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Amebiasis Vaccine

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1. Introduction

Amebiasis is still a major health problemin the world, especially in developing countries, low income, poor sanitation, lack of clean water, such as South Africa, Bangladesh, and Vietnam. *Entamoeba histolytica* is a major agent of amebiasis. Protoza intestinal parasites have caused dysentery and liver abscesses (Quach, Jeanie et al., 2014). When *E.histolytica* invade the intestinal epithelium, it will activate an immune response in a human host. To survive in a human host, *E.histolytica* repression of the host immune system and environmental control parasites. For example, when *E.histolytica* survive in vascular and liver environment contains a lot of oxygen, *E.histolytica* must subvert detection by antibodies and complement. This is against oxidative and nitrosative attack. The mucosal lining of the digestive tract generally serves as a major physical barrier against intestinal pathogens and secondary defense against the immune response of *E. histolytica infection*. Mucosal immunoglobulin (Ig) is a major component of the human intestinal defense mechanisms. Among them, IgA is one of the most abundant Ig produced by plasma cells (N.Kumiko-Tsukui and Tomoyoshi N, 2016).

In the lumen of the large intestine, the intestinal epithelial cell layer is covered by a layer of mucus that contain mucin, IgA, and microbiota. Infiltration trofozoit attacked by the complement of circulation, ROS and NO from neutrophils and macrophages. Gal / GalNAc lectin and LPPG in surface *E.histolytica* which is binding TLR2 and leads to activation of NFκB. Other than, Gal / GalNAc lectin and LPPG activate the CD4, CD8 T cells, and NKT cells, thus increase the protective cellular immunity. CD4 T cells produce IFNγ, IL-4, IL-5 cells, IL-13, and CD8 T produce IL-17. IL-17 induced neutrophil infiltration and increase the secretion of mucin, antimicrobial peptides, and IgA into the lumen of the colon. When *E.histolytica* in the liver, IFNγ secreted by NKT cells is causing inactivation *E.histolytica* whereas TNF-αsecreted from macrophages resulting in liver abscess. The mechanism of colonization and invasion *E.histolytica* can be seen in the picture below (N.Kumiko-Tsukui and Tomoyoshi N, 2016). Based on the mechanism of colonization and invasion of E. histolytica, the vaccine strategy of amebiasis was developed.

2. Methode

Studies have antigen and targets of different antigens. Adjuvants are used is also different. More details are described in Table 1.

3. Result

Interaction *E.histolytica*with the intestine is mediated through the binding of theintestinal mucin and epithelium via a galactose and N-acetyl-D-galactosamine(Gal/GalNAc) lectin comprised of a disulfide linked heavy (ca. 180 kDa) and light chain (ca. 35 kDa) and a non covalently bound intermediate subunit (ca. 150 kDa). L. Barosso*et.al*was researchedvaccine candidate which focused on an internal 578 amino acid fragment, designatedLecA, located within the cysteine-rich region of the heavy chain subunit because it is a majortarget of adherence-blocking antibodies of seropositive individuals and vaccination with histagged LecA provides protection in animal models.

The Gal/GalNAc lectin is a 260 kDa heterotrimer of highly conserved disulfide-linked heavy (Hgl) and light (Lgl) subunits non-covalently associated with an intermediate subunit (Igl). The carbohydrate recognition domain (CRD) is a cysteinerich region within Hgl recognized by adherence-inhibitory Mab. They have focused on a region located within Hgl designated “LecA” (aa 578–1154) as a vaccine candidate. The results of this study between the control group (EM014 adjuvant only), the EM014 adjuvant + LecA group, and the tagged EM014 + adjuvant + group showed vaccination with the LecA tagged group resulted in a reduction in amoeba ability in binding cells better than the other groups. The average OD value for vaccinated rats is 1.17 ± 0.5 while for control rats the average is at point 5,4,1,1. The infection rate in the growth of TYI-S-33 media was a control group of 12/15, the LecA group 6/25, and the LecA group tagged 5/12 (L. Barroso *et al*., 2014).

