27O-ISMS39 **Auranofin, an Inhibitor of Thioredoxin Reductase, Exhibits Preferential Cytotoxicity Under Nutrient-deprived Conditions in Human Pancreatic Cancer Cells**

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Cancer tissues are frequently exposed to hypoxia and nutrient-deprived conditions. We focused on the nutrient-limiting environment in solid tumors, and then screened small molecular cytotoxic agents which preferentially decreasing the survival of cancer cells under nutrient-deprived conditions. Auranofin showed preferential cytotoxicity and significantly induced apoptosis toward human pancreatic cancer cells in nutrient-deprived conditions. Auranofin, a gold complex used in clinical treatment of rheumatoid arthritis, is known to inhibit thioredoxin reductase (TrxR) in the thioredoxin (Trx) system. Therefore, we examined the relationship between the Trx system and the cytotoxicity of auranofin under nutrient-deprived conditions. Auranofin significantly suppressed TrxR activity in PANC-1 cells in nutrient-deprived conditions. In addition, auranofin increased the level of intracellular reactive oxygen species (ROS). The cytotoxicity of auranofin was reduced by ROS quenchers such as *N*-acetyl-L-cystein; therefore, the accumulation of ROS is attributed to the cytotoxicity induced by auranofin. Our findings suggest that the Trx system in cancer cells is an important target for anticancer drugs and that auranofin has a potential to be a unique therapeutic agent against human pancreatic cancers.