

Mitochondrial Redox Homeostasis in Hypoxia via a Microfluidic Platform

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Abstract

Significant research has been conducted on cancer, the molecular basis of metastasis, malignancy, and the signaling pathways that lead to these conditions. However, limited research has been conducted regarding the tumor microenvironment, specifically its constraints and limitations. Researchers have found that the study of tumor molecular genetics is limiting because the heterogeneity of DNA mutations associated with cancer make it difficult to develop innovative treatments that target every specific gene. Our approach targets aspects of the tumor microenvironment that are common in every cell. One such aspect is mitochondrial metabolism. Mitochondria are universal in every cell. It is well known that mitochondria have DNA that is passed down from mother to offspring. Mutations of this DNA can also lead to cancer transformation. This research will determine if certain characteristics of the tumor environment, such as the partial pressure of oxygen, affect mitochondria, as a part of a larger project explaining the relationship between mitochondrial REDOX homeostasis and tumor cell metabolism. The effects that the condition called hypoxia, or a reduction of oxygen supply, has on mitochondria will be specifically studied. A novel 3D culture model will be constructed and validated, that allows the observation of tumor cells in real time. This model will be specially designed to allow the investigator to control the levels of O₂. The mitochondrial glutathione redox cycle will be targeted via genetically programmed redox-sensitive GFP-based fluorescent proteins in order to assay the chemical environment involved in metabolism. The results of this study could shed light on additional mechanisms by which cancer cells can overcome hypoxia and progress into aggressive malignancy.