# Regulation of the PPAR? Pathway Using Antagonists and Inverse Agonists Across 2D and 3D Lung Cancer Models

Nunnery, Parker (School: John Overton High School)

Lung cancer is the leading cause of cancer-related deaths and is known to effectively colonize other parts of the body, often evading the immune system as it metastasizes or spreads. Pre-liminary data from our lab indicated that the PPAR? pathway may enhance lung cancer cells' ability to adapt and survive in new microenvironments resulting in metastasis. To test this, three lung cancer cell lines were treated with PPAR? antagonists (GW9662, T0070907) and the inverse agonist BAY-0069. In 2D monolayers, all three compounds significantly reduce cell proliferation in a dose-dependent manner in two of three lines. However, growth inhibition was markedly weaker when cells were cultured as neurospheres or 3D tumor organoids, suggesting that PPAR?'s role in proliferation is highly dependent on model complexity and tumor microenvironment. These findings highlight the importance of using complex relevant models for drug testing. a complex model such as a cerebral organoid could be utilized in future studies to test whether proliferation and colonization of the brain could be reduced with PPAR? pathway inhibition. If successful, targeting PPAR? signaling may offer a novel therapeutic strategy to improve outcomes in patients with lung cancer brain metastasis.

**Awards Won:**
National Anti-Vivisection Society: Awards of $3,000