

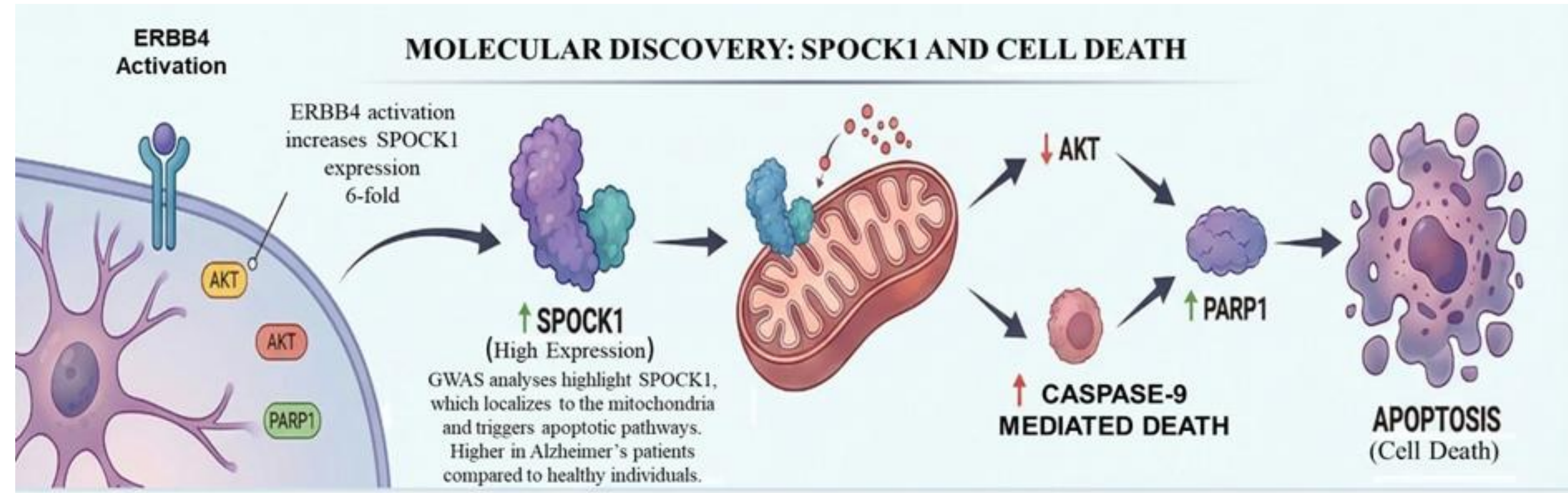
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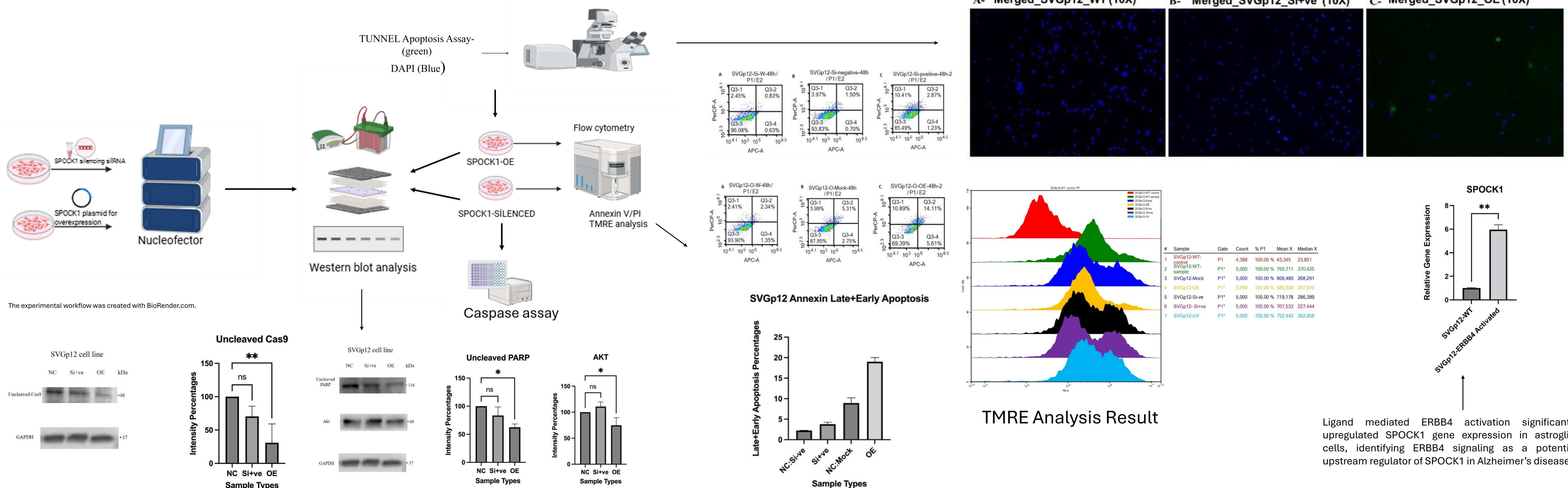
PROPOSED MECHANISM



INTRODUCTION

Astrocyte dysfunction and cell death are increasingly recognized as key contributors to Alzheimer's disease (AD) pathogenesis. SPOCK1, a member of the SPARC family, is highly expressed in breast, lung, prostate, and liver cancers. Several studies have reported that SPARC family proteins may play a role in the development of central nervous system (CNS) diseases. In our group's previous studies, SPOCK1 variants were associated with late-onset Alzheimer's disease (LOAD); however, its cell type specific functions and molecular mechanisms remain poorly understood.

EXPERIMENTAL DESIGN AND SELECTED RESULTS DEMONSTRATING A PRONOUNCED PRO-APOPTOTIC EFFECT OF SPOCK1 EXCLUSIVELY IN ASTROCYTE CELLS



CONCLUSION

For the first time, these findings demonstrate that SPOCK1 selectively triggers mitochondrial apoptosis in astroglia via caspase-9 activation and AKT pathway suppression, while causing distinct effects in other neural cell types. Our study provides the first comprehensive evidence that SPOCK1 may contribute to Alzheimer's disease pathogenesis through astrocyte-specific apoptotic mechanisms downstream of ERBB4 signaling.

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