Determination of Cell Death Mechanisms Initiated during Gold Nanoparticle-mediated Photothermal Therapy

Varun P. Pattani* (1) and James W. Tunnell (1)
(1) The University of Texas at Austin, Department of Biomedical Engineering, 107 W Dean Keeton, Austin, TX 78712

Gold nanoparticles (GNPs) exhibit a property known as surface plasmon resonance, which allows for the use of GNPs as a contrast agent for two-photon imaging and a heating agent for photothermal therapy. Recent studies have shown that GNP-mediated photothermal therapy is effective in treating cancer; however, the cell death mechanisms involved during photothermal therapy are not fully understood. Photothermal therapy utilizes localized heat from the GNPs within the tumor to induce cellular damage. The purpose of this study was to determine whether the efficacy of photothermal therapy depends on GNP localization and to elucidate the cell death mechanisms involved.

We determined the threshold laser power to induce cell death during photothermal therapy for GNPs targeted extracellularly and intracellularly. GNP localizations were confirmed with three-dimensional imaging using two-photon microscopy. Furthermore, we measured the change in cellular temperature (ΔT), using a thermal imaging camera, that correlates with the laser power threshold. Finally, we probed specific cell death pathways initiated for both GNP localizations during photothermal therapy, using fluorescent stains. Necrosis and apoptosis were investigated as the primary pathways of cell death. Necrosis is cell death due to external injury, which can result in undesired surrounding tissue inflammation. Apoptosis, conversely, is programmed cell death that occurs naturally without external inflammation.

We found that cell death required a 50% higher fluence rate for membrane-bound GNPs (30 W/cm^2) than for internalized GNPs (19 W/cm^2). Similarly, we measured a significantly higher ΔT ($p < 0.01$) for membrane-bound GNPs (8.3°C) than internalized GNPs (6.6°C) to induce cell death. These results suggest that GNP cellular concentrations alone did not solely account for the threshold fluence rate differences observed. Therefore, the GNP localization does seem to have a significant impact on the cell death pathways during photothermal therapy. A better understanding of the cell death mechanisms involved in GNP-mediated photothermal therapy may allow for increased efficiency and selectivity of such treatments and nanovector design.