FEATURES

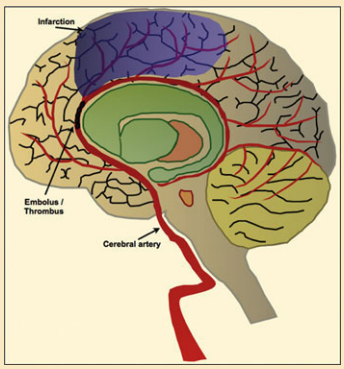
VOLUME 114 • NUMBER 4

Stem Cells as Promising Therapeutic Options for Neurological Disorders

743

Jongman Yoo, Han-Soo Kim, and Dong-Youn Hwang

ACCEPTED MANUSCRIPT ONLINE 23 OCTOBER 2012



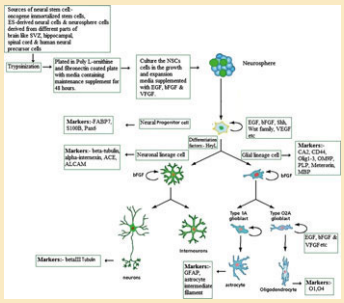
Due to the limitations of pharmacological and other current therapeutic strategies, stem cell therapies have emerged as promising options for treating many incurable neurologic diseases. A variety of stem cells including pluripotent stem cells (i.e., embryonic stem cells and induced pluripotent stem cells) and multipotent adult stem cells (i.e., fetal brain tissue, neural stem cells, and mesenchymal stem cells from various sources) have been explored as therapeutic options for treating many neurologic diseases, and it is becoming obvious that each type of stem cell has pros and cons as a source for cell therapy. Wise selection of stem cells with regard to the nature and status of neurologic dysfunctions is required to achieve optimal therapeutic efficacy. To this aim, the stem cell-mediated therapeutic efforts on four major neurological diseases, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and stroke, will be introduced, and current problems and future directions will be discussed.

Neural Stem Cells—Trends and Advances

764

Denis English, Neel K. Sharma, Kaushal Sharma, and Akshay Anand

ACCEPTED MANUSCRIPT ONLINE 5 DECEMBER 2012



For many years, accepted dogma held that brain is a static organ with no possibility of regeneration of cells in injured or diseased human brain. However, recent preclinical reports have shown regenerative potential of neural stem cells using various injury models. This has resulted in renewed hope for those suffering from spinal cord injury and neural damage. As the potential of stem cell therapy gained impact, these claims, in particular, led to widespread enthusiasm that acute and chronic injury of the nervous system would soon be a problem of the past. The devastation caused by injury or diseases of the brain and spinal cord led to wide premature acceptance that "neural stem cells (NSCs)" derived from embryonic, fetal or adult sources would soon be effective in reversing neural and spinal trauma. However, neural therapy with stem cells has not been realized to its fullest extent. Although, discrete population of regenerative stem cells seems to be present in specific areas of human brain, the function of these cells is unclear. However, similar cells in animals seem to play important role in postnatal growth as well as recovery of neural tissue from injury, anoxia or disease.

Journal of Cellular Biochemistry

Identification of Candidate Downstream Targets of TGFβ Signaling During Palate Development by Genome-Wide Transcript Profiling 796

Richard C. Pelikan, Junichi Iwata, Akiko Suzuki, Yang Chai, and Joseph G. Hacia

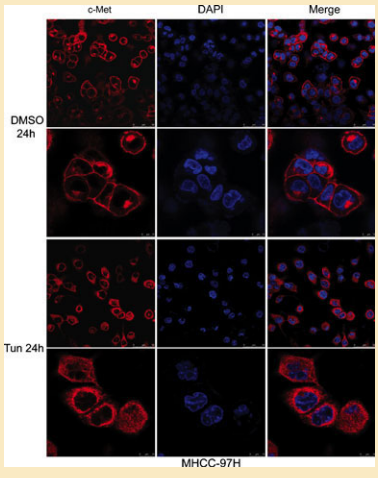
ACCEPTED MANUSCRIPT ONLINE 11 OCTOBER 2012

Nonsyndromic orofacial clefts are common birth defects whose etiology is influenced by complex genetic and environmental factors and gene–environment interactions. Although these risk factors are not yet fully elucidated, it is known that alterations in transforming growth factor-beta (TGFβ) signaling can cause craniofacial abnormalities, including cleft palate, in mammals. To elucidate the downstream targets of TGFβ signaling in palatogenesis, we analyzed the gene expression profiles of *Tgfbr2*$^{fl/fl}$;*Wnt1-Cre* mouse embryos with cleft palate and other craniofacial deformities resulting from the targeted inactivation of the *Tgfbr2* gene in their cranial neural crest (CNC) cells. Relative to controls, palatal tissues obtained from *Tgfbr2*$^{fl/fl}$;*Wnt1-Cre* mouse embryos at embryonic day 14.5 (E14.5) of gestation have a robust gene expression signature reflective of known defects in CNC-derived mesenchymal cell proliferation. Groups of differentially expressed genes (DEGs) were involved in diverse cellular processes and components associated with orofacial clefting, including the extracellular matrix, cholesterol metabolism, ciliogenesis, and multiple signaling pathways. A subset of the DEGs are known or suspected to be associated with an increased risk of orofacial clefting in humans and/or genetically engineered mice. Based on bioinformatics analyses, we highlight the functional relationships among differentially expressed transcriptional regulators of palatogenesis as well as transcriptional factors not previously associated with this process. We suggest that gene expression profiling studies of mice with TGFβ signaling defects provide a valuable approach for identifying candidate mechanisms by which this pathway controls cell fate during palatogenesis and its role in the etiology of human craniofacial abnormalities.

c-Met Function Requires N-Linked Glycosylation Modification of Pro-Met 816

Run Chen, Juan Li, Chun-Hong Feng, Shao-Kun Chen, You-Ping Liu, Chun-Yan Duan, Hong Li, Xian-Ming Xia, Tao He, Mei Wei, and Rong-Yang Dai

ACCEPTED MANUSCRIPT ONLINE 11 OCTOBER 2012



c-Met, the receptor for hepatocyte growth factor (HGF), is cell surface tyrosine kinase that controls cancer cell growth, survival, invasion and metastasis. Post-translational modification, such as glycosylation, plays an essential role in regulating the function of cell surface molecules. Whether glycosylation modification regulates the enzymatic properties of c-Met is unknown. In this study, we investigated the effect of glycosylation on the function of c-Met. We found that c-Met is an N-linked glycosylated protein. Both pro-Met and p145Met (the β subunit of mature c-Met) have N-linked glycosylation. Glycosylation inhibitor studies revealed that the *N*-glycosylation modification of p145Met is from pro-Met, but not due to the further modification of pro-Met. Importantly, blocking the *N*-glycosylation targets pro-Met to cytoplasm and initiates its phosphorylation independent of HGF engagement. Nonglycosylated pro-Met activates c-Met downstream pathways to a certain extent to compensate for the degradation of p145Met induced by glycosylation blocking-mediated endoplasmic reticulum (ER) stress.