

## The Role of Txnrd2 Deficiency in Epithelial-to-Mesenchymal-Transition (EMT) and Tumor Formation in Pancreatic Cancer

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**Abstract :** Thioredoxin reductase 2 is a mitochondrial enzyme that belongs to the cellular defense against oxidative stress. We deleted mitochondrial Txnrd2 in a KrasG12D-driven pancreatic tumor model. Despite an initial increase in precursor lesions, tumor incidence decreased significantly. We isolated cancer cell lines from these genetically engineered mice and observed an impaired proliferation and colony formation. Reactive Oxygen Species, as determined by DCF fluorescence, were increased. We detected a higher mitochondrial copy number in Txnrd2-deficient cells (KTP). However, measurement of mitochondrial bioenergetics showed no impairment of mitochondrial function and comparable O<sub>2</sub>-consumption and extracellular acidification rates. In addition, the mitochondrial complex composition was affected in Txnrd2 deleted cell lines. To gain better insight into the role of Txnrd2, we deleted Txnrd2 in clones from parental KrasG12D cell lines using Crispr/Cas9 technology. The deletion was confirmed by western blot and activity assay. Interestingly, and in line with previous RNA expression analysis, we saw changes in EMT markers in Txnrd2 deleted cell lines and control cell lines. This might help us explain the reduced tumor incidence in KrasG12D; Txnrd2 $\Delta$ panc mice.

**Keywords :** PDAC, TXNRD2, epithelial-to-mesenchymal-transition, ROS

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