AP-2α, also known as Activating Protein 2 alpha, is a transcription factor encoded by the TFAP2A gene. It belongs to the AP-2 family of transcription factors and plays important roles in the regulation of gene expression during embryonic development and tissue-specific differentiation.

Here are some key features and functions of AP-2α:

Structure: AP-2α is a DNA-binding protein consisting of a conserved DNA-binding domain known as the AP-2 domain. This domain enables AP-2α to bind to specific DNA sequences in the promoter regions of target genes.

Gene regulation: AP-2α functions as a transcriptional activator or repressor depending on the context and the target gene. It can interact with other proteins and cofactors to modulate the expression of downstream target genes. AP-2α recognizes and binds to specific DNA sequences known as AP-2 binding sites.

Developmental roles: AP-2α is crucial for embryonic development and is involved in the formation of various tissues and organs. It is expressed in numerous embryonic structures, including the neural crest, craniofacial structures, limb buds, and sensory organs. AP-2α helps regulate the expression of genes that control cell proliferation, migration, and differentiation during development.

Tissue-specific functions: AP-2α is also important for tissue-specific differentiation in various organs and systems, such as the mammary gland, skin, eye, and adrenal gland. It regulates the expression of genes involved in these tissues' development, maintenance, and function.

Cancer and disease: Dysregulation of AP-2α has been associated with various types of cancer. It can act as a tumor suppressor or an oncogene depending on the cellular context. Changes in AP-2α expression or function can impact cell proliferation, apoptosis, and other cancer-related processes. Additionally, AP-2α has been implicated in certain developmental disorders and congenital diseases.

Overall, AP-2α is a transcription factor that plays a vital role in embryonic development, tissue-specific differentiation, and the regulation of gene expression. Its functions extend to various physiological and pathological processes, making it an important molecule for research and understanding of development and disease.

Long et al. show that low expression of AP-2α is correlated with high expression of PD-L1 in high-grade glioma tissues. AP-2α binds directly to the promoter of the CD274 gene, not only inhibits the transcriptional activity of PD-L1 but enhances endocytosis and degradation of PD-L1 proteins. Overexpression of AP-2α in gliomas enhances CD8+ T cell-mediated proliferation, effector cytokine secretion, and cytotoxicity in vitro. Tfap2a could increase the cytotoxic effect of Cd8+ T cells in CT26, B16F10, and GL261 tumor-immune models, improve anti-tumor immunity, and promote the efficacy of anti-PD-1 therapy. Finally, the EZH2/H3K27Me3/DNMT1 complex mediates the methylation modification of AP-2α gene and maintains low expression of AP-2α in gliomas. 5-Aza-dC (Decitabine) treatment combines with anti-PD-1 immunotherapy to efficiently suppress the progression of GL261 gliomas. Data support a mechanism of epigenetic modifications of AP-2α that contributes to tumor immune evasion, and reactivation of AP-2α synergizes with anti-PD-1 antibodies to increase antitumor efficacy, which may be a broadly applicable strategy in solid tumors [1)]

1)

Long S, Huang G, Ouyang M, Xiao K, Zhou H, Hou A, Li Z, Zhong Z, Zhong D, Wang Q, Xiang S, Ding X. Epigenetically modified AP-2α by DNA methyltransferase facilitates glioma immune evasion by

upregulating PD-L1 expression. Cell Death Dis. 2023 Jun 17;14(6):365. doi: 10.1038/s41419-023-05878-x. PMID: 37330579.