Frontiers in Medical Science Research
ISSN 2618-1584 Vol. 1, Issue 4: 62-66, DOI: 10.25236/FMSR.2019.010411

Feasibility Study of Bacterial Hull as Immunological Adjuvant

Huiwen Kan, Xiaojing Shi, Qiuning Liu, Yanyan Bao, Yiming Chen, Jin Wang, Zhenqiu Gao***

School of Pharmacy, Yancheng Teachers University, Xiwang Road, Yancheng 224007, China
**Corresponding Author*

ABSTRACT. *Bacterial hulls are used as bacterial shells that do not cover any nucleic acid cost and nucleus, especially in recent years. Studies on the surface of BGs have confirmed that many intact natural immune pattern recognition receptor agonists can be retained as immunological adjuvants. The resulting immune or non-immune secreted cytokines achieve effective activation of the adaptive immune response. This study will summarize the preparation technology of bacterial hulls, and analyze the mechanism of action as an immunoadjuvant, explore its application potential, and provide reference for similar research.*

KEYWORDS: *Bacterial capsid; Immune adjuvant; Feasibility*

1. Introduction

At present, the preparation technology of BGs has been applied to a variety of Gram-negative bacteria, such as Escherichia coli, Salmonella, Brucella, Aeromonas veolitica, Klebsiella, Haemophilus parasuis, pleuropneumonia Phytobacteria, delayed Edwards, Pasteurella multocida, etc., can achieve considerable lysis effect[1], usually by repeated freeze-thaw or hypertonic solution treatment to obtain bacterial hull, as a non-denatured inactivated vaccine It has ideal immunogenicity compared to traditional formaldehyde inactivated vaccines. Existing bacterial shell preparation techniques overcome the limitations of past expression of resistance-dependent marker plasmids, such as residues of antibiotic resistance genes and genetic instability of recombinant plasmids. In addition[2], a lytic system for nutrient-inducing punishment has been reported, that is, the expression efficiency of the cleavage E gene is controlled by the iron-inducible promoter PviuB, and finally the Vibrio anguillarum shell is prepared based on the system. In addition to the cleavage of the E gene expression system, Hu Bengang used antibacterial skin combined with ultra-high pressure device to prepare Haemophilus parasuis and Klebsiella pneumoniae shells, respectively[3], which were superior in immunogenicity to conventional inactivated bacteria. seedling. However, whether the genetic shell or physicochemical method is used to prepare the shell, the purpose

ISSN 2618-1584 Vol. 1, Issue 4: 62-66, DOI: 10.25236/FMSR.2019.010411

is to obtain a complete bacterial shell, which is an important prerequisite for ensuring the immunogenicity of the bacteria itself and the functional activity of the surface immunostimulatory molecules.

2. Bacteria Can Be Used as an Immunoadjuvant Mechanism

Immunological adjuvants typically enhance the immunogenicity of the vaccine by stimulating the immune receptors on the surface of the host's immune cells. Among them, the immune immune cells mediate the immune response through a series of pattern recognition receptors, such as Toll-like receptors (TLRs)[4], which recognize bacteria, viruses, parasites, and mold infections. In recent years, certain components of bacteria have the ability to enhance the immune response of weak antigenic vaccines, and have been applied to the development of vaccines.

The production of BGs is non-denaturing, retaining intact cell membrane and cellular Yif structure, which contains known immunostimulatory components (LPS, flagella, etc.), and is a highly promising high-efficiency immunological adjuvant[5]. These extracellular structures of BGs can be effectively recognized and presented by immune cells or non-immune cells, and activate immune cells mainly through TLR2 and TLR4 signaling pathways, including induction of activation and maturation of dendritic cells, thereby promoting their lymphoid organs. Recruitment of T cell regions; BGs transmit signals to downstream MAPK or 1kB cascade molecules via TLR2 and TLR4 linker molecules via MyD88 or TRIF-dependent (non-dependent MyD88), and activate nuclear transcription factors such as NF-kB, AP-1 , IRF3 / 7, eventually produced a variety of pro-inflammatory cytokines and chemokines[6].

