A PROTEIN OF SHIGELLA FLEXNERI CIRCUMVENTS INNATE IMMUNITY

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Abstract- Shigellaflexneri is able to invade and replicate within the epithelial cells, leading to severe inflammation and epithelial damage in which the transmission process through the fecal-oral route. Epithelial cells in the intestinal tract are the first barrier that haveimmunocompetent cells to responsible for the innate immune response. However, S. flexnerysecretes virulence protein through the Type III Secretion System (T3SS) for disarming the innate immunity system. This review focus on the mechanisms of S. flexneriin manipulating the innate immunity by epigenetic regulation.

Keywords- Innate immunity, Shigellaflexneri**,** OspF, T3SS

I. INTRODUCTION

Shigella is a gram-negative, non-motile, non-spore bacteria that infect intestine tract on human [1][2]. There are four serogroups of *Shigella: Shigellaflexneri, S. dysenteriae, S. boydii*, and *S. sonnei.S. flexneri*is the most common cause intestinal infections called Shigellosis, also known as bacillary dysentery, with symptoms of abdominal pain, diarrhea, fever, vomiting, and blood or mucus in the stool. Shigellosis, gastroenteritis caused by *Shigella*spp., is a major public health problem in both developing and develop countries. Approximately 164.7 million cases of shigellosis occur annually worldwide in 1.1 millian deaths, primarily among children aged < 5 years. Bacterium caused by Shigellosis accour mainly in developing countries due to poor hygiene and limited access to clean driking water; industrialized countries the disease mainly results from travel to developing countries and exposure to contaminated foods and/or food handlers. Foods contaminated with bacteria survive in the stomach environment and move on to the colon. They penetrate and adhere to intestinal epithelial cells, causing severe inflammation and disrupting cellular integrity of the intestine[1],[3],[4],[5].

In the human body, there is an immune system that serves to protect the skin, respiratory tract, digestive tract and other areas to antigen, such as bacteria, fungi, parasite, virus, cancer cell, and toxin. Immune system can be divided two parts : innate and adaptive immunity. Innate immunity is the first line of defense against pathogen, with characteristic of an antigen-independent (non-specific), defense mechanism used by the host immediately or within hours of encountering an antigen. The innate immune system has no immunologic memory and, therefore, it is unable to recognize or memorize the same pathogen should the body be exposed to it in the future [6]. In physical or mechanical defense system, skin, mucous membranes, airway cilia, coughing and sneezing are the leading line of defense against infection. Keratinocytes and layers of healthy skin epidermis and intact mucosal epithelium can notbe penetrated by most microbes. However, many entric bacterial pathogen, including *Shigella*, can do bacterial evasion of the immune system of host. As a result, pathogens efficiently colonize the intestinal epithelium [7],[8].

II. METHOD

Systematic review

III. DISCUSSION

Shigella infections are almost found in the gastrointestinal tract, rarely an invasion of blood flow. *Shigella* is highly contagious; the infective dose of about 10^3 organisms [2]. Attachment of *S. flexneri*to submucosa is divided by three mechanisms; (1) transcytosis through M cells, (2) *S. flxneri* induced tight junction distruption, or (3) *S. flexneri*-induced polymorphonuclear (PMN) lecukocytetransepithelial migration[9]. Once the bacteria are endocytosed by the M cells, they are transcytosed toward the M cell pocket, where resident macrophages receive the bacteria. However, *Shigella* can distrupt the vacuolar membranes, disseminate into the cytoplasm, and multiply therein[10].

Epigenetic Modification

Mitogen-activated protein kinase (MAPKs) are protein Ser/Thr that convert extracellular stimuli into a wide range of cellular responses. MAPKs are important signal transduction pathways [11] which highly responsive to specific chemical with receive, process, and respond to information from environment (Figure 1), [11], [12].

Signal transduction pathways control pivotal cellular processes including proliferation, differentiation, survival, apoptosis, gene regulation, and motility [13]. Host transcriptional program plays a

predominant role in triggering inflammation and eliminating bacterial infection [14], *S.flexneri* is bacterial pathogen that causes bacillary dysentery in humans by invading colonic epithelial cell by remitting a subset of *Type III Secretion System* effector protein that regulate gene expression that is encoded by a 220-kilobase virulence plasmid and prevent host immune responses[15]. Moreover, restricting with NF-kB signaling. NF-kB (The immunoglobulin kappa light-chain of activated B cells) is a protein in transcription factors that have an essential role in inflammation and innate immunity[16].

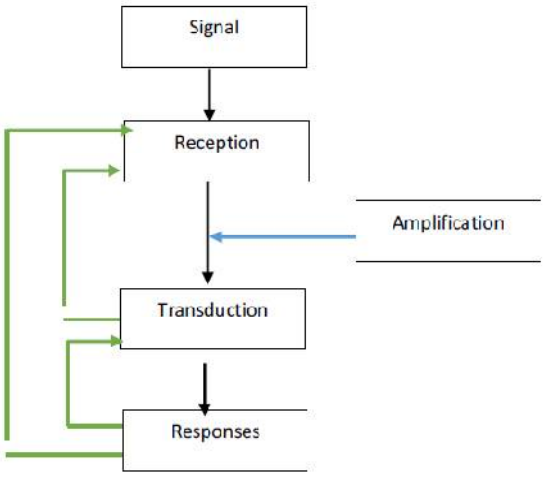

Fig. 1 Principle of Signal Transduction

A protein of *S. flexneri* avoid host transcriptional responses via epigenetic modifications : (1) diminishing the level of phosphorylated histone H3. Phosphorylation of histone at Ser10. Protein effector OspF of *S. flexneri* as a dually specific phosphatase that dephosphorylated mitogen-activated protein kinases in the nucleus, preventing histone H3 phosphorylation at Ser10 in a gene-specific way. That activity of OSpF enabled *Shigella* to block the activation of a subset of NF-kB-responsive genes, leading to compromises recruitment of polymorphonuclear leukocytes to infected tissues. *S. flexneri*has thus evolved the capacity to precisely modulate host cell epigenetic information as a strategy for repressing innate immunity (Figure 2),[15].

Figure2 : Coming Soon

CONCLUSIONS

Pathogenic enteric bacteria, especially *S. flexneri*, some researchers know how the bacterial manipulation of innate immunity in humans that is modified epigenetically, and this also needs further understanding so that it can develop a genomic drug-making process to prevent Shigellosis in the group which has less health and a developing country.

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