Materials Today Bio 20 (2023) 100684

Contents lists available at ScienceDirect

Materials Today Bio

journal homepage: www.journals.elsevier.com/materials-today-bio

Immunosuppressive dead cell as lung-targeting vehicle and cytokine absorption material for cytokine storm attenuation of pneumonia

Tianyuan Ci [1,*], Yaoxuan Xiong [1], Jinniu Zhang, Jing Zang, Nianping Feng [**]

School of Pharmacy, Shanghai University of Traditional Chinese Medicine, Shanghai, 201203, China

ARTICLE INFO

Keywords:
Dead cell
Pneumonia
Immunosuppression
Lung targeting
Cytokine storm

ABSTRACT

Effectively controlling cytokine storm is important to reduce the mortality of severe pneumonia. In this work a bio-functional dead cell was engineered by one-time quick shock of live immune cells in liquid nitrogen, and the obtained immunosuppressive dead cell could server as both lung-targeting vehicle and cytokine absorption material. After loading the anti-inflammatory drugs of dexamethasone (DEX) and baicalin (BAI), the drug-loaded dead cell (DEX&BAI/Dead cell) could first passively target to the lung after intravenous administration and quickly release the drugs under high shearing stress of pulmonary capillaries, realizing drug enrichment in the lung. Then, the immunosuppressive dead cell acted as the camouflage of normal immune cells with various cytokine receptors exposing on their surface, to "capture" the cytokines and further reduce the state of inflammation. With above formulation design, a synergic anti-inflammatory effect between drugs and carrier could be achieved. In a lipopolysaccharide-induced pneumonia mice model, this system could calm down the cytokine storm with high efficacy and elongate the survival of mice.

1. Introduction

Pneumonia is a widespread infection disease of respiratory system, which is generally caused by the invasion of bacteria or virus, causing inflammation in the lung tissue [1,2]. When the invaded pathogens are numerous or severe, these exogenous substances will lead to imbalance of immune homeostasis with over-activation of immune cells and excessive production of various cytokine [3–5]. Cytokine storm is considered as the main lethal factor of severe pneumonia [6–8], and efficient inhibition of uncontrolled inflammatory responses and reducing the level of inflammatory cytokines are important to control severe pneumonia and reduce mortality.

Clinical strategies of attenuating cytokine storm include immunosuppressive drugs such as glucocorticoids [9,10], or neutralizing antibody such as Tocilizumab [11,12]. However, above two schemes still have some limitations in practical applications. The use of high dosage of corticosteroids may lead to serious adverse reactions, such as osteonecrosis of the femoral head [13–15]. And single neutralizing antibody treatment may have limited anti-inflammation efficacy, regarding the cytokine storm is usually the results of various inflammatory factors [16].

Immune cells play an important role in mediating the occurrence and development of cytokine storm [17–19]. For example, the macrophages in the lung can recognize the exogenous stimuli at the first time and recruit neutrophils in blood circulation by secreting cytokines to enhance immune response [20,21]. Our previous work engineered functional dead cells *via* treating the live cell by one-time quick shocking with liquid nitrogen [22]. The obtained cells lost proliferation capability but maintained the cellular structure and protein-related bioactivities. Thus, we designed the immunosuppressive dead cells with similar strategy by shocking the immune cells with liquid nitrogen, and utilized this kind of dead cell as delivery vehicles of the anti-inflammatory drugs of dexamethasone (DEX) and baicalin (BAI).

In this system, the immunosuppressive dead cell first acted as the lung targeting vehicle due to its cellular size and quickly released the loaded anti-inflammatory drugs in the lung, then behaved as "mixed antibodies" of inflammatory cytokines to further decrease the cytokine levels (Fig. 1). The drugs and immunosuppressive dead cells worked synergistically to calm down the cytokine storm of severe pneumonia.

* Corresponding author.
** Corresponding author.
E-mail addresses: tianyuanci@shutcm.edu.cn (T. Ci), npfeng@shutcm.edu.cn (N. Feng).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.mtbio.2023.100684
Received 8 February 2023; Received in revised form 26 May 2023; Accepted 26 May 2023
Available online 27 May 2023