Glioblastoma (GBM) is the most common primary human malignant tumor and is almost incurable. Treatment of GBM is challenging, partly due to apoptosis evasion and drug resistance. We recently showed that Nuclear Factor I-A (NFIA), a glial fate determinant, promotes GBM malignant behavior and inhibits cell death. Our subsequent analysis showed that NFIA-induced survival is mediated in part by NFkB. Further, we showed that the levels of NFIA and NFkB are highly correlated in the primary GBM tumors. Using gain- and loss-of-function approaches, we demonstrated that NFIA induces NFkB transcription and increases the level of NFkB and its downstream anti-apoptotic factors. Interestingly, NFIA expression also increases in response to ectopic NFkB or to the NFkB activator TNFa, suggesting a feed-forward effect. Moreover, both genetic and pharmacologic inhibition of NFkB blocks the anti-apoptotic effect of NFIA. Together, these data suggest that NFIA-induced survival is mediated in part by NFkB. These novel observations place NFIA at the center of a signaling network that controls GBM progression. This is the first evidence to link between NFIA and NFkB in glioma biology and thus facilitate our understanding of emerging role of NFIA in cancer, which may open new insights into therapy by targeting relevant pathways.