CHAPTER I
INTRODUCTION

1.1 Background

Osteoarthritis is prevalent among elderly individuals, obese patients, and physically active people who exert significant stress on their knee joints. The incidence of osteoarthritis increases with age and obesity. According to the World Health Organization's (WHO) Global Burden of Disease Study 2010, over 70 million Europeans suffer from osteoarthritis, which hampers normal joint function due to the low self-repairing capability of cartilage. Knee and hip osteoarthritis are also the causes of disability (Cucchiarini et al., 2016). Osteoarthritis can be triggered by a range of factors, including non-genetic factors e.g. age, sex, occupational activities, sports activity, high body mass index, obesity, diabetes mellitus, muscle weakness, mechanical instability, bone marrow lesion, and bone mineral density (Jones et al., 2019; Kong et al., 2017). Genetic factors may also play a role, such as changes in gene expression in cartilage and subchondral bone. These factors can impact joints in the body, particularly in the hands and limbs that are subjected to greater weight-bearing stress, resulting in pain and functional impairment in adults. Initial symptoms involve deterioration of articular cartilage leading to pain, bone dysfunction, and difficulties in performing daily activities. Articular cartilage is a specialized type of connective tissue composed of cartilage cells and typically found in synovial joints. These cells produce extracellular matrix (ECM) and preserve the function of the tissue. Articular cartilage does not possess self-healing ability due to the absence of blood vessels, lymphatic vessels, and the nervous system (Sophia Fox et al., 2009). Arthritic cartilage degeneration can cause various symptoms, including growth abnormalities in children, injuries caused by stress from trauma, and age-related osteoarthritis (Song et al., 2004).

Current OA treatments are commonly determined based on disease severity, and the physician's recommendations including pharmacological and non-

pharmacological therapies. The first-line pharmacologic treatment is acetaminophen to cure mild and intermittent symptoms, and then followed by non-steroidal anti-inflammatory drugs (NSAIDs) when acetaminophen is ineffective to alleviate pain. However, NSAIDs prescription should be considered due to their gastric ulcer complication, and cardiovascular risk (Yusuf, 2016). Combination of pharmacological and non-pharmacologic treatment, namely diet and weight loss, physical therapy and exercise, and nutritional supplements (glucosamine and chondroitin sulfate) is a common advice for OA treatment to reduce symptoms and improve functional performance of the joint. Surgery is an invasive procedure that should be conducted when the combined therapy is unsuccessful to produce desired outcomes (Yusuf, 2016). Additionally, there is a possibility of recurrence and complications after surgery in many patients. Consequently, a novel and more effective procedure for osteoarthritis is indispensable, like application of cartilage cells. However, extraction of these cells from a human requires invasive surgery, which is complicated and expensive (Ebihara et al., 2012; Wong et al., 2020). Research is currently underway to explore the potential use of mesenchymal stem cells (MSCs) in treating osteoarthritis. The stem cells possess the unique ability to stimulate the growth of cartilage cells and other types of cells. MSCs are utilized in treating various disorders and can be sourced from several different locations, including bone marrow, blood, adipose tissue, and dental pulp. They can be isolated and cultured with a high level of proliferation activity. Previous studies have identified Wharton's jelly, found in the umbilical cord of humans, as a common source of MSCs. This tissue can be collected from pregnant women following childbirth, without complex collection process required (Troyer et al., 2008). As a result, MSCs isolated from the Wharton's jelly of human umbilical cords are a promising area of interest for future clinical trials.

The use of Dunkin Hartley guinea pigs as an animal model for studying spontaneous cartilage degeneration in the knee joint, which is similar to osteoarthritis in humans, has been well established (Tessier et al., 2003; Yan et al., 2014). Researchers reported that the knee joint of guinea pigs closely resembles that of humans affected by osteoarthritis (Fernandez et al., 1997; Kraus et al., 2010). Moreover, spontaneous cartilage degeneration in the Dunkin-Hartley guinea pigs are used for study (Bendele and Hulman, 1988). Previous studies demonstrated that

injecting mesenchymal stem cells (MSCs) with hyaluronic acid (HA) into the articular cartilage of guinea pigs with osteoarthritis led to recovery (Sato et al., 2012). HA-based formulations are currently delivered into the joint to relieve pain and improve joint mobility of OA patients by partial restoration of the rheological properties of the synovial fluid (La Gatta et al., 2021).

In this study, we isolated MSCs from human Wharton's jelly of the umbilical cord and induced them into cartilage cells. We then transplanted the early chondrogenic differentiated MSCs into the guinea pigs which have osteoarthritis and monitored their progress to evaluate the effectiveness of the treatment. The results demonstrated promising outcomes in the experimental animals, suggesting that this treatment approach using early chondrogenic differentiated MSCs could be developed.

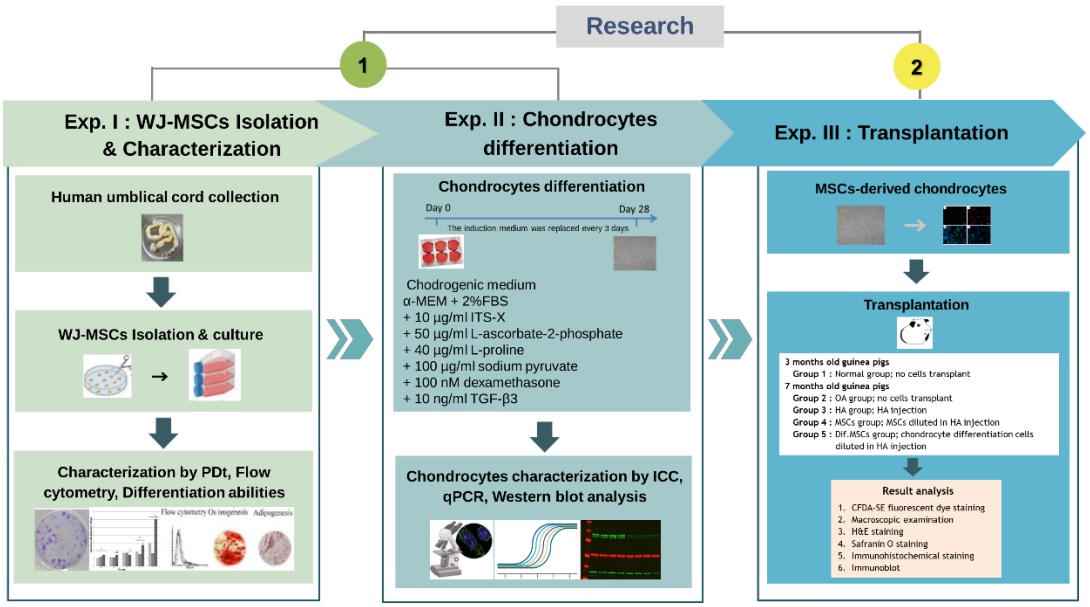
1.2 Research objectives

1.2.1 To isolate and characterize mesenchymal stem cells (MSCs) derived from the Wharton’s jelly of the human umbilical cord.

1.2.2 To investigate the potential of WJ-MSCs for differentiating into chondrocytes.

1.2.3 To investigate the potential therapeutic effects of chondrocytes derived from Wharton’s Jelly mesenchymal stem cells (WJ-MSCs) in the treatment of osteoarthritis using an animal model.

1.3 Experimental design



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