IDH2 MUTATION IN CHONDROSARCOMA: SHEDDING LIGHT ON MITOCHONDRIAL METABOLISM AND CELLULAR PHYSIOLOGY. Caleb C. J. Wyckoff, Michael W. Stacey, & Christopher J. Osgood, Old Dominion University. Chondrosarcoma (CS) stands as the second most prevalent form of bone cancer, notorious for its resistance to conventional chemotherapy and radiation treatments. CS has mutually exclusive gain-of-function mutations in the enzymes IDH1 and IDH2. IDH1 mutant enzymes function in the cytosol whereas IDH2 functions in the mitochondria. Cells with the IDH2 mutation convert α-ketoglutarate in the citric acid cycle into high levels of D-2-hydroxyglutarate (D2HG). D2HG is a potent oncometabolic byproduct that aids in the malignant progression of the cancer and elicits changes in the epigenetic profile of DNA. Recent work shows CS capable of sabotaging healthy cell metabolism in the tumor microenvironment by transferring mutant mitochondria via formation of intracellular nanotubular highways; a significant event that could negatively impact receiving cell metabolism. Our initial metabolic analysis shows our CS cell line SW1353 (IDH2 mutant) has a two-fold higher mitochondrial metabolic activity compared to wild-type cells. Using relevant Mitrotracker dyes (Green FM and Red FM), our lab has validated the creation of nanotubular highways between SW1353 chondrosarcomas and primary fibroblasts and verified transfer of mitochondria using fluorescent microscopy and flow cytometry. We hypothesize that mitochondrial transfer between chondrosarcoma and normal cell types occurs through nanotube formation between the cells. Understanding the effects of mitochondrial transfer on cell metabolism and epigenetic alterations (such as hypermethylation) could pave the way for novel, targeted treatment strategies. Author contact: cwyckoff@odu.edu