Gabriella Webster: TAMU Student Research Week: Agriculture and Life Sciences Category, 1st Undergraduate Oral

Title: Illuminating molecular mechanisms by which dietary DHA aids in colon cancer prevention

Abstract: Epidermal Growth Factor Receptor (EGFR) is a receptor tyrosine kinase located in the cell plasma membrane, which regulates epithelial tissue growth and development and is hyperactivated in cancer tissues. Binding of EGFR ligands promotes receptor oligomerization (clustering), which is required for efficient signal propagation. Currently, inhibition of EGFR signaling, which suppresses uncontrolled cell growth, is used as a chemotherapeutic strategy. This is relevant because the long-chain n-3 PUFA, docosahexaenoic acid (DHA, 22:6?4,7,10,13,16,19), attenuates EGFR signaling, making it of interest as a potential colon cancer therapeutic. Although the mechanism by which DHA attenuates EGFR activity is unclear, it is known that DHA can modulate plasma membrane spatiotemporal dynamics. Therefore, we hypothesized that DHA inhibits EGFR driven cell proliferation by reducing EGFR nanocluster size/frequency. To visualize EGFR nanoclusters, we utilized two complementary super-resolutio n microscopy platforms. A labeling protocol for EGFR was developed for use in stimulated emission depletion (STED) microscopy experiments using SW48 human colorectal cancer cells. It was determined that anti-human EGFR antibody (Cetuximab) labels EGFR with high fidelity after showing that membrane cholesterol depletion reduces the size of EGFR nanoclusters in the epithelial cell membrane, as expected. Future studies will employ this labeling protocol to examine the effect of DHA on EGFR nanoclustering using Stochastic Optical Reconstruction Microscopy (STORM).