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Review

Recent development in cell encapsulations and their therapeutic applications

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ABSTRACT

Chronic and degenerative diseases are the main causes of death in the aging population worldwide. These diseases are currently maintained using long term administration of conventional drugs which are not curative and reduce the life quality of patients. It is urgent to develop new therapeutic approaches for the treatment of these diseases. Cell therapy that involves the injection of viable cell into patients is a promising therapeutic strategy in chronic and degenerative diseases. However, the survival of injected cells in host tissue is limited due to immunoresponse. Cell encapsulation potentially improves treatment approaches using viable cells and overcome the immuno-rejection following cell transplantation. In this review, we first present the main components and their different functions in the cell encapsulation, including semi permeable membrane, types of cells and matrix. Then, the recently developed technologies and approaches employed to encapsulate cells are summarized and compared in benefits and flaws. More importantly, the insights and significance of the encapsulated cells are also discussed in the application of treating various diseases.

Contents

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1. Introduction

With the increasing life expectancy over the past century due to better nutrition and medical advances, another problem arises. The increased life expectancy brought about new problems, one of them being chronic and degenerative disease such as degenerative bone disease, diabetes, Alzheimer's disease, gene related diseases and cancer to name a few. This new enemy does not have an absolute counter and many people fall victim to it every day. In 1933, Vincenzo Bisceglie discovered the first step of a possible solution through his experiments. In his experiment, he proposed that since his transplant of tumour cells into the host body were still surviving after a long period of time, the polymer structure that is used to encase the tumour cells showed an ability to prevent immunoresponse in the host body to foreign cells [1]. In 1964, Thomas Chang proposed the concept of 'artificial cells' for his idea of encapsulating cells to prevent the immunoresponse of the body [2]. This lead to a surge in encapsulation technology in the 70s and 80s where it is used to test islet cells to control diabetes in small animals [3]. Cell encapsulation is based on the concept of immobilizing the cells in a matrix which is surrounded by a semi permeable and biocompatible membrane. The membrane serves to protect the cell from immunoresponse and a pathway for nutrients in the body to enter the matrix. The matrix, on the other hand, serves as a scaffold to promote cell proliferation, provides mechanical strength and control the release of drugs from the matrix to the body (Fig. 1) [4].

2. Semi-permeable membrane in cell encapsulation

The membrane has one main function which is to prevent immunoresponse from the host body to the encapsulated cells. However, there are also other factors that should be considered when choosing the membrane, such as morphology, biocompatibility, degradability and mechanical strength. In this section, different factors of the membrane materials that have significant influence in the cell encapsulation are discussed.

2.1. Semi permeable membrane factors

The main function of the membrane is to prevent immunoresponse from the body reaching the cells in the encapsulation. The morphology of the membrane such as wall thickness, pore size distribution, surface structure and porosity will affect the transport mechanism of nutrient and drugs [5]. As the membrane must be selective in its permeability whereby only nutrients are able to diffuse past the membrane and block out all immunoresponse, the surface morphology would be very important in determining the permeability. The permeability of the membrane determines what kind of therapeutic drugs are able to diffuse into the host body as different drugs have different sizes and the sizes of the drugs have to be taken into account for when choosing the permeability of the membrane. In addition, the membrane has to be biocompatible as it is in contact with the host body and the encapsulated cells. As the membrane is in contact with the host tissues, it should not cause any immunoresponse by the body to the encapsulated cells such as inflammatory response or tissue encapsulation. It should also be non-cytotoxic as there should not be any tissue or cell death caused by the encapsulated cells.

In another aspect, some membranes are degradable over time and this will lead to immunoresponse breaching the membrane to reach the matrix and then the cells. If this is not planned, it could lead to the failure of the encapsulated cells. However, in some cases, the encapsulated cells are meant to degrade over time so as to remove the requirement for another surgery to remove the encapsulated cells. It should be noted that when the membrane starts to degrade, it will lose mechanical strength and increased permeability of the membrane, hence, plans should be made if the membrane were to degrade. On top of the degradation behaviour, the mechanical strength is also considered as different sites of the body experience different amount of stress from daily activities, hence, a suitable membrane with the required mechanical strength is needed for the success of the implant. If the membrane was to break due to lack of mechanical strength, it will lead to the failure of the encapsulated cells as immunoresponse will be able to affect the cells.

2.2. Representative types of semi permeable membranes

The semi permeable membrane is made of many different materials and these materials are chosen to suit the function of the encapsulated cell for drug releases [6]. In general, there are three main types of materials used as semi permeable membranes, including hydrogels, thermoplastic polymers and non-polymeric materials. Hydrogels are made of hydrophilic polymers that are able to absorb water without dissolving [7–13]. They are used due to their high viscoelasticity and water content which is similar to biological tissues in a living organism [14–16]. The close resemblance makes hydrogels have a less inflammatory response in vivo compared to the rest. The permeability properties of hydrogels can be controlled by changing the amount of crosslinks within the hydrogels where a higher crosslinking will lead to higher perm-selectivity and lower diffusion rates [8,17–23]. In addition to hydrogels,

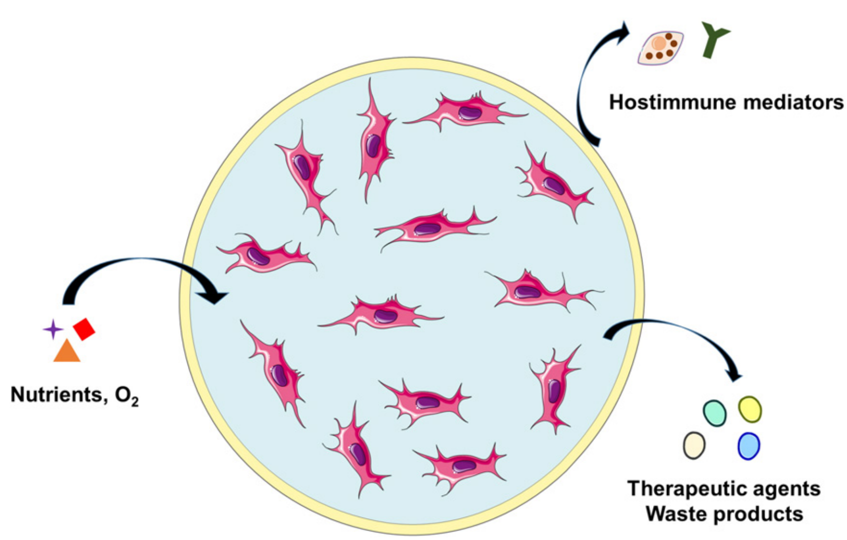

Fig. 1. Schematic illustration of cell encapsulation and its interactions within the body.