



ASHLEY'S ANGELS FUND

Your Investment. Your Impact.

Ashley's Angels' support of the Transplant and Regenerative Medicine Centre helps SickKids improve outcomes for children with transplants by integrating cutting-edge research, innovative education, and exemplary care. Thank you for your tremendous generosity.

We are delighted to report on the impact of your gift over the past year.

IMPROVING OUTCOMES FOR CHILDREN FACING ORGAN FAILURE

The Transplant and Regenerative Medicine Centre provides the best in complex and specialized care by delivering scientific and clinical advancements, sharing knowledge and expertise, and advocating on behalf of the children who need it most.

60%

of all children's liver transplants in Canada take place at SickKids

#1

SickKids Liver Transplant Program is the largest of its kind in Canada, and one of the largest in North America

25+

years SickKids has been performing life-saving liver transplants in infants and children with end-stage liver failure in Canada

~75

transplants performed at SickKids per year

The Transplant and Regenerative Medicine Centre

SickKids' Transplant and Regenerative Medicine Centre is Canada's most research-intensive paediatric transplant program and the largest centre in the country to offer comprehensive transplant care. Case volumes have grown to within the top five to 10 per cent in North America, and survival rates match or exceed the most prominent programs, worldwide.

Health professionals from all disciplines make up the world-renowned Centre. The team provides the best in complex and specialized care by developing scientific and clinical advancements, sharing knowledge and expertise, and advocating on behalf of children who need it most.

This year, your meaningful donation has supported three individual pilot competition research projects.

Assessing School Readiness and Health-Related Quality of Life in Children Transplanted Under the Age of Two
Drs. Vicky Ng, Alaine Rogers, Anna Gold, and Binita Kamath

Excellent long-term survival after paediatric liver transplantation is now the rule rather than the exception. As a result, survival is no longer the best metric of success, and paediatric liver transplant teams must focus on functional outcomes such as neurocognitive development, school

readiness, academic performance, and health-related quality of life to more fully optimize the quality of life restored for these children. Special emphasis on the youngest recipients (who are under the age of two years at the time of their liver transplantation surgery) is appropriate, given that this age group represents over half of the transplant volumes performed in paediatric liver transplant programs. The impact on the developing brain of being so sick so young, and then proceeding to undergo a significant surgical procedure followed by the need for prolonged immunosuppression, remains unknown.

The specific aims of this research study are:

- to determine the prevalence of developmental and neurocognitive delays in a population of children who underwent liver transplantation before the age of two years at SickKids, and compare them to age-matched children who have not yet undergone liver transplantation; and
- to identify variables that may be predictive of impairments in the multiple established domains of school readiness.

Support received from Ashley's Angels has been critical in moving this research study forward, including funding for trained neuropsychometrists and occupation therapists to complete these assessments based on best availability of the patients and

Meet Elyana

Genetic testing at SickKids confirmed a diagnosis of ABCA3 deficiency in Elyana—a rare cause of Respiratory Distress Syndrome. Elyanna's older sibling was diagnosed with the same disorder in 2009, and died at six weeks of age. At that time, the infant lung transplant program at SickKids did not exist. After two months, a non-compatible donor became available for Elyanna and SickKids' team performed the second ever ABO-incompatible infant lung transplant. Her surgery was a success and she is recovering at home.



their parents. Funding also supported the purchase of dedicated, age-appropriate psychology assessment batteries which were critical for efficiencies.

To date, full neurocognitive and developmental assessments have been performed on 15 patients—including six children with chronic liver disease before transplantation and nine children after liver transplantation. Plans are in place to assess an additional five children, bringing the total to 20 children tested.

We are now in the process of setting up our final analysis programs so that once all the assessments are finished, we will be ready to expedite the completion of the data analysis strategy. Dr. Ng was an invited speaker for a scientific talk entitled “Neurocognitive Outcomes After Paediatric Liver Transplantation” at the ILTS (International Liver Transplantation Society) Annual Congress in Sydney, Australia, a high profile meeting for the international liver transplant community (both adult and paediatric). Preliminary data from this research study was presented and highlighted SickKids' leadership role in optimization of outcomes after paediatric liver transplantation. The goal was to submit this research for publication in a peer-reviewed academic transplantation journal, ultimately, changing practice with the adoption of detailed neurocognitive and school readiness testing as standard of care in the monitoring and surveillance of the paediatric liver transplant recipient.