In another study conducted by Burgess, S.L et al. It showed thatcolonization of the gut with the commensalClostridia-related bacteria known as segmented filamentous bacteria (SFB) is protective during *E. histolytica* infection. SFB colonization in this model was associated with elevated cecal levels of interleukin 17A (IL-17A), dendritic cells, and neutrophils. Bone marrow-derived dendritic cells (BMDCs) from SFB-colonized mice had higher levels of IL-23production in response to stimulation with trophozoites. Adoptive transfer of BMDCs from an SFB+ to an SFB- mouse was sufficient to provide protection against*E. histolytica*. The results showed the control group (PBS) with the test group (Giving SFB) an increase in IL-17, Il-23, neutrophils, CD11c +, MHCII +, and serum SAA. SFB present of the intestine may induce soluble mediators, including SAA, which can have local effects as well as trigger systemic changes in bone marrow that support increased IL-23 production from dendritic cell subsets and downstream IL-17A-mediated innate and adaptive immune

responses. So that, protect against intestinal E. histolytica infection.

Research from Min, X *et al*., focused on immune effectiveness and immunological characterization of recombinant IGL and its fragments. The fragments are GL-1 (gll-1) and N-Igl, M-Igl, and C-Igl. This fragment is evaluated in the formation of ALA (Abscess Liver Amebiasis). The results showed that the 1st fragment vaccinated ALA 14 out of 15 hamsters, the N-Igl fragment had no protective effect on the occurrence of ALA on 8 hamsters, the M-Igl fragment vaccinated the ALA 2 out of 8 hamsters, and the C-Igl fragment provided a protective effect the occurrence of ALA in all hamsters, namely 8 hamsters. So that the fragment 1 and C-Igl can interfere with the ability of the tropozoid in binding to CHO cells. In addition, C-Igl fragment can also accelerate amebic lysis by complement activation. In addition, the C-Igl fragment vaccine showed an increase in the expression of IL-4 and IL-10 cytokine mRNA genes, whereas a decrease in the production of Th1 IFN-γ, pro-inflammatory TNF-α, and IL-8 production.

Increasing the effectiveness of vaccines can combine antigens that are highly purified by adjuvants. Therefore, the selection of adjuvants is very important, such as aluminum salts, emulsions, liposomes and TLR agonists. The Abhyankar *et al*. Study describes TLR ligand agonist nanoformulation to increase vaccination against E. histolytica. Leca antigen is mixed with each adjuvant (Figure 4). Of the eight adjuvant formulas, a mixture of GLA(TLR-4) agonists and 3M-052 (TLR-7/8 agonists) was chosen for further studies because of the high IgG2a / IgG1 ratio. The results show that the adjuvant formula can increase IFN-γ and IL-17 cytokines, which can play a role in vaccinating Amebiasis.

4. Conclusion

The most widely used amebiasis vaccine strategy is Gal / Gal Nac Lectin inhibition. To et a good vaccine, purification is needed and the determination of C-terminal fragment must be precise. Adjuvants selection is also important because it increases the immunogenicity and protective efficacy. Besides the development of the Gal / GalNac Lectin vaccine, there is a development based on intestinal colonization with certain commensal bacteria. However, the most logical candidate vaccine agent while this is Gal / GalNac Lectin. Current challenges in developed vaccines are trials in non-human primates and clinical trials in humans.

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Table 1

No	Antigen	Target	Animal Model	Adjuvant	Dosis	Refrence
1	Recombinant AcNPV-LC3 baculovirus	Gal-Lectin LC3 Fragment	Male Hamster 3-6 week old (20 hamsters for test gorup and 10 hamsters for control group)	Not mentioned	Vaccine is given for 2 weeks, with 3 doses, 20μL respectivley	(M.D.Meneses -Ruiz *et al*., 2015)
2	Recombinant rIgl-1, N-Igl, M-Igl, and C-Igl	Gal-Lectin LC3 Fragment	Male Hamster 3-4 week old (15 hamsters for rIg1-1 gorup, 24 hamsters for N-Igl, M-Igl, and C-Igl gorup, and 12 hamsters for control gorup)	TiterMax Gold	50µg	(Min, X *et al*., 2016)
3	Recombinant lec A	Th1 responses (IFN-γproduction)	Male Mice 5 weeks old	EM014	20 µg antigen per mice per immunization, in a 100 µl final volume	(L.Barroso *et al*., 2014)
4	Segmented filamentous bacteria (SFB) colonization, *Clostridia*	IL-17A, dendritic cells, and neutrophils	Mice 4 weeks old	Not mentioned	150µl	(Burgess, S.L *et al*., 2014)
5	LecA	IFN- γ, IL-17A, IL-2 and IL-4	Mice 4-6 weeks old	Agonis TLR	5 µg mixed with the adjuvant and volume brought up to 100 µl	(Abhyankar *et al*., 2017)