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Abstract

The central nervous system (CNS) is generated from progenitor cells that are recognized as neural stem cells (NSCs). The mammalian CNS is generally believed to lack the capacity to regenerate itself after damage. As a result, patients with CNS injury and disease are suffering from immense pain, immobility, and inconveniences, which usually burden the family and the society. On the other hand, the adult fish and salamander have a remarkable capacity for repair after damage. During neural development, dramatic and consistent changes in the composition of glycolipids occur. Interestingly, c-series gangliosides appear only transiently in mammalian embryonic brain but extremely low amount in adult brain. Whereas, c-series gangliosides are abundant in brains that have a high capacity to regenerate, such as adult fish. My long-term goal is to promote adult neurogenesis of the endogenous NSC pools with curative glycoconjugate compositions to achieve neural repair and functional recovery in our mammalian brains after damage. To improve our knowledge on ganglioside functions of regulatory mechanisms in NSC self-renewal and differentiation, we took advantages of rodent NSC culture and zebrafish regenerable brains. The damaged zebrafish brain spontaneously recovered at one month post-injury. After brain injury of adult zebrafish, an increase of A2B5 expression and increased numbers of A2B5+/GFAP+ cells were observed. In our mammalian brain, a limited endogenous neurogenesis, spontaneously occurred following various insults, such as ischemic stroke, traumatic brain injury (TBI) and amyloid-beta peptide (Aβ), in an attempt to repair in the mammalian brain. However, the adult mammalian brain has a low ability to regenerate, making it difficult to fully recover the lost neurons and their functions. In proliferating mouse NSCs after insults, the expression of ST-III (an enzyme for the synthesis for c-series gangliosides) and A2B5 antigens were elevated. Increased A2B5+/GFAP+ cells might have a role for brain regeneration. Interestingly, we found that A2B5+/GFAP+ cells from rodents have a lipid composition distinct from mature astrocytes, but they are more similar to progenitor cells. Further experiment revealed that EGF-signaling and gangliosides are necessary components on insult-induced NSC proliferation. Our research will be useful in providing novel strategies for disease treatment and neural repair by NSCs and gangliosides.