

Cancer cells possess several unique features compared to healthy cells, such as faster growth, higher protein levels, and acidic surroundings. These differences help scientists to develop drugs that specifically attack and destroy cancer cells. However, current cancer treating drugs also attack healthy cells, causing side effects such as hair loss, nausea, decrease in blood cell count etc. Because of these problems, there is a strong requirement to develop new drugs that can specifically invade cancer cells while leaving healthy cells minimally affected. An important feature of cancer cells is their increased use of copper (Cu) ions for survival. Humans receive Cu through diet, and it exists in two ionic forms in the human body: cupric (Cu^{2+}), the predominant form in the bloodstream, and cuprous (Cu^+), which is mainly found inside the cells. Cancer cells have higher demand for Cu^+ , which supports their progression in multiple ways such as to produce energy and defend against stress-induced damage. Therefore, by focusing on this unique Cu^+ dependency of cancers, researchers aim to develop treatments that harm only cancer cells but not healthy cells. However, the way Cu^+ moves and is stored inside of a cell is carefully controlled by natural molecules that hold onto it very tightly. This strong control makes it challenging for synthetic molecules to disturb intracellular Cu^+ transfer, which has slowed progress in Cu^+ -focused therapies. Therefore, this research proposal aims to bypass the existing challenges of the field by developing innovative approaches to specifically target Cu^+ transfer process in cancer cells. Our focus will be on developing molecules that function both individually and jointly by forming superstructures (supramolecules) within the cancer cells to sequester Cu^+ to kill them. This goal will be achieved through three major aims. First, it aims to develop small protein-like molecules (called peptides) that can enter the energy-producing part of cancer cells, known as the mitochondria. Once inside, these peptides come together to form superstructures that can trap Cu^+ and damage the mitochondria, leading to cancer cell death. This approach focuses on treating cancers that strongly rely on Cu^+ to make energy (known as OXPHOS), laying the groundwork for personalized treatments tailored to these unique cancer types. The second goal is to design small molecules that can capture Cu^+ from defined areas of the cells called organelles. By studying how Cu^+ removal in different areas affects cancer cell behavior, this work will help build the foundation for Cu^+ -based cancer therapies with high spatial control within the cell. The molecules we design (called Bca derivatives) are able to recognize Cu^+ specifically, without interfering with Cu^{2+} that is important for normal body function. This specificity for Cu^+ over Cu^{2+} position them safer than conventional drugs, which often bind both forms, leading to the Cu-deficiency associated side effects. In addition, when Bca-derivatives capture Cu^+ inside cancer cells, they produce a unique signal and color that allows us to track the process in real time using advanced imaging techniques. The final goal is to design Bca-derivatives to capable of producing supramolecules within the cancer cells upon binding to Cu^+ within the cell to form defined structures like fiber or particle. This allows tiny therapeutic materials to form directly inside cancer cells, avoiding common problems with externally made treatments, like instability, difficulty entering cells, or unwanted side effects. Together, these strategies aim to put Cu^+ -based treatments at the cutting edge of cancer therapy, opening the way for precision medicines that selectively work on cancer cells. The proposed research will be carried out through a combined approach of chemistry, materials science, and biology.