As a full-time antigen-presenting cell, DCs can effectively ingest and process BGs, mediate the production of pro-inflammatory cytokines, and then up-regulate the expression of co-stimulatory factors in DC cells, which is beneficial to the efficient delivery of foreign antigens to unsensitized cells. T cells. Studies have found that BGs can provide effective early maturation signals to DCs, and secrete Th1 cytokines in large quantities, thereby activating NK and Th1 cells. In addition, the expression level of MHC-11 on DCs was significantly up-regulated after DCs exposed to BGs for 12 h, indicating that BGs have the potential to stimulate early immune response, which may be a new finding for emergency immunization strategies. Moreover[7], LPS of BGs can also enhance the expression of MHC-1 in DCs, allowing DCs to cross-represent antigens to CD8+ T cells, thereby contributing to the induction of effective cytotoxic T cell responses. The bacterium can up-regulate the expression of intercellular adhesion molecule-1 (1CAM-1) on the surface of DCs, which provides the necessary basis for stimulating high-efficiency CD8+ T cell responses. Studies have shown that both Salmonella BGs and S. Enteritidis BGs cause potent CD8+ T cell responses and protect immunized birds from lethal doses of virulent strains. In addition to being able to act on DC cells[8], BGs can also efficiently activate monocytes and macrophages, and promote immune responses to a Th1-type response. In addition, BGs induce many lymphoid and non-lymphocyte production of cytokines and chemokines, which promote the reflux and migration of T, B lymphocytes and immune cells to lymph nodes, thereby fully

ISSN 2618-1584 Vol. 1, Issue 4: 62-66, DOI: 10.25236/FMSR.2019.010411

stimulating the immune response by contact with homologous antigens. These results indicate that the autoimmune adjuvant effect of BGs can effectively induce humoral and cellular immune responses in the body.

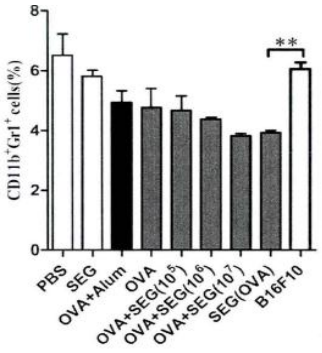

Figure.1 Bacterial Shell Test Results

BGs can also stimulate non-professional antigen-presenting cells, such as conjunctival epithelial cells, fibroblasts, keratinocytes, melanoma cells, and the like. Thus, BGs are able to provide non-specific resistance to pathogenic microorganisms[9], and BGs can also activate downstream signaling pathways using TLR5 molecules (recognizing flagella). Abtin et al found that the bacterial shell of wild-type Escherichia coli (NK 9373) was more easily captured by keratinocytes than the mutant flagellar E. coli, suggesting that bacterial flagellin can mediate cell activation pathways via TLRS or inflammatory bodies. Activate any of the signal paths. In addition, BGs can also act on lymphocytes[10]. After stimulation of T cells by Actinobacillus BGs in vitro, a specific T cell response can be detected. There are also related studies showing that BGs can induce T cell proliferation, and with the help of antigen-presenting cells, their ability to activate T cells is stronger than that of BGs alone. Therefore, BGs can not only activate T cells through antigen-presenting cells, but also directly activate T cells through the '1' LR molecule. At present, the biggest cause of BGs as an immunoadjuvant is mainly LPS[11]. Some studies have found that DCs treated with flagellar hair have weaker T-cell ability than LPS-treated DCs, but can also mediate T cell secretion of cytokines. . It has been found in the literature that Salmonella BGs containing Escherichia coli heat labile B subunit enterotoxin have the ability to induce humoral and cellular immune responses more efficiently than BGs alone.

3. Bacterial Shell Application Potential

Most immune cells or epithelial cells generally express TLR4 and TLR5, and LPS and flagella as their ligands are inherently present on BGs, which enables BGs to effectively induce mucosal immune responses. The adjuvant properties of BGs themselves make it a potential vector platform for assembling foreign DNA on its surface or loading DNA fragments inside it. In addition, the targeting of BGs also

ISSN 2618-1584 Vol. 1, Issue 4: 62-66, DOI: 10.25236/FMSR.2019.010411

makes it a good carrier for small molecule drugs[12].

