

The project aims to discover more about cellular senescence and improve its detection. In any experiment involving senescent cells, we must first create them in a laboratory setting and confirm them by making a few tests for characteristic markers. One of these markers is that senescent cells do not divide. Another is for the protein called  $\beta$ -galactosidase that just so happens to be more abundant in senescent cells than non-senescent cells. Generally, checking for these markers uses two different assays. To make the detection process more efficient, we will create nanotechnology that simultaneously gives both characteristics in one assay. The basis of our invention is on nanoparticles that transmit fluorescence when a cell becomes senescent as a result of stress or damage. The assay can essentially tag live senescent cells within a population for downstream quantification by flow cytometry. The project plan has three major tasks and involves interdisciplinary research in biology with its links to medicine, chemistry, and some physics. First, we will synthesize the fluorogenic nanoparticles. We will explore the best ways to produce them and pioneer protocols to check for their quality. In the second task, we will examine the biological fate of nanoparticles inside target cells. To demonstrate the capabilities of an NP-based reporter system to sense out senescence, we will test it on various cell line models. Notably, our team recently observed that senescence markers could appear in cancer cells, requiring the need to include other methods to confirm it. The third task of the proposal will study the new concept of how dormant tumor cells (senescent cells) reprogram to cancer stem cells (CSCs) that cause disease. Developing our NP-based reporter system can help us realize how the same types of cells in the body might behave or respond to different conditions. The origin of CSCs is poorly understood. With more understanding at the molecular level, we could find new ways to identify their source and block their formation. Some of the potential outcomes for the concept of our nanotechnology are its application in biomedical research applications, drug discovery, and diagnosis for age-related diseases.