Chapter 1

Introduction

1.1 Background

T cell-mediated diseases are a major problem in clinical medicine, as pathological T cell activation and proliferation causes the pathology of many autoimmune, inflammatory, and transplant-related disorders. Standard immunosuppressive therapies, such as corticosteroids and calcineurin inhibitors, are often limited by incomplete efficacy and significant side effects, highlighting the need for novel approaches to immune modulation (Bulliard et al., 2024). Mesenchymal stem cells (MSCs) have appeared as prospective candidates for the treatment of T cell-mediated disorders due to their potent immunomodulatory properties. MSCs can inhibit the proliferation and activation of both CD8+ and CD4+ T cells, promote the creation of Tregs, and suppress the secretion of pro-inflammatory cytokines such as IL-2, IFN-γ and TNF-α (Zhou et al., 2020). These effects are mediated through both direct cell-cell interactions and the secretion of soluble factors, including IL-6, PGE2, and TGF-β. Additionally, MSCs can affect other immune cells, such as dendritic cells and monocytes, further contributing to an immunosuppressive environment (Song et al., 2020).

One of the examples of a T cell-mediated disorder where MSCs have shown therapeutic promise is graft-versus-host disease (GvHD), a complication of allogeneic hematopoietic stem cell transplantation. In both acute and chronic GvHD, donor T cells attack recipient tissues, leading to significant morbidity and mortality. Multiple preclinical and clinical studies have demonstrated that MSC infusion can reduce GvHD symptoms, through their capacity to modulate T cell responses and reduce inflammatory cascades (Zhao et al., 2019). However, while MSCs are being actively investigated for GvHD, their immunomodulatory mechanisms are relevant to a broad spectrum of T cell-driven diseases. Recent research also highlights that MSC-derived extracellular vesicles (EVs) may contribute to these immunosuppressive effects by delivering regulatory molecules to immune cells,

although this area remains under active investigation (Zhou et al., 2020). Given these properties, it is important to continue investigating how MSCs interact with activated T cells. A deeper understanding of these mechanisms could provide valuable insights that support the advancement of more effective and targeted cell-based therapies. Such advancements could benefit a wide range of T cell-mediated conditions by improving treatment outcomes and reducing harmful immune responses.

1.2 Objective

This study aims to study the effect and mechanisms of Wharton's Jelly MSCs and Amniotic Fluid MSCs on activated T cells isolated from mice with different activation systems.

1.3 Hypothesis

MSCs mediate immunosuppressive effects on activated T cells that decrease the severity of T cell-mediated diseases through mechanisms that include modulation of T cell function, secretion of anti-inflammatory cytokines and change in immune cell morphology.