Thymidine kinase 1

Thymidine Kinase 1 (TK1) is an enzyme that plays a crucial role in DNA precursor synthesis by phosphorylating thymidine to thymidine monophosphate (dTMP). This reaction is part of the **salvage pathway** for nucleotide synthesis, allowing cells to recycle nucleosides for DNA replication.

Key Characteristics

- **Cellular Localization:** TK1 is primarily found in the **cytoplasm** during the **G1 phase** of the cell cycle and moves to the **nucleus** in the **S phase**, where DNA synthesis occurs. - **Cell Cycle Regulation:** Its expression is tightly regulated, increasing significantly during the **S phase** and being degraded during the **G2 and M phases**. - **Diagnostic Marker:** TK1 is used as a **biomarker for cell proliferation** and is elevated in various cancers, including leukemia, lymphoma, and solid tumors. Its presence in **serum** can indicate tumor activity.

Clinical Significance

- **Cancer Biomarker:** Elevated **serum TK1 (sTK1)** levels correlate with tumor growth and progression. - **Therapeutic Target:** TK1 is involved in the activation of nucleoside analogs used in chemotherapy, such as **acyclovir (ACV)** and **ganciclovir (GCV)** in antiviral treatments.

Preclinical experimental study with molecular and transcriptomic analysis

A study aimed to establish radio-resistant meningioma cell lines and uncover molecular mechanisms driving radioresistance to identify potential biomarkers and therapeutic targets.

Radio-resistant meningioma cell lines (IOMM-Lee-RR, CH157-RR) were developed using a progressive radiation dose (cumulative 90 Gy). Cell morphology, radiosensitivity, apoptosis, viability, migration, invasion, cell cycle, and DNA damage repair were analyzed via clonogenic assays, flow cytometry, and Western blotting. Transcriptome sequencing was performed to identify differentially expressed genes (DEGs), followed by KEGG and GO enrichment analyses. Protein-protein interaction (PPI) analysis was conducted to identify hub genes. TK1 expression was further validated in a cohort of 350 meningiomas and the GSE189672 dataset.

Radio-resistant meningioma cell lines exhibited enhanced survival, reduced apoptosis, increased cell viability, and superior migratory and invasive abilities compared to parental cells. Under radiation, these cells showed G0/G1 phase accumulation and reduced G2/M phase arrest, along with enhanced DNA repair capacity, as evidenced by lower γ-H2AX expression and fewer DNA damage foci. Transcriptome analysis revealed significant enrichment in metabolic pathways, DNA repair, and cell cycle regulation. Among 34 hub genes identified, TK1 emerged as a key gene, being highly expressed in recurrent and high-grade meningiomas and positively correlated with Ki67. Analysis of the GSE189672 dataset confirmed TK1 as a poor prognostic factor associated with tumor recurrence.

Radio-resistant meningioma cells exhibit enhanced DNA repair, migration, invasion, and altered cell cycle dynamics. Thymidine kinase 1 was identified as a promising biomarker and therapeutic target for overcoming radio-resistance in meningiomas [1)]

1)
Yu J, Ren L, Wu T, Hua L, Wang D, Wang Y, Xie Q, Deng J, Gong Y. Establishment and transcriptomic characteristics of radio-resistant meningioma cell lines. J Neurooncol. 2025 Feb 28. doi: 10.1007/s11060-025-04966-6. Epub ahead of print. PMID: 40019713.