The maintenance of water balance is critical for survival. Humans are exquisitely sensitive to changes in osmolality, with slight derangement eliciting physiologic compromise. When the loss of water exceeds dietary intake, dehydration - and in extreme cases, death - can occur. Far from uncommon, millions of people die every year as a direct result of dehydration. In contrast to humans, animals living in desert habitats thrive without water and endure extreme heat and intense drought, as a direct result of unique adaptations. These adaptations allow them to survive conditions fatal to humans and most other animals. Despite being a well-known ecological phenomenon with obvious implications for human health, we know very little of the underlying mechanisms that allow for survival in desert environments. **The proposed research uses an innovative approach integrating physiology, evolutionary genomics, and computational biology to better understand how desert-adapted animals survive in what appear to be non-survivable conditions.** Ultimately, understanding the mechanisms underlying extreme osmoregulation in desert-adapted rodents may suggest novel treatment strategies for conditions resulting in acute dehydration in humans.

To accomplish this, a series of laboratory manipulations of environmental conditions will be conducted, exposing desert-adapted rodents to various levels of heat and aridity, the most extreme being 110F and 10% Relative Humidity. The response of these animals to extreme environmental conditions will be studies from physiologic and genomic perspectives. Regarding physiology, many types of data will be collected, including serum and urine electrolytes, urine concentration, fecal water content, body weight, temperature, rates of metabolism, as well as other parameters. On top of these data, extensive genomic data from three different tissues - pulmonary, renal, and hypothalamus (brain) tissue will be collected. These data will consist of information regarding gene expression, and patterns of methylation and isoform use and will allow us to identify putative mechanisms underlying desert-animals amazing ability to avert physiological compromise despite dehydration. In addition to the study of the response to extreme environments, research aiming to understand the development of dehydration resistance will be performed. Though desert rodents are able to survive without drinking water as adults, they depend on oral fluid intake (milk) as infants. Given this, data collected along a developmental series from fetal to post-weaning animals will be extremely informative.

Together, these data will allow the PIs to understand the physiologic and genomic mechanisms underlying extreme dehydration resistance in desert animals. This insight will provide meaningful insights and novel treatment strategies for an important human condition, dehydration.