disease, may find treatment more distressing. When a staff member detects that a patient is having trouble with a procedure, or if they believe the patient may need a specific form of support, they are referred to Child Life.

The aim of this initial appointment is to create a profile of the patient—a type of medical history—but focusing more on their communication needs, how they interact with their surroundings, or the sensory aspects of the child to determine what difficulties or developmental aspects should be taken into consideration when they require a medical procedure.

'We ask the parents what happens when the child is agitated and then pass that onto staff, or ask what the best way to give medication is – with a syringe and syrup or by mixing tablets with something they like the taste of? Are they touch-averse or do they struggle to understand waiting times?' explains Sonia Tordera, Coordinator of the Child Life team. 'All this information is hugely useful, as we learn what we can do to keep the patient calm at all times during a medical procedure or when administering medication.' This profile is added to the patient's medical history notes and is shared with any staff members who will be treating the patient at one time or another.

The team at Child Life have various strategies and resources at their disposal to improve the hospital experience for these patients. 'It is hugely calming and important to have a support person or the parents present with the child at all times. In other cases, having a distraction, like a device or a toy, can be a great help. In some cases, music can be a big help. Other times, when the child has had previous contact with dog support at school or if they like animals, dog-assisted activities can also be a useful way of keeping the child calm', explains Sonia.

Juan José Lázaro, Head of the SJD Anesthesiology Department highlights how extremely simple measures like the ones mentioned by Sonia can influence how a small procedure like an injection plays out. It can be the difference between just another normal procedure or a traumatic experience that makes the child not want to come back to the hospital. 'Years ago, children with autism who had to undergo dental treatment had to be sedated and taken to theatre. Now, thanks to Child Life, they are better prepared for these procedures and know what to expect, so they can be treated in the normal consultation room', he notes.

Lázaro also stresses that the sensory clinical history provided by Child Life helps to avoid anything that could have a negative effect on the child. 'For example, if the child does not like crowded rooms, there will only be one or two staff members, whoever is most necessary, with the child in theatre. The rest will enter afterwards. If the child has a special toy they are attached to and that they do not like to be away from, we check whether it can be taken into theatre so the child does not get nervous, then we remove the toy once the child is sedated', he adds.

Carla, with her ragdoll and the mask that Child Life used to explain one of her medical treatments in a simple way.

Carla's story

Carla, who has autism, had tonsil surgery when she was just three years old at a facility in Barcelona. For her mother, Cristina, it is a bad memory. 'They ended up strapping her to the stretcher because she didn't want the line to be inserted', she recalls.

A few months ago, she had to have surgery again. 'This time, we asked our pediatrician to refer us to SJD because we knew that there was a unit for children with autism here', says the mother.

A few days before the procedure, a Child Life staff member got in touch with the family to book an appointment to prepare Carla for the procedure. Using symbolic play with a ragdoll and some pictures, Child Life explained the surgery to Carla in a simplified way, suited to her age and her special requirements. They also took her to see where she would be staying during her time there, to help alleviate some of her fear and uncertainty.

'For us, as parents, it really put us at ease seeing how they treated Carla. They tried to understand her, even though she doesn't speak, and find out what she needed and what she was scared of. It was also good for us since they told us ways that we could help her ourselves. We took the ragdoll back home with us, the lines, the mask and the pictures, and every day we would play the game Carla had played with Child Life, and we explained what would happen at the hospital. This meant that, on the day of the procedure, everything went smoothly. It was so easy and she was much calmer. It was less traumatic for everyone involved', recalls Cristina.

For Carla, like many children with autism, injections and needles are particularly frightening. This fear, as well as other special requirements, were recorded in her medical history. So, when she arrived at the Surgical Wing, staff treating the girl already knew about her particular case. To stop her from getting nervous, they decided to insert the line after she was already under anesthesia. 'They seem like small things, but they are so important. The work that Child Life does with kids with autism like my daughter turn what could be a traumatic experience into something far from it, better for her and for everyone involved', Cristina says.

