THE HARTWELL FOUNDATION

2012 Individual Biomedical Research Award

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Identifying Children at Risk of Chronic Kidney Disease: Utilizing Contrast-Enhanced Magnetic Resonance Imaging to Count Nephrons

In the U.S., approximately 500,000 infants are born prematurely each year and as a consequence, critical organs such as the kidneys haven't fully developed. The kidneys play a critical role in the filtering of blood and the removal of body breakdown products that are excreted in the urine. The key structures in the kidney responsible for filtering blood are called nephrons and their loss will lead to the dangerous buildup of fluid and waste products throughout the body. Fewer nephrons results in elevated blood pressure and dialysis of the blood to remove the waste products. Unfortunately, dialysis also promotes further nephron loss and increases the possibility of a required kidney transplant. Every normal child is born with up to several million nephrons, which if damaged can not regenerate and which number declines naturally with age. By contrast, premature infants born before 36 weeks begin life with fewer nephrons and as a result have a 70% increased risk of developing chronic kidney disease (CKD). In addition, children with cancer, heart disease, sickle cell disease and diabetes are also at high risk for developing CKD. Unfortunately, the early stages of CKD are clinically silent and physicians lack the tools to diagnose the disorder until irreversible kidney damage has occurred. Blood biomarkers believed to be predictive of CKD do not increase until more than half the nephrons are damaged. Current methodologies to determine nephron number rely on posthumous and destructive techniques, which can not benefit clinical therapy. The lack of early diagnosis of CKD results in late stage very aggressive treatment strategies. To address this unmet need, Jennifer proposes to deploy nondestructive MRI technology to quantify the number of available and functional kidney nephrons in a rabbit animal model. Unlike standard MRI, she will use a special contrast-dye that interacts with nephrons to enhance their detection. If she is successful, the clinical translation of her approach will benefit children at risk for CKD because they will be identified in time to allow preventative therapy before extensive and irreversible kidney damage occurs. The ability to nondestructively quantify the number of functional nephrons by contrast-enhanced MRI will enable the determination of any correlation between known biomarkers of CKD and nephron number, including the potential to develop new biomarkers. Quantifying nephron number will also provide an objective measure of organ transplant suitability.