

**RESEARCH PROGRAM**  
**Medical Research Abstracts**  
**for Grants Awarded in December 2020**

*Fred Hutchinson Cancer Research Center*

*The George Washington University  
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previous stress event and respond to future episodes with more rapid gene activation. This self-educating ability based on past experience endows organisms with enhanced survival and fitness under fluctuating and adverse environmental conditions. How cells store records of past experience remains incompletely understood, but the current paradigm centers around chromatin-based epigenetic mechanisms. A team from George Washington University and the University of Texas Health San Antonio, will test the hypothesis that paused RNA polymerase II (Pol II) at genes that are activated by a past stress signal can prime future gene activation, thus potentially endowing multiple cell types with enhanced responsiveness to repeated stress attacks. This model for cellular memory is a departure from the current chromatin-centered paradigm. To establish proof-of-principle, the investigators will focus on two cell types with cellular memory: memory T cells and skin epithelial stem cells. Using mouse genetic models, they will interrogate the impact of Pol II pausing on the ability of these cells to preserve records of past experience of infection and injury. Furthermore, the researchers will use cutting-edge genomic tools to survey the dynamics of Pol II movement and transcriptional activation in

associated with cell division, and cardiomyocytes do not divide. The investigators will determine whether mechanical stress drives telomere shortening and subsequent pathogenic signaling, leading to cardiomyocyte death. They have developed a novel hydrogel platform that can be stiffened and softened on demand to tune mechanical load, which will be used in