Optimising venous access to improve the patient experience

Progress in care provision has given rise to greater specialisation in venous access, which is a crucial aspect of caregiving, for administering treatments and obtaining samples, for instance. In response to changing needs and new, emerging challenges, hospitals like the SJD Barcelona Children's Hospital have implemented teams that specialise in venous access. These teams, made up of highly specialised nurses, improve both technical precision and the experience of the patient thanks to their advanced techniques and experience in ultrasound-guided venepuncture.

Healthcare is moving forward in leaps and bounds, and as a result, new needs and challenges are appearing along the way with regard to improving patient safety and the quality of healthcare. One of the key aspects of patient care is venous access, which is crucial for administering medication and taking samples. However, for some patients, inserting a venous access point can be a difficult and painful task. It is here where specialisation and innovation play a decisive role.

'In many pediatric healthcare facilities, venous access lines are inserted by nurses. For some complex patients, however, like chronic patients or those with exhausted vascular capital, a more specialised approach may be needed', explains Sara Palou, Vascular Access Nurse at the SJD Barcelona Children's Hospital. In this context, specialist equipment for venepuncture must be used.

As such, the SJD Barcelona Children's Hospital has recently implemented a team of nursing staff with specialist vascular access training to help safeguard vascular capital in venepuncture and venous catheter placement procedures. This nursing team has had specific training and uses techniques such as ultrasound guidance to ensure safe, precise access in patients with difficult venous access.

'Not only does this approach improve the patient experience, reducing pain and complications associated with several puncture attempts, but it also optimises clinical results, ensuring correct, timely administration of treatments', adds Sara Palou.

Sara Palou, Vascular Access Nurse.

Improving both the safety and experience of the patient

Creating teams that specialise in venous access has not only revolutionised the way this procedure is approached in hospitals, but it has also had a significant impact on the safety of the patient and their experience. It is because one of the most highlighted aspects of this approach is that treatment is personalised. 'Every patient is unique, and the vascular access team makes sure to use the device best suited to each case, considering the duration and type of treatment, as well as the patient's characteristics', comments Sara Palou.

'Before, venous access was a painful and stressful procedure for many patients, especially those whose veins were hard to locate. However, introducing expert staff in venepuncture has made this experience much less traumatic', she adds. Vascular access nurses use techniques such as ultrasound guidance to more precisely locate hard-to-find veins.

This means that patients do not have to suffer through several puncture attempts, which significantly reduces the pain and discomfort associated with the procedure, as well as preserving vascular capital.

Veins are a valuable, limited resource, especially for patients with chronic illnesses or for pediatric patients, whose veins are subject to continuous stress due to long-term treatments. As such, it is fundamental to adopt practices that minimise vascular damage, and preserve the integrity of the patient's veins in the long term. This not only guarantees there will be veins accessible for future treatments, but also reduces the risk of complications associated with repeated insertion of venous access devices. Finally, preserving vascular capital not only improves quality of life for the patient, but it also contributes to safer, more sustainable healthcare.

Another important aspect of specialist venepuncture is the focus on correct maintenance and removal of venous access devices. This helps to prevent long-term complications such as infection or thrombosis, and guarantees that the patient can continue to receive treatment in a safe and effective way.

Specialisation backed by data

'Creating this specialist team has proven to be a significant step forward in clinical healthcare, setting a new standard of care in hospital. Continuing education, standardisation of protocols and the use of advanced technology are all key aspects of this initiative, which could act as a model for other hospitals hoping to improve their venous access procedures', adds the specialist.

Moreover, this approach is backed by data. A study done at the SJD Barcelona Children's Hospital found that devices inserted by expert nursing staff resulted in 25% fewer insertion-related complications compared to devices inserted by general nursing staff with basic knowledge of ultrasound-guided venepuncture.

To conclude, specialist teams in vascular access are transforming the way this procedure is approached in hospitals, improving both the safety and experience of the patient and ensuring high quality healthcare with excellent results. This progress is proof of healthcare staff's ongoing commitment to improving patient care and striving for healthcare excellence.

SJD

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