What is the role of Atf3 in the brain?

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ATF3 is a transcription factor that is activated by various types of stress, such as nerve injury, hypoxia, inflammation, and infection. ATF3 plays different roles in the brain depending on the cell type and the context. In neurons, ATF3 is mainly expressed after axonal damage and promotes neuronal survival and regeneration by regulating the expression of genes involved in anti-apoptotic, pro-regenerative, and anti-inflammatory pathways [1] [2]. For example, ATF3 suppresses the expression of carboxyl-terminal modulator protein (CTMP), which inhibits the Akt/PKB signaling cascade that protects neurons from apoptosis [3]. ATF3 also enhances the expression of growth-associated protein 43 (GAP-43), which is essential for axonal growth and guidance [4]. Moreover, ATF3 inhibits the production of pro-inflammatory cytokines, such as TNF-α and IL-6, by interfering with the activation of NF-κB [2]. In glial cells, such as astrocytes and microglia, ATF3 is also induced by various stimuli, such as ischemia, lipopolysaccharide (LPS), and interferon-γ (IFN-γ). However, the role of ATF3 in glial cells is less clear and may depend on the duration and intensity of the stress. Some studies have suggested that ATF3 may have anti-inflammatory and neuroprotective effects in glial cells by inhibiting the expression of inducible nitric oxide synthase (iNOS), cyclooxygenase-2 (COX-2), and matrix metalloproteinase-9 (MMP-9) [2]. Other studies have reported that ATF3 may have pro-inflammatory and neurotoxic effects in glial cells by enhancing the expression of IL-1β, IL-6, TNF-α, and nitric oxide (NO) [2]. Therefore, ATF3 may have dual functions in the brain depending on the cell type and the stress condition.

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