

miR-26a-5p/PTEN/AKT Pathway Overview

The **miR-26a-5p/PTEN/AKT pathway** is a critical signaling pathway involved in cell proliferation, survival, and metabolism. It plays a significant role in various biological processes, including cancer progression, neuroprotection, and tissue regeneration. Below is a breakdown of its key components and their functions.

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1. miR-26a-5p: A MicroRNA Regulator - **miR-26a-5p** is a microRNA (miRNA), a small non-coding RNA molecule that regulates gene expression by binding to target mRNAs and inhibiting their translation or promoting their degradation. - It has been implicated in multiple cellular processes, including apoptosis, cell cycle regulation, and differentiation. - miR-26a-5p is often **upregulated in cancers** and plays a dual role, acting as an **oncogene or tumor suppressor** depending on the cellular context.

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2. PTEN: A Tumor Suppressor - **PTEN (Phosphatase and Tensin Homolog)** is a tumor suppressor gene that negatively regulates the **PI3K/AKT pathway**. - PTEN functions as a **lipid phosphatase**, dephosphorylating **PIP3 (phosphatidylinositol 3,4,5-trisphosphate)** to **PIP2 (phosphatidylinositol 4,5-bisphosphate)**, thereby preventing AKT activation. - Loss or downregulation of PTEN leads to **uncontrolled cell growth**, resistance to apoptosis, and increased tumorigenesis.

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3. AKT: A Key Cell Survival Kinase - **AKT (Protein Kinase B, PKB)** is a central player in cell survival and metabolism. - It is activated through phosphorylation by **PI3K (Phosphoinositide 3-Kinase)**. - Once activated, AKT promotes:

1. **Cell survival** by inhibiting pro-apoptotic factors such as BAD and caspase-9.
 2. **Cell proliferation** by modulating the mTOR pathway.
 3. **Metabolism regulation** by influencing glucose uptake and glycolysis.
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How miR-26a-5p Regulates the PTEN/AKT Pathway - **miR-26a-5p directly targets PTEN mRNA**, leading to its **downregulation**. - Reduced PTEN expression results in increased **PIP3 accumulation**, leading to **persistent AKT activation**. - This promotes **tumor growth, resistance to apoptosis, and enhanced cell migration/invasion**. - Conversely, in some contexts, miR-26a-5p may act **anti-oncogenically**, depending on the tissue type and microenvironment.

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Clinical Significance - **Cancer:** Overexpression of miR-26a-5p is linked to enhanced tumor progression in breast, liver, and lung cancers due to PTEN suppression. - **Neuroprotection:** In the nervous system, miR-26a-5p might have protective effects, promoting neuronal survival through AKT activation. - **Therapeutic Potential:** Targeting miR-26a-5p could be a strategy for cancer therapy by restoring PTEN levels and inhibiting AKT hyperactivation.

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Conclusion The **miR-26a-5p/PTEN/AKT pathway** plays a crucial role in cell fate determination, particularly in cancer biology. Understanding this pathway provides insights into tumor development and potential therapeutic interventions targeting miRNAs to modulate PTEN and AKT signaling.

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Last update: **2025/01/31 07:52**