Immunization of the body through mucosal immunization is a hot spot in current mucosal vaccine research, but it has been in a bottleneck stage due to the lack of sufficient immunogens to stimulate this pathway. One of the major advantages of BGs as a vaccine candidate is that it can elicit effective antigen-specific mucosal immunity and systemic immune responses. Among them, oral vaccine research with Helicobacter pylori as a carrier is particularly prominent. Some studies have implanted its own protective antigen Omp18 protein on the surface of H. pylori BGs. After oral immunization of mice, mice produce high levels of anti-Omp18 antibody. In addition, the number of live Helicobacter pylori in the stomach was also significantly reduced. Small particles such as BGs are also easily taken up by antigen-presenting cells, and are therefore often used as loading enzymes, antibiotics, and anti-tumor drugs 4a. Studies have shown that the enzymes loaded by BGs still have their enzymatic activity. By loading specific enzymes, BGs not only help to treat metabolic disorders caused by enzyme deficiency, but also regulate intestinal tract by loading enzymes with partiality. Flora. In addition, researchers have successfully used M. haemolytica BGs to mount anti-tumor factors (DOX) to target human colon adenocarcinoma cells, which have significantly better anticancer effects than DOX alone and do not cause healthy cells. Pathological damage. It can be seen that the application potential of BGs that retain the biological activity of bacteria is constantly being explored.

4. Conclusion

BGs is a new type of inactivated bacteria with good safety and immunogenicity. It retains its surface structure and possesses the characteristics of autoimmune adjuvant. Based on the BGs vector platform, it develops multiple chimeric vaccines and targets. Vaccines and tumor immunotherapy offer new strategies.

References

[1] Nakaoka R, Tabata Y, Ikada Y (2015). Potentiality of gelatin microsphere as immunological adjuvant. Vaccine, vol.13, no. 7, pp. 653-661.

[2] Hawkins L D, Ishizaka S T, Lewis M, et al (2017). Immunological adjuvant compounds compositions and methods of use thereof. Official Gazette of the United States Patent & Trademark Office Patents, vol. 28, no. 1, pp. 647-650.

[3] Finger H, Emmerling P, Bertz R (2017). The Reactivity of Aged Mice to Bordetella pertussis as an Immunological Adjuvant. Gerontology, vol. 17, no. 5, pp. 323-332.

[4] Andrews A E, Lofthouse S A, Bowles V M, et al (2014). Production and in vivo use of recombinant ovine IL-1β as an immunological adjuvant. Vaccine, vol. 12, no. 1, pp. 14-22.

[5] Takahashi K, Kato Y, Sugiyama T, et al (2019). Production of Murine Collagen-Induced Arthritis Using\r, Klebsiella pneumoniae\r, O3 Lipopolysaccharide as a Potent Immunological Adjuvant. Microbiology and

ISSN 2618-1584 Vol. 1, Issue 4: 62-66, DOI: 10.25236/FMSR.2019.010411

Immunology, vol. 43, no. 8, pp. 795-801.
[6] Overwijk W W, De Visser K E, Tirion F H, et al (2016). Immunological and Antitumor Effects of IL-23 as a Cancer Vaccine Adjuvant. The Journal of Immunology, vol. 176, no. 9, pp. 5213-5222.
[7] Mariano-Neto F, Matos J R, Silva L C C D, et al (2018). Physical properties of ordered mesoporous SBA-15 silica as immunological adjuvant. Journal of Physics D Applied Physics, vol. 47, no. 4, pp. 366-370.
[8] Popescu C, Durbaca S, Ivanov D (2018). Negatively charged liposomes as immunological adjuvant for tetanus and diphtheria toxoids. Roumanian archives of microbiology and immunology, vol. 57, no. 3, pp. 255-261.
[9] Miconnet I, Coste I, Beermann F, et al (2017). Cancer Vaccine Design: A Novel Bacterial Adjuvant for Peptide-Specific CTL Induction. The Journal of Immunology, vol. 16, no. 7, pp. 4612-4619.
[10] Jensen O M, Koch C (2018). On the effect of Al (OH)3 as an immunological adjuvant. Apmis, vol. 96, no. 3, pp. 257-264.
[11] Stevenson, James P, Kindler, Hedy L, Papasavvas, Emmanouil (2016). Immunological effects of the TGF â-blocking antibody GC1008 in malignant pleural mesothelioma patients. Oncoimmunology, vol. 28, no. 8, pp. 262-268.
[12] Shawky M, Mohamed A A, Hind M, et al (2016). Immunological Effect of Levamisole As Immumostimulant in Vaccination with Bivalent Oil Adjuvant Foot and Mouth Disease Vaccine in Sheep. vol. 37 no. 3, pp. 383-383.