### Chapter 21

# Chitosan-Based Biomaterials for Tissue Engineering of Glial Cells

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#### **ABSTRACT**

Glial cells play a remarkable structural and functional role in the nervous system compared to neurons. However, damage to glial cells leads to degeneration and the onset of numerous neurodegenerative diseases. It is well known that the central nervous system (CNS) has a limited capacity for tissue regeneration. The use of chitosan-based biomaterials has emerged as a potential alternative solution to overcome these limitations. Interest in these biomaterials for CNS biomedical implementation has increased due to their ability to cross the BBB, their mucoadherence, and especially their hydrogel-forming capacity. In addition, their ability to form porous scaffolds and to carry cells and biomolecules has offered a means of achieving glial cell regeneration. Thus, this chapter aims to bring together recent work that highlights the potential of chitosan-based biomaterials suitable for glial cell tissue engineering.

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#### INTRODUCTION

Neurological and neurodegenerative diseases (NDD) are a major public health problem. Neurodegeneration refers to the progressive loss of structure and function of the central nervous system (CNS), leading in particular to cognitive dysfunction and motor impairment (Amor et al., 2014). Neurodegeneration, or the death of neuronal cells, is the histopathological hallmark of neurodegenerative diseases such as Alzheimer's disease (AD), multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS) and Parkinson's disease (PD). Neurodegeneration has also been reported in stroke, neurotrophic infection, prion disease, traumatic brain and spinal cord injury, as well as in neuropsychiatric and genetic disorders (Choi, 1988; Amor et al., 2014).

During both normal and pathological development of the nervous system, glial cells play an essential role in the remodeling of neural tissue. They are also involved in tissue regeneration after injury (Kim et al., 2016; Song et al., 2018). However, in certain pathological conditions, their contribution to neuronal regeneration may be limited. Consequently, various strategies have been developed to safeguard neurons from damage, apoptosis, and neurodegeneration, aiming to achieve neuroprotection (Pangestuti & kim, 2010; Kostrzewa & Segura-Aguilar, 2003). Neuroprotection seeks to minimize neurodegeneration or impairment of neurons after CNS injury, aiming to maintain neuronal integrity and functionality as much as possible (Tucci & Bagetta, 2008). Based on these mechanisms, several neuroprotective agents have been explored for the management of neurological conditions (Pellicciari et al., 1998; Chandrasekaran et al., 2003).

Potential therapeutic biomolecules have not received much attention in the treatment of neurodegenerative disorders, although they could play an important role. For example, the marine environment is known for its nooks and crannies in the structures of bioactive compounds with promising applications (Alonso et al., 2005). Recent reports on chitosan (CTS) and its derivatives as plausible molecules to target neurodegenerative disorders are well documented in several studies (Hao et al., 2017; Hamdan et al. 2023a). This chapter, reviews recent advances in the use and applications of CTS in neuronal tissue engineering involving glial cells to target neurological and neurodegenerative disorders.

#### GLIAL CELL DEGENERATION AND PATHOLOGY

Neurodegenerative diseases are conventionally characterized by progressive neurological disorders marked by the selective loss of distinct populations of neurons. Parkinson's disease, Alzheimer's disease (AD), epilepsy, and amyotrophic lateral sclerosis (ALS) are among the conditions historically associated with the degeneration of dopaminergic, cholinergic, GABAergic, and motor neurons, respectively (Davies and Maloney, 1976; Leenders et al., 1990; Xu-Friedman et al., 2001; Buskila et al., 2019b). However, a growing body of evidence suggests that dysfunction in glial cells may also play a significant role in the pathology of these diseases. In this section, we will provide an overview of how glial dysfunction contributes specifically to various neurodegenerative diseases (Figure 1).

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