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The effect of VEGF and PDGF growth factors in olfactory regeneration

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Background: The olfactory system has a unique ability to regenerate throughout life. The nerve cells that detect odours are directly exposed to bacteria, viruses and toxic chemicals which cause an estimated 1-3% of nerve cells dying each day. Luckily stem cells that reside in the olfactory epithelium within the nasal cavity produce new olfactory neurons which send long fibres up through the cribriform plate of the ethmoid bone and terminate within the olfactory bulb to make new connections. However, when extensive damage to the olfactory nerve occurs such as skull base surgery, regenerating olfactory axons cannot find their targets and are unable to make functional connections to the olfactory bulb which causes anosmia. This is due to axonal mis-targeting in the forebrain or scar tissue formations which make a physical barrier and prevent axons reach the target tissue.

Loss of smell (anosmia) can be devastating for patients. Smell dysfunction significantly influences physical wellbeing, quality of life, nutritional status as well as everyday safety and is associated with increased mortality. Currently there is no effective treatment to

restore olfaction (sense of smell). One of the major causes of anosmia is skull base surgery which uses the intranasal transsphenoidal approach to remove tumors. Despite care to minimise damage to the olfactory region during surgery, patients can suffer permanent reduction or complete loss of olfaction. It has been shown that anosmia can reduce life-expectancy of individuals by up to 5 years. Therefore, there is a need to find a treatment for anosmia.

Methods: We have investigated the effects of combined two growth factors (VEGF) and (PDGF) in regeneration of the olfactory neurons and restoration of sense of smell in mice animal models. The degeneration of olfactory neurons was induced by surgical removal of the olfactory bulb which mirrored the skull base surgery. The animals were divided into two groups: the treatment animals group received 0.5 μg of the combined growth factors over three days; however the control group only received PBS. The animals were harvested at different time points post- injury and histology was used for analysis of neuronal and astrocytes cells.

Results: We have found that olfactory regenerating axons significantly projected deeper to the brain in the treatment group compared to the control group at day 10 and 14 ($P < 0.05$) and regeneration of the olfactory receptor neurons significantly increased in the treatment group ($P < 0.05$). Our results also showed that the growth factor treatments changed the morphology of astrocytes which improved axonal regeneration (identified by GFAP immunohistochemistry).

Conclusion: Our results indicated that the combined delivery of VEGF and PDGF growth factors treatment has a therapeutic potential for anosmia and restoration of sense of smell.

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