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Metabolic adaptations in non-model organisms yield cardiac pathophysiology insights

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The African naked mole rat (*Heterocephalus glaber*) is unique among mammals, displaying extreme longevity, resistance to cardiovascular disease and an ability to survive long periods of complete hypoxia. The metabolic adaptations required for this spectacular cardiac resistance to low O_2 are hotly debated. Whilst a recent report provides evidence that they are able to switch from glucose to fructose driven glycolysis in the brain, other systemic alterations in their metabolism are largely unknown. Using an unbiased metabolomics ^{1}H nuclear magnetic resonance spectroscopy on cardiac tissue from the naked mole-rat (NMR)a, we demonstrate for the first time a range of metabolic adaptations in the naked mole rat heart that are relevant to their ability to survive extreme environmental pressures and the resultant metabolic stress: enhanced glycolytic, reduced oxidative metabolism intermediates and enhanced ROS protection. However, the most striking observation are the supra-physiological glycogen stores resulting from glycogen turnover. These metabolites are undetectable in wild type C57/BL6 mouse heart and above the levels found in the mouse liver, the primary systemic glycogen storage site. Thus, we identified a range of metabolic adaptations in the NMR heart that are relevant to their ability to survive extreme environmental pressures and metabolic stress. Our study underscores the plasticity of energetic pathways and the need for compensatory strategies to adapt in response to the physiological and pathological stress including ageing and ischaemic heart pathologies.