[Biliary Complications after Paediatric Liver Transplantation: Incidence, Impact and Opportunities for Improvement](#)

Drs. Anand Ghanekar and Binita Kamath

To date, data has been reviewed and collected from the clinical records of all children who received liver transplants at SickKids between 2000 and 2010, with a focus on biliary complications. A preliminary analysis of this data has been performed, which reveals the frequencies of different types of biliary complications that have occurred, and their associated risk factors. Different strategies that were used to treat these complications have been analyzed for success. The goals of this study include:

- measuring how often and what types of biliary complications occur in children after liver transplantation
- identifying risk factors for the development of these problems
- evaluating how effective different treatments have been in correcting these problems
- using these findings to develop the best strategies for treatment with biliary complications in the future.

part of organ transplantation. IRI occurs when the blood supply of the donor liver is cut off when the liver is removed. Loss

Funds granted by Ashley's Angels were used to support the hiring of a research assistant to collect data, and were critical in allowing this important research to move forward.

Data analysis and preparation for publication that describes these findings are in progress. The manuscript proposal includes an algorithm for the optimal management of biliary complications in children after liver transplantation that is based on the results of this study. The goal is to submit this research for publication in a peer-reviewed academic transplantation journal as well as for presentation at international transplantation conferences within the next six months.

[Delineating the Role of Autophagy in Ischemia Reperfusion Injury and Chronic Graft Dysfunction in Children with Solid Organ Transplants](#)

Drs. Nicola L. Jones, Lisa A. Robinson, Christiane Sokollik, Divisions of Gastroenterology, Hepatology and Nutrition and Nephrology, Department of Paediatrics, University of Toronto

Despite improved short-term outcomes due to advances in drug treatments that prevent rejection of the transplanted organ, long-term liver graft survival remained unchanged over the last decade. There is convincing evidence that ischemia reperfusion injury (IRI) significantly affects the long-term success of liver transplants. IRI is an inevitable part of organ transplantation. IRI occurs when the blood

supply of the donor liver is cut off when the liver is removed. Loss of blood and oxygen supply to the liver causes injury and damage to mitochondria, the cell batteries that produce energy for the cell to survive. Damaged mitochondria release toxic material called reactive oxygen species (ROS), which can kill cells. When the blood vessels of the liver are reconnected to the recipient, immune cells recognize the injury resulting in inflammation and graft damage. The overall goal is to develop mechanisms to reduce the injury caused by ischemia reperfusion injury, ultimately improving long-term outcomes.

Recent studies indicate that a cellular recycling pathway called autophagy may help to remove the toxic metabolites including ROS. Therefore, it is suspected that enhancing autophagy may reduce IRI. The aim of this pilot project was to employ an in vitro model system of IRI and determine the effect of enhancing autophagy with a drug called rapamycin, which is already in use as an immunosuppressive agent in liver transplantation. Below are the key deliverables arising from the support of our Ashley's Angels, as well as the future direction of the research.

Leveraging of funds from Ashley's Angels: Through the support of Ashley's Angels, an additional \$7,000 in funding has been leveraged from the Sickkids Research Institute and the Canadian Liver Foundation to support the research goals of improving outcomes for children with liver transplants. We obtained additional support to allow Dr. Christiane Sokollik to visit the "Canadian Institute Of Health Research Scientist of the Year" and Dr. Paul Kubes' laboratory to develop an animal model of IRI and learn an innovative method for studying inflammation in the animal model. We can employ this knowledge in our ongoing studies. We also obtained support from the Canadian Liver Foundation for a summer student salary for Ms. Emma Torbicki to assist in the pilot project.

Advancing knowledge in the field: In a model of IRI in blood vessel cells, rapamycin treatment increased the autophagy pathway and this resulted in a decrease in generation of toxins and a decrease in cell death. In addition, preliminary studies indicate that rapamycin treatment decreased inflammation when immune cells were added to the blood vessel cells.

Significance to children with liver transplants: The pilot studies have identified a possible mechanism to reduce injury during IRI and thereby improve the long-term outcome of liver transplantation in children and adults. Although more research is still needed, findings suggest a novel treatment for IRI.

Moving Forward: Additional studies are now needed to determine if increasing autophagy is beneficial in an animal model and understand the reasons why it is beneficial. Using the necessary pilot data generated by the support from Ashley's Angels we will continue to seek funding from the Canadian Liver Foundation (CLF) and Sickkids' Transplant and Regenerative Medicine Centre to support these ongoing studies.

Thank you

As innovators in transplantation led by world-renowned medical staff, SickKids is uniquely positioned to make life-changing discoveries that can be rapidly translated into clinical practice. These transformative changes hinge on the generosity of donors such as Ashley's Angels. Your contribution is a testament to our shared vision: Healthier Children. A Better World. We greatly appreciate your continued support.

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