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Opinion Paper

CAN MICROBIAL SCFA, BUTYRATE BE THE ALTERNATE SAVIOR AGAINST COVID-19?

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Abstract

Gut microbial metabolites such as short-chain fatty acids rule our immune system and might have therapeutic roles in the Corona Virus Diseases. Production of these metabolites particularly butyrate is indispensable for its hostility against viral diseases. This viral disease, predominantly initiated from the Wuhan city, China in the year 2019 has its mechanism in the host cells that embrace the binding of the spike protein with the angiotensin converting enzyme-2 (ACE2) receptors of the hosts via damaging the alveolar epithelial type 2 cells leading to inflammations and butyrate and its derivatives play a significant role in suppressing these factors, thereby act as a potential therapeutic target.

Keywords: Gut microbiome; metabolite; anti-inflammatory; SCFA

Short Chain Fatty Acids (SCFAs) including butyrate, propionate, and acetate are produced by the gut microbes, which help in the regulation of the host immune system. Recently, orally administered SCFAs showed promising anti-inflammatory effects [1]. SCFAs may also act as potential therapeutics in Corona Virus Disease, 2019 (COVID19) management. The COVID19, which was primarily originated from the Wuhan city, China in the year 2019 and drastically spread around the world with more than 5,000,599 positive cases and 325,156 mortality as on date [2]. The common symptoms include fever, dry cough, and difficulty to breath in most

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cases and headache, muscle pain, diarrhea, loss of smell and taste in a few [3, 4]. The entry mechanism of the virus in the host cells includes the binding of the spike protein with the angiotensin converting enzyme -2 (ACE2) receptors of the hosts followed by damaging the alveolar epithelial type 2 cells causing inflammation of the epithelial linings of the lungs [4]. The patients suffering from the disease have further been observed to have reduced CD8T and CD4 T- cell population, which is important to maintain the host immunity [4]. Also the dysregulation of IFN-γ has been reported in the cases [4]. SCFAs especially butyrate may be considered as therapeutic agents in this context. Several studies have suggested the potential role of SCFAs in the maintenance of the functions of CD4-T cells and antigen presenting cells [5]. Luu *et al*., in 2018, have shown the potential impact of butyrate and propionate (to a lesser amount) in direct modulation of the CD8+ cytotoxic T lymphocytes (CTLs) and Tc17 cells gene expressions. Moreover, the authors also reported the significant effect of butyrate in elevation of the CTLs mediated expressions of IFN-γ and granzyme B and molecular switch of Tc17 cells towards the CTL phenotype as well, engaging the specific SCFA-receptors e.g. GPR41 and GPR43. Butyrate has also been found to inhibit histone-deacetylases in CD8-T cells affecting its gene expression, which might have significant implications in the adoptive antiviral immunity of the host [6]. COVID19 has also been found to damage the alveolar epithelial cells followed by inflammation [4]. Studies have shown the effect of SCFAs especially butyrate and propionate in controlling the inflammation by inducing FOXP3 [7]. Also, these are found to promote regulatory T cells and suppression of Th2 responses. Additionally, butyrate treatment also observed to attenuate lung inflammation and mucus production in the mice model [7].

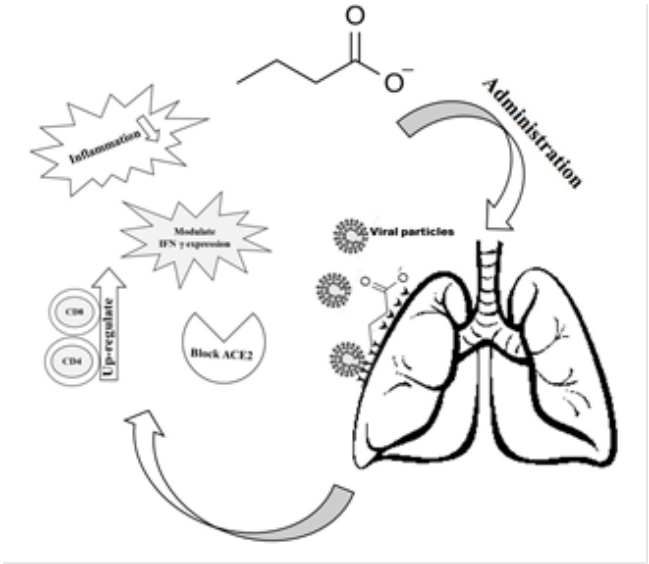

Fig. 1: Prospective protective mechanism of butyrate and its derivatives.

Moreover, the derivative of butyrate viz.; sodium butyrate has also been found to play a major role in suppressing the angiotensin-II expression [8]. These findings provide possible therapeutic strategies for 2019-nCoV by using the butyrate, although detailed research is needed before concluding about the drug target (Fig. 1). Additionally, a suitable dosage regimen should be designed within the therapeutic window for human use, along with a suitable drug delivery system.

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