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Connexin 30 down-regulates insulin-like growth factor receptor-1, abolishes Erk and potentiates effects of an IGF-R inhibitor in a glioma cell line

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Connexins (Cx) play a crucial role in cell communication through regulation of cell growth and proliferation. In recent decades, both suppressive and enhancing roles of gap junction proteins in malignancy have been proposed, though mechanisms remain unclear. We intend to evaluate the impact of Cx30 on dysregulated growth of glioma owing to an aberrant expression of Insulin-like growth factor-1 receptor (IGF-1R). The study also examined whether Cx30 expression influenced sensitivity of glioma cells to Picropodophyllin (PPP), the potent inhibitor of IGF-1R. C6-cells transfected with full length Cx30 resulted in complete abolition of colony-forming efficiency. Interestingly, PPP-supplemented cells behaved differently with and without exogenous Cx as confirmed by wound closure assay. The expressions of phosphorylated and unphosphorylated IGF-1R along with its key signaling enzymes, pAkt/pErk, were also varied significantly in transfected and non-transfected C6 cells. pIGF-1R and IGF-1R were significantly reduced on Cx30 transfection when compared with that of non-transfected cells. pErk expression was abolished in transfected C6 with no significant difference in the expression of pAkt. The potency of PPP against C6 was more pronounced in the presence of Cx30. We demonstrate that Cx30 has the potential to alter the IGF-1R mediated pathway thereby influencing the growth, proliferation and migration of glioma cells which could further enhance the effect of therapeutic intervention. Though it could not be corroborated that the observations made are due to Cx30-mediated channel-dependent and/or independent impact, we stress the impact of significance of Cx30 on IGF-1R in glioma and in therapeutic aspects.

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