Added Value on Sade Village and Bau Nyale Festival in Autoimmune Diseases Immunization Travel: Supported by Aptamers Technology

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Abstract—Prevalence of Autoimmune diseases (AD) are high in developed countries and low in developing countries. Wall of worm were associated with lower level of allergy and support the hygiene hypothesis (HyHy). Long term use of Interferon as drug for AD and synthetic vaccine made by epitope mapping are global economic burden. Adolescence from developed countries traveling to Ghana forwarding AD-HyHy. Fecal microbiota transplantation (FMT) for fighting AD have been developed in hygiene countries such as UK, Japan and Korea, meanwhile the aims of this study are reveal an added value to Sade village ‘FMT culture’ and Bau Nyale/Mandalika Princess festival for Nature Vaccination on AD. These local nature vaccination needs to be known by policy maker and political doer and could be a translational-medicine education topic to lessen AD economic global burden. Method: Systematic-review and Bayesian network analysis. EBSCO host search engine were used. Result: Description of 9 Publications of meta-analysis are chosen. Conclusions: The increasing of immunity in developing countries and decreasing in clean habit educated family is based on hygiene hypothesis, could be answered by local life-style and festival. These added value for local tour package has been supported by affirmers and aptamers contemporary technology based on bacteria and worm epitope mapping.

Keywords—hygiene hypothesis-autoimmune diseases, bacteria and worm cell wall, aptamers, epitope mapping, Fecal Microbiota Transplantation (FMT).

I. INTRODUCTION

Wall of worm cell have many epitope as well dormant bacteria (Fecal Microbiota Transplantation or FMT),¹⁻⁵ is now locally neglected and globally abandoned. Usage of natural antigen for vaccination is hygiene hypothesis (HyHy) based on prevention such as in allergy epidemic in US.⁶⁻⁸ Decreasing autoimmmune disease (AD) by natural AD vaccination as added value of Sade and Bau Nyale festival, could lessen AD burden. Meta-analysis on Rheumatoid Arthritis (RA) molecule has ethnicity relation⁹ parallel with new loci RA in Japan¹⁰,¹¹ and Korean and European eight new RA risk loci.¹¹ Meta-analysis on FMT in IBD¹² and hygiene lifestyle are associated with allergic, atopic sensitization,⁷ and asthma. Hand vs. machine dishwashing have significantly different AD prevalence.¹³ A number of references show that AD and climate,¹⁴,¹⁵ and socioeconomic status¹⁶ are related to HyHy.⁸,¹⁶ Do these factors contribute to the occurrence of increasing prevalence of AD in developed countries? Meanwhile, protocols in synthetic vaccine industry for AD or treatment strategies for people with AD, with interferon longterm usage are still unclear. No publication before that summarizes and describes the association of HyHy, AD, FMT, Genome Wide RA,¹⁷ RA in developed countries,¹⁸⁻²⁰ Epitope-RA-SLE,²¹ Helminth-Hygiene-AD,²²,²³ vaccine-epitope/antigen.²⁴,²⁵ Just by implementing local wisdom such as Sade village and Bau Nyale–Mandalika Princes festival can lower risk of AD. Effective preventive activities and treatments could be initiated for high risk person’s AD caused by clean habit of living.⁵,¹³,²⁷,³³ This prevention and therapy model is the first effective natural vaccination idea published.

II. MATERIAL AND METHOD

Systematic review and Bayesian network analysis using EBSCOHos search engine. The search was performed up to Sept 2016 in 3 steps. First, searching with Google search engine for the definition of known key words, then with CINAHL plus with full text for developing the knowledge for the aims of study. Using the following search terms: Autoimmune Diseases, Hygiene Hypothesis, Epidemiology and AD, Atopic Sensitization, Asthma, T1D, IBS, MS, Rheumatoid Arthritis, Ulcerative
Colitis, Allergic Diseases. AD AND Meta-Analysis (372), high prevalence in UK (Epidemiology and AD and UK (237), Japan (247), Korea (51). Low in Sierra Leone (0, SL ancestor (1), Egypt (0), Ghana (0). Where FMT are growing in high prevalence 3 countries, FMT (554), FMT AND UK (14), FMT AND Japan (12), FMT AND Korea (9). In molecular level using terms of: exposure of unhygienic bacteria, worm, epitope with some topics: high in tropical rainforest area (wet and warm) and savana dry and warm climate; combination of worm antigen-prevent T1D37; Epitope E. coli-vaccine33; wet and warm countries: Ghana4; making of synthetic vaccination HBV aptamers: next generation sequencing34; synthetic long peptide vaccine24; long peptide synthetic vaccines with just one protective epitope22; FMT for extra-intestinal disorders AD35 (FMT industrialization)35; recent therapy and education on HyHy: Exposure 1: sade village cultural: bacteria and parasitic cell wall as natural ligand1; Exposure 2: bau nyale-putri mandalika cultural event (annelids): Effect of helminth-induced immunity on infections,36; helminth can protect IBDS, an Meta-analysis (MA)36; Schitosoma induce Treg37; Ghana: Longitudinal studies increase in immunological disorders as it grew cleaner37; helminth therapy for allergy39; probiotic-helminth1; the ability of countries to respond of infectious and chronic diseases40; lower prevalence on asthma and allergies in childhood exposed to infections, as postulated in the HyHy to fight AD31; School children in the beginning and the end of rainy season: wake up of dormant cell (April-October is the dry season) in Flores could be the Next Prevention on Autoimmune and TB vaccine42; Immunizations by Traveling.

In the second Step, searching for meta-analysis of 2 key words related to the researcher Okada and Orenstein and one key words of helminth AND Autoimmune; EBSCO:CINA HL plus (Medline/PubMed) for FMT-MA (12), Helminth AND AD (137), Worm AND AD (33), Worm AND HyHy (17); Epitope AND Helminth AND Vaccine (80); and in the molecular level RA (Epidemiology AND MA AND RA (28.). All are Screening abstract or title: excluded the not relevant and the duplicates by Bayesian analysis. Since we were interested in explanatory factors of bacteria and worm epitope sequencing are filtered.

In the third step, screening full text publications, excluded since not relevant and publications has been filtrated for table 1. The selection was mainly performed by one reviewer and confirmed by the co-authors.

III. RESULTS AND DISCUSSIONS

3.1 Discussion

From clinical to molecular clue of inflammation markers in savanna (warm and dry climate) with dormant bacteria and worm in dry season, and also in tundra (cold and dry) where no worm no bacteria in all season are searched by us. Meanwhile AD have been found in low prevalence in wet and warm or hot and humid countries, whereas epidemic in clean countries. Dormant bacteria in dry season are specific physics-chemistry antigens and broad spectrum of variable microbiota implies rich of epitope of protein from known FMT. Fig. 1 and Table 1. showed the association of HyHy-allergy and AD.3,6-8,13,15,22,24,32,35,36,39,42,43 Whereas deepest understanding of inflammation reaction increase correlation with the generation of antibody and affimers based product based product induced by antigen based on epitope mapping31,56 Immune Modulation and Prevention of Autoimmune Disease by Repeated Sequences from Parasites Linked to Self Antigens has reported. 56

Studies that have developed FMT and helminth probiotic for prevention and therapy of these diseases1, and has been supported by recent studies,32,43,56 The association of Epitope mapping of similarity structure and the size length to the making of immunological properties has been reported57-60 Reduced Asthma produced from early childhood exposure is relied in developing country.61 Clean habit has support these AD and any potential association between bacteria and helminth infection.35 In Sade village area which peoples expose to dormant bacteria and Bau Nyale cultural event in which sea-worm were catch to eat, prompt us to propose a specific HyHy to explain how dormant bacteria and helminth wall cell play a role as good antigen similar to high technology for making vaccine and antibiotics. Basically, using small or length peptide sequence from parasites has been an industrial economic income.22,24,35,46 People resistant from AD and the broad range of bacteria and worm might have contributed to the uprising national economic income for the most common infectious diseases burden countries like Ghana and Indonesia. 38,40,42,55 With the recognition that FMT as well treatment for ulcerative colitis due to supported by epitope mapping-immunology technologies, and parallel with urban rich-urban poor epidemiology.62-64 Traveling to Sade village and participate in Bau Nyale–Mandalika princess festival will be good for AD patients, family, tribe and country with high prevalence of atopic sensitization, asthma, IBD, SLE, MS, psoriasis, Rheumatoid Arthritis,9,13,15,16,29,40,49,55,61,65
### Table 1
Description of 9 Identified Literatures on Meta-analysis in AD-FMT-Genome Wide Very Similar-Epitope-One Shoot Vaccine-Primary Therapeutic Agent

<table>
<thead>
<tr>
<th>Study</th>
<th>Variables of Interest</th>
<th>Adjustment for other variables</th>
<th>Comparative risk measures for HyHy</th>
<th>Influence of co-morbidities</th>
<th>Influence of infectious and worm parasite</th>
</tr>
</thead>
<tbody>
<tr>
<td>Okada 2016</td>
<td>Ethnic Rheumatoid Arthritis Molecule</td>
<td>Ethnology, genetics, metabolism</td>
<td>Genome-wide Association</td>
<td>Hygiene Hypothesis of Autoimmune Diseases</td>
<td>In Human meta-analysis</td>
</tr>
<tr>
<td>Sakai-Bizmark 2016</td>
<td>Autoimmune in Developing countries</td>
<td>Asthma, allergic diseases, world wide</td>
<td>Industrialized countries in Childhood</td>
<td>More prevalent in affluent countries</td>
<td>Epidemiology reduce in developing countries</td>
</tr>
<tr>
<td>Shi 2016</td>
<td>FMT</td>
<td>Efficacy</td>
<td>Ulcerative colitis</td>
<td>Clinical remission</td>
<td>Clinical response</td>
</tr>
<tr>
<td>Lopez-Isac 2016</td>
<td>Genome wide RA Systemic Sclerosis</td>
<td>same direction, opposite-direction</td>
<td>Allelic effect Rheumatoid Arthritis</td>
<td>Incl. several genomic regions identified T1 Interferon and IL-12</td>
<td>Usefulness of a cross-disease GWAS meta-analysis strategy in the identification of common risk loci</td>
</tr>
<tr>
<td>Burr 2010</td>
<td>Rheumatoid Arthritis UK vs. Asian</td>
<td>RA in an independent group of RA cases and control</td>
<td>PADI4_94 Anti-CCP ab PTPN22</td>
<td>-</td>
<td>R PADI4-RA In Asian pop but no R in European ancestry</td>
</tr>
<tr>
<td>Dieguez-Gonzalez 2008</td>
<td>Epitope Meta-analysis RA and SLE</td>
<td>ACPAs anti-citrullinated protein antibodies – vs.+</td>
<td>Rs2004640 IRFS Shared epitope OR 0.88 vs. controls</td>
<td>Very similar in SLE</td>
<td>OR haplotype 1.8 vs. controls, protective haplotype OR 0.76 vs. controls</td>
</tr>
<tr>
<td>Gorman 2004</td>
<td>Epitope Meta-analysis RA</td>
<td>SE shared epitope</td>
<td>Erosive disease in many ethnic groups OR 2.0; Greek )R0.8, South Eu Caucasians 6.2, Asians OR 5.4 with 2 SE alleles</td>
<td>Genetic and environmental differences in the clinical expression of RA</td>
<td>DRB1*0401 frequency among different ethnic group</td>
</tr>
<tr>
<td>Colman 2014</td>
<td>FMT Meta-analysis</td>
<td>Primary therapeutic agent for IBD</td>
<td>Donor selection and microbiome analysis</td>
<td>Ulcerative Colitis, Crohn’s diseases</td>
<td>Clinical remission and or mucosal healing</td>
</tr>
<tr>
<td>Orenstein 2014</td>
<td>Vaccine IBD</td>
<td>Additional diseases</td>
<td>Supply and delivery</td>
<td>Improving global health one shot at a time</td>
<td>Particularly in developing countries</td>
</tr>
</tbody>
</table>

**Meta-analysis**
2. Orenstein AND MA (9): 2011
3. helmint AND autoimmune (253), + MA: -

**EBSCO: CINA HL plus (Medline/PubMed) with full text**
FMT^MA (12), Helminth^AD (137), Worm^AD (33), Worm^HyHy (17), Epitope^H^V (80)

**Bacteria envelope and wall of worm cells range of Epitopes**
(Antigen and antibody): Epitope AND Meta-analysis AND RA (28)

**Screening abstract or title: 44-30 excluded since not relevant or duplicates analyzed by Bayesian network**

**Screening abstract or title: 279-256 excluded since not relevant or duplicates analyzed by Bayesian network**

**Screening abstract or title: 28-20 excluded since not relevant or duplicates analyzed by Bayesian network**

**9 Publications of Meta-analysis AD-FMT-vaccine-primary therapeutic**

**Figure 1. Flowchart of the Identified Literature**
RA: Rheumatoid Arthritis; MA: Meta-analysis; ^: AND
The historic antibody level in developing countries is closely associated with worm enteric infection and in the other hand the emerging allergic epidemic is associated with low exposure of epitopes. In 2015, AD affects up to 50 million Americans, according to the American Autoimmune Related Diseases Association has 80 types, 70% women, and in the last few decades increase in the global prevalence.38 A better comprehension of the association between helminthes and allergies is pressing as research orientation progress closer to harnessing the preventive potential of worms and derivational relations in also allergic disorders therapy.39

The body produces Antibody against some of own tissue is the definition of AD. Epidemiology of T1D16 and AD to geography4 vs. HyHy32, helminth infection has associated negatively with AD5,14,23,39,42,43 has proven that geography and HyHy associate with socioeconomic status. FMT associate with AD was in HyHy topic,16 where as helminth associate with AD was in Epitope mapping topic.9,57,58,60 The increasing of inflammation cytokine associated with AD is also reveal in Anti TNF antibody; anti TNF-a treatment response in RA has been reported46 and supported by others.43,56,67

The same trends of HyHy-AD association in developing countries is proven in schoolchildren,38 whereas animal studies demonstrated that worm antigens increase the protective effect and represent a new potential management therapy fighting AD.33 The use of pills of frozen microbiota are already used in clinical trials, will be effective as the leading for abundant use and large industrialization of FMT.35 These pills of frozen microbiota are similar with dormant bacteria in dry and hot area like Sade village, which is forbidden done in early rainy season where the dormant bacteria become active living bacteria (pagebugl/epidemic disease). Synthesis vaccine of HBV are produce by Aptamer AND miRNA (43 publications). Aptamer AND vaccine (23); aptamer AND antibiotic (54); vaccine AND epitope (6941); antibiotic AND epitope (135) are found with EBSCOhost search engine. Treatment of several AD with worm and worm eggs mitigate the clinical symptoms and inhibited production of proinflammation cytokines and increase anti-inflammatory cytokines.43 The hopes of creating vaccine based on new protective antigens not only for AD, but also in TB vaccine.41 Vaccination for Mycobacterium tuberculosis37 and antimicrobial peptides for vaccine nanolipoprotein have been reported 24,25 but for AD were already answered by meta-analyses36; and supported by others in table 1. Since 2010, de-Graft40 convinced the double burden of infectious and chronic diseases which is a risk by FMT diversity microbiota but could be safe in Sade village and Bau Nyale festival. It is eastern to Wallace’s Line, between tropical rainforest area (Bali island, humid and hot) and Savanna area (Sumbawa Island, dry and warm). One shot contemporary vaccine challenges could be improving global health vaccine, at a time,49 cross diseases44 and same IRF5 polymorphisms could influence RA similar to SLE patients.21

3.2 Bacterial and Parasite wall

Prevention of AD with immune modulation using repeated sequences from parasites associated to anti TNF or decrease TNFα associate with T cell epitope in RA Therapy known as affimer technology,66 and Jhonson 201251 made affimer which linked with impedance CRP immunoassay and TNFα.43,51,56,67 An intestinal worm infections longitudinal studies and allergy in rural vs. semi urban areas of Flores, Indonesia have been reported,42 which could help develop evidence-based policy making.52

FMT beyond intestinal disorders,22 is supported by allergy reduction due to increase microbial exposure.13 Caucasian RA were lower than Japanese, which is statistically significant in the Japanese population15 by HyHy approach could now be simply understood. Another autoimmune reaction associate preeclampsia-EBV epitope54 and the global multimorbidity pattern in multi country has been made.55 Epitope mapping of tuberculosis antigen,57 and other epitope mapping,58 could now be help by Mass Sepctrometric epitope mapping39 and short non-epitope vs. epitope prediction antibody binding,60 but FMT is an effective therapy for recurrence CDI reduce the cost effectiveness therapy for CDI,50 Qualitative and quantitative antigen induce immune responses,7 and a linear surface epitope in a proline rich reg of HeV could be a model.4 Invariant NKT cells on Parasitic HyHy and cell wall of Bacterial and Parasit is a cellular structure in variety highly enriched of glycolipids and lipoprotein, is a cross talk of Th1, Th2, Th17, Treg, inate lymphoid cells.3

IV. LIMITATION

These Systematic review has several limitation 1) Non published literature on Sade village and bau nyale/princess Mandalika may limit the validity of our findings, but these cultural indigenous study are a real phenomenon which is already attracted peoples from developed and clean countries with AD burden. However, we used meta-analysis with partly overlapping data bases for our literature search on bacteria and worm cell wall antigens. And we found a large number of papers fulfilling the criteria of our search in these HyHy-AD prevention, diagnosis and therapeutic. 2) Another potential problem in this systematic review is that studies mainly used in the searching steps are depended on the vocabulary synonyms (not find in
general, but many in specific such as autoimmune diseases could be Rheumatoid arthritis, recurrent CDI, IBS, T1D, atopic sensitization, asthma etc.). Different changes chances choices give different results may be misleading. We intended to manage this problem in an additional work, by dividing the using chosen specific to generic into 2 broad categories: measurements and epidemiological findings.

V. CONCLUSION

Epitope of FMT, dormant bacteria, protein from the wall of worm are all rich of ranges epitopes and could present in cultural event like Sade village and Bau Nyle ‘Mandalika princess’ festival. These indigenous study from local, present to global is similarly paralleled with epitope mapping and contemporary industrial affimers and aptamers based on epitope biotechnology for diagnostic, vaccination and therapeutic fighting against autoimmune diseases. Further education to policy maker and global politic doer from local to global will support this added value idea.

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DISCLOSURE

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REFERENCE


