Development of Coherent Anti-Stokes Raman Scattering (CARS) Cytometry for Characterizing the Low-Dose Tissue Response

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Optical microscopy is one of the most widely-used analytical techniques in the life sciences and it is probably one of the most natural ways to connect the physical sciences with the biosciences. Its main attraction is that it allows researchers to study *living* samples in real-time with a high spatial resolution of ~200–250 nm. Non-linear optical signal detection methods such as second harmonic generation (SHG), two-photon fluorescence (TPF), and coherent anti-Stokes Raman scattering (CARS) can offer rapid measurements of the chemical composition and molecular order of materials with sub-micron resolution. By examining these signals, we can quantitatively probe changes within and across specific cell and tissue types both *in vivo* and *ex vivo*. We propose to demonstrate this capability by characterizing low dose radiation-induced changes and remodeling of the extracellular matrix of tissues and characterize membrane-level signal transduction of protein complexes previously identified as low dose responsive (<10 cGy). Coupled with chemometrics and other analytical methods, CARS can be developed into a highly-sensitive and accurate tool that would be inexpensive and simple to operate that could characterize relevant cellular and tissue-level responses at these low IR doses. The groundwork for this research has recently been laid by the development of a CARS microscope at LLNL, and we are actively pursuing biological changes associated with various environmental and genotoxic stressors.

This work was performed under the auspices of the U.S. Department of Energy by Lawrence Livermore National Laboratory under contract DE-AC52-07NA27344 and supported by grant FWP SCW-0551 from the Low Dose Radiation Research Program.