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Journal of Cellular Signaling Editorial

Connecting Molecular Regulation to Cellular Function

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Editorial

Cell signaling is a complex, interconnected system that controls vital cellular processes such as proliferation, post-translational modifications (PTMs), and, ultimately, cell fate, controlling protein degradation and apoptosis. Alterations in these pathways can lead dysregulation. The recent issue of Journal of Cellular Signaling, **Volume 6, Issue 4**, touches on potential players that may affect apoptotic signaling such as PAX-Interacting Protein 1 (PTIP), as well as PTMs and mutations that can lead to neurological disorders and chronic illnesses such as Autosomal Dominant Polycystic Kidney Disease (ADPKD). Further research into the molecular mechanisms behind cell signaling pathways and the major players involved is vital for a deeper understanding of how disorders may lead to diseases, as well as how they may be harnessed therapeutically.

PAX-Interacting Protein 1 (PTIP) Promotes Apoptosis

The article *'PAX-Interacting Protein 1 (PTIP) Promotes Apoptosis'* (Huang, C., *et al*., 2025) [1] chronicles the exploration of the previously unrecognized apoptotic function of PTIP. Huang and colleagues were prompted by observations that PTIP manipulation appeared to influence apoptotic outcomes. To further investigate this interaction, enforced overexpression was employed. Due to the cytotoxicity of PTIP at high levels, a GFP-PTIP fusion was designed to allow higher levels of expression before reaching a critical toxicity point. With this newly generated fusion, Huang *et al*. report that elevation in PTIP expression facilitates a mitochondrial apoptosis cascade. PTIP translocates from the nucleus and associates with mitochondria, resulting in aggregation. This triggers the release of Cytochrome C, which in turn activates caspase-9 and begins the intrinsic apoptotic pathway. Notably, these events only occur under forced overexpression conditions; no known cell lineage exhibits comparable PTIP behavior or expression levels. As a result, the broader biological significance of these findings remains unclear. The study demonstrates that PTIP can initiate apoptosis when artificially overexpressed, but the authors do not articulate a physiological context or rationale that would clarify why this phenomenon matters.

A Newly Characterized, Two BRCT Domain-Containing Isoform of PAX-Interacting Protein (PTIP) Generated via Frame Shift and Alternative Pre-mRNA Splicing

With *'A Newly Characterized, Two BRCT Domain-Containing Isoform of PAX-Interacting Protein (PTIP) Generated via Frame Shift and Alternative Pre-mRNA Splicing,'* Huang and team [2] begin the work of characterizing a newly designed, truncated PTIP protein (PTIP576). This variant is identified by the presence of a two-base frameshift and alternative splicing across exons 12–14. The resultant protein retains only BRCT3 and BRCT4 and terminates with a novel, disordered 50-amino-acid C-terminus. The authors demonstrate that the expression of PTIP576 is heavily restricted: detectable in fetal CD19*IgM$^+$ B cells and inducible in mature B cells only under combined antigen and IL-5 stimulation. Overexpression in transgenic mice resulted in a developmental bottleneck wherein B-cell progenitors were reduced by 40–45%, while later B-cell populations were increased correspondingly to the earlier reduction. Furthermore, thymic expression of the transgene revealed a three-fold increase in the number of CD4 single-positive thymocytes without changes in CD8 or double-positive cells. Overall, these findings indicate that

the structurally truncated PTIP576 exerts measurable effects on B- and T-cell development, even though the underlying mechanisms remain unresolved.

Pathogenic Pathways and Therapeutic Strategies in Autosomal Dominant Polycystic Kidney Disease (ADPKD)

In *'Pathogenic Pathways and Therapeutic Strategies in Autosomal Dominant Polycystic Kidney Disease (ADPKD)'*, Preval *et al*. [3] review the molecular mechanisms and mutations underlying ADPKD, as well as ways these are or could be used in potential treatments. ADPKD is most often caused by mutations in PKD1 or PKD2, which encode for polycystin-1 or polycystin-2, respectively. These proteins are vital for calcium signaling, and these mutations lead to increased cAMP signaling which can promote cyst formation and kidney enlargement via activation of pathways that alter proliferation and fluid secretion. Other major signaling pathways that promote cyst formation via increasing cell proliferation include mTORC1, Src, and tyrosine kinase. Preval et al. also explore experimental treatment options for ADPKD, highlighting approaches that focus on decreasing fluid accumulation, improving protein folding and maturation, and mTOR inhibition. The review paper emphasizes the need for further research into the various drug targets for ADPKD, as well as a deeper understanding of the molecular mechanisms and alterations in signaling pathways underlying the disease.

Ubiquitination of Metabotropic Glutamate Receptors and Associated Synaptic Proteins In vitro and In vivo

Mao and Wang's review article [4], *'Ubiquitination of Metabotropic Glutamate Receptors and Associated Synaptic Proteins In Vitro and In Vivo'*, explores the role of ubiquitination on metabotropic glutamate (mGlu) receptors and other mGlu-associated proteins such as Homer1, Arc, and PICK1 which are involved in synaptic signaling. Ubiquitination is a post-translational modification implicated in degradation of proteins via the ubiquitin-proteasome system (UPS) or lysosomal pathway, as well as non-degrading roles like regulation of trafficking, mGlu function, and protein-protein interactions. Specific postsynaptic group I (mGlu1/5) and presynaptic group III (mGlu7) mGlu receptors are especially regulated by ubiquitination in UPS-dependent and -independent manners. Dysregulation of ubiquitination may lead to an impairment of synaptic plasticity in various chronic brain diseases. This review highlights the need for further research into ubiquitination and specific E3 ligases involved with mGlu receptors, as well as research into the less studied deubiquitination enzymes, other post-translational modifications, and the potential crosstalk between these various modifications.

Collectively, cell systems involve closely regulated and precisely balanced networks of gene expression, protein modification and signaling transduction, and disease arises when cellular homeostasis breaks down.

References

1. Huang CJ, Cho H, Li C, Kim K, Yu D, Park D, et al. PAX-Interacting Protein 1 (PTIP) Promotes Apoptosis. J Cell Signal. 2025;6(4):126–41.
2. Huang CJ, Li C, Yu D, Cho H, Kim K, Zhang YJ, et al. A Newly Characterized, Two BRCT Domain-Containing Isoform of PAX-Interacting Protein (PTIP) Generated via Frame Shift and Alternative Pre-mRNA Splicing. J Cell Signal. 2025;6(4):142–55.
3. Preval KM, Smith AO, Pazour GJ. Pathogenic Pathways and Therapeutic Strategies in Autosomal Dominant Polycystic Kidney Disease (ADPKD). J Cell Signal. 2025;6(4):156–69.
4. Mao LM, Wang JQ. Ubiquitination of Metabotropic Glutamate Receptors and Associated Synaptic Proteins In Vitro and In Vivo. J Cell Signal. 2025;6(4):170–7.