Las Madrinas Impact at Children's Hospital Los Angeles
October 4, 2023

Las Madrinas generosity and commitment to research discovery at Children's Hospital Los Angeles has had an impact that is almost indescribable. The support has provided the flexible funds for investigators to be innovative and risk-taking to make new discoveries that cannot be done with traditional funding from the federal government, such as the National Institutes of Health (NIH). NIH provides the sustaining support for projects, but Las Madrinas provides the foundational support for the research discoveries that will bring new treatments to children, youth and their families. The investments have resulted in dozens of NIH and other private foundation grants in the tens of millions of dollars.

Las Madrinas Endowed Chairs currently are held by Dr. Shafali Jeste (Chief, Division of Neurology and Co-Director of the Neurological Institute) and Dr. Elizabeth Sowell Director of the Adolescent Brain and Cognitive Development consortium study, a national effort to discover the factors that promote healthy brain development for youth, and the challenges that may result in difficulties from adolescence to young adulthood. Each of these faculty investigators have been successful in garnering multiple NIH and private foundation grants due to the Las Madrinas support.

The Las Madrinas Endowment for Molecular Pathology (Drs. Jaclyn Biegel, Tim Triche, Alex Judkins) has throughout its history played an outside role in our continuous grant funding to study childhood cancer since its inception over 30 years ago. Unlike typical grant funds which are required to be spent on specific expenses like salary, reagents, equipment, and so forth, the inherent flexibility of the Las Madrinas funds has enabled us to support programmatic needs as they arise. This would not be possible with typical grant funds, and as a result, we have repeatedly been able to undertake pilot projects supported by Las Madrinas funds that have eventuated in committed grant funding. The most recent activities of the program are focusing on new treatments for two highly challenging pediatric cancers, Ewing Sarcoma and various brain cancers. The group is developing the use of RNA molecules that regulate genes to turn off those that are responsible for the tumor growth. The side effects from this will be much less than current standard radiation and chemotherapies.

The Las Madrinas Endowment for Experimental Therapeutics for Ophthalmology (Dr. Aaron Nagiel) bolsters research efforts by supporting novel laboratory investigations. Most recent, the use of a model system, produced from human stem cells, to monitor human retina development has led to a greater understanding of how connections, or synapses, form between neurons in the retina. These synapses are required for information from the environment to be conveyed to the brain areas that process scenes for visual perception to occur. By gaining a deeper understanding of how cells connect during development, researchers hope to pinpoint when this process goes awry in children with eye diseases and triggers various inherited retinal diseases. As a direct result of support from Las Madrinas.

Las Madrinas Simulation Center (Dr. Todd Chang) is a 5,000 square foot facility and infrastructure funded by the Las Madrinas Foundation and enables for both systems improvement, education, and

innovative research studies. The studies are supported by Center investigators' success in obtaining extramural funding to pursue innovative research, all of which is fully dependent upon having the modern infrastructure of the Simulation Center. In a recent study focused on the Extended Reality Simulation for Basic Life Support education among lay people. Partnerships with external companies was now possible with the infrastructure funding that enabled in-kind equipment and training for a XR-based solution for BLS training. The Center is underway on a multinational randomized controlled clinical trial to determine the advantages of adding technology-based simulation to CPR education. Finally, for Neonatal Resuscitation Program Virtual Reality Training, VR training is prevalent, but it is unknown whether solo or group training confers advantages in provider knowledge and performance. A research project is addressing this important issue.

Las Madrinas Molecular Oncology, Hematopoietic Stem Cell, Gene, Immune and Stem Cell Therapy Research Programs (**Drs. James Amatruda, Alan Wayne**) has supported the recruitment of three physician-scientists, Drs. Babak Moghimi, Rongfu Wang and Sarah Richman. The funds provide protected time outside of their clinical work to be able to develop and implement cutting-edge research programs. Moghimi's laboratory examines that factors that improve success in cancer therapies using cell transplantation approaches. Wang's laboratory focuses on the improving the ability of the immune system to target malignancies for particularly challenging types of cancers. Richman is using a combination of brain imaging and cell transplantation to battle pediatric brain cancers. Finally, Dr. Amatruda's research program has received support to utilize a powerful model system in zebrafish to discover the factors that cause sarcoma tumors, and the drug treatments that can successfully treat this very challenging pediatric cancer.

The Las Madrinas Endowment for Autism Research, Interventions and Outcome currently support two outstanding investigators and their research programs:

The Study of Autism Risk in Siblings (StARS) focuses on developing biomarkers for early identification of autism in infants who are at very high risk because they have an older sibling with autism. The study is led by **Dr. Sahana Nagabhushan Kalburgi**. The project applies a multi-modal research strategy of high density recording of brain activity (EEG), simultaneous eye tracking, and developmental assessments. Dr. Kalburgi develops and applies advanced machine learning and artificial intelligence to 'big data' analysis to identify brain development 'red flags' that are indicative of later onset ASD.

Training and Research to Empower NeuroDiversity (TREND) Laboratory is directed by **Dr. Jessica Schwartzman**, a clinician-scientist who does clinical service for neurodivergent youth, including those diagnosed with autism, who experience depression and even thoughts of suicide. The research program designs and tests the effectiveness of new interventions that engage the brain circuits that control mood and reward to promote best outcomes. Multi-modal strategies are used to understand how the brain changes with improved behaviors.