THE HARTWELL FOUNDATION

2007 Individual Biomedical Research Award

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Pathogenesis and Therapy of ARVD, a Common Cause of Sudden Cardiac Death in Young Athletes

Nothing can stir the emotions more than the sudden loss of life. The unexpected death of an otherwise healthy child is even more devastating. Frequently, the cause of sudden death is attributable to a genetically inherited disorder called arrhythmogenic right ventricular dysplasia (ARVD). The prevalence in the US is about one per 5000 individuals. With nearly 20,000 affected children, 5-10% will experience sudden death each year. ARVD produces structural heart muscle disease in the lower-right chamber of the heart (right ventricle) that creates fatal or life-threatening disturbances in the natural rhythm of the heart, causing progressive failure of the heart to pump blood adequately. Although it runs in families, it may also occur with no prior family history and is frequently responsible for sudden death in young athletes. In most cases however, symptoms do not appear until patients are in their 30s or 40s, when sadly, recognition of the disorder first occurs following a fatal heart attack. There are at least ten known genetic variants of ARVD, including five genes and their exact gene changes. Non-genetic causes of the disorder may include viral infections of the heart muscle. The incidence of ARVD in the US is approximately 1 in 5,000, with about a third of all cases recognized in childhood and representing 19,200 affected children in the US. In comparison, there were 1,411 children in the US living with AIDS at the end of 2005 and there were 9,500 new cases of pediatric cancer in the US in 2006. Dr. Judge proposes to identify and alter the sequence of events preceding the development of ARVD by creating a novel strain of genetically modified mice, similarly affected. He will deploy several technologies to measure the size and function of the right ventricle of these mice, including high-resolution echocardiography, micro-computed tomography scanning, and 3.0 Tesla cardiac magnetic resonance imaging. Thoroughly characterized, the mouse model will provide the basis for developing new, targeted medications that Judge hopes will ameliorate this condition. If successful, the research will translate directly to improved therapy for children with existing ARVD and importantly, those with an inherited genetic predisposition to this condition.