

Supplementary Table 1. Role of the gut microbiota in the protection or induction of inflammation diseases.

Microbe	Subject	Disease	The possible role of macrophages	Reference
Microbiota that promote the development of inflammation disease				
<i>E. coli</i>	Rats	NASH	Escherichia Coli-LPS induces liver macrophages activation towards pro-inflammation phenotype through the TLR4 pathway	(Zhu et al., 2013; Carpino et al., 2019)
<i>Prevotella copri</i>	Human	RA	The activated macrophages are the main source of pro-inflammatory cytokines and chemokines such as TNF and IL-1 β	(Bernard, 2014; Siouti and Andreakos, 2019)
<i>Bacteroides fragilis</i>	NOD mice	T1DM	<i>B. fragilis</i> enhances the phagocytic functions of macrophages and polarize them to an M1 phenotype.	(Deng et al., 2016; Sofi et al., 2019)
<i>Clostridium difficile</i>	Child	Asthma	<i>C. difficile</i> release TcdA and TcdB toxins, which induce the recruitment of macrophages, and survive in the macrophages	(Paredes-Sabja et al., 2012; Salameh et al., 2020)
<i>Adherent-invasive Escherichia coli</i>	Human	CD	Adhere to intestinal epithelial cells, invade epithelial cells, survive and replicate within