The Food and Drug Administration's (FDA's)
2015 ORSI Science Symposium
April 27, 2015
SPEAKER ABSTRACTS AND BIOGRAPHIES

Session 6: CORES Scientific Intramural Grant Presentations – 4:10 -5:00 PM

Speaker	**Julian E A Leakey, PhD, DABT**
Title	**Research Biologist**
Biography	**Julian Leakey is a research biologist and toxicologist who has worked at NCTR since 1985. He received his PhD in Biochemistry in 1976. His areas of expertise include: drug metabolism, effects of diet and body weight on aging and cancer, toxicology of antiviral drugs, toxicity and efficacy of dietary supplements and immunotoxicology of nanomedicines.**
Subject	**Complement assays for detection of immune-sensitizing activity of nanomaterials**
Presentation Abstract	**The ability to activate the serum complement cascade is a major determinant as to whether a nanoparticle used as a drug or drug-carrier will evoke immunotoxicity. Recently, an in vitro assay for nanoparticle-induced complement activation was developed by G Lanza et al (Pham et al, Nanomed. 10, 651-60, 2014). This Nanotechnology CORES research project is part of an FDA program to beta-test this assay for general use in nanotoxicology research, we have evaluated the assay using a spectrum of coated gold nanoparticles and compared the response of human serum with that of cynomolgus monkey, beagle dog and Sprague-Dawley rat serum. The assay measures residual complement activity in a serum sample by titrating the serum with hemolysin-sensitized sheep erythrocytes and determining the level of hemolysis. The serum samples are pre-exposed to nanoparticles so that the degree of nanoparticle-dependent complement depletion can be determined. The positive control in the assay was coated perflurooctylbromide (PFOB) nanoemulsions (Lanza et al., 2014). The assay provided quantitative and reproducible results with commercially available cryopreserved human and animal serum and with both commercially available and freshly prepared sensitized erythrocytes. Results with PFOB emulsions were correspondent to published data. Species differences were observed in complement activating potential of gold nanoparticles. Human and monkey serum was more sensitive to complement activation than that of dog and rat. In certain cases, particles that activated complement also aggregated in ionic buffers. The data suggests that in vitro species comparisons should be performed prior to designing animal studies to evaluate nanoparticle immunotoxicity. Further work is being conducted to develop a high throughput version of the assay and to develop other ELISA-based assays that can be used to detect complement activation in plasma from experimental animals exposed in vivo.**