

**TITLE:** Evidence of a metabolic switch in patients with squamous cell carcinoma of the oral cavity

**BACKGROUND/PURPOSE:** A Metabolic reprogramming, a switch to anaerobic glucose metabolism, known as “Warburg effect” exclusively seen in cancer cells highlight demand for nutrients to support its proliferation rate. This study aims to investigate the role of glucose-6-phosphate dehydrogenase (G-6PDH), lactate dehydrogenase (LDH) in tumor cell lysate along with glutathione (GSH) levels as a surrogate measure of cellular redox potential in the oral cancer cell metabolism.

**METHODS:** We report Total GSH, G6PDH and LDH enzyme activity in tumor samples from 26 tumor/normal tissues from oral cancer patients (stage IV oral cancer patients , Male: 20, Female: 5) surgically treated at Kailash Cancer Hospital and Research Centre were analyzed.

**RESULTS:** Total GSH decreased by 1.7- fold in tumor samples ( $16.2 \pm 3.14$  moles/mg protein) as compared to the paired normal tissue ( $26.5 \pm 3.0$  moles/mg protein). This was correlated and supported by with the 7.3-fold increase in G6PDH activity seen in tumor tissue ( $5.64 \pm 1.19$   $\mu\text{M}/\text{mg}$  protein) compared to normal tissue ( $0.774 \pm 0.179$   $\mu\text{M}/\text{mg}$  protein).

**DISCUSSION AND CONCLUSION:** No significant change was observed in LDH activity in tumor tissue ( $700.4 \pm 67.95$   $\mu\text{M}/\text{mg}$  protein) when compared to normal tissue ( $630.8 \pm 54.66$   $\mu\text{M}/\text{mg}$  protein). Our data suggest that increased flux of glucose through G6PDH pathway protects tumor cells from heightened oxidative stress. Pentose phosphate pathway and glycolysis operates as a metabolic switch between hypoxia and oxygenation with the upregulation of G6PDH. Low GSH supports with patient’s history of tobacco intake and thereby oxidative stress mediated by hypoxic condition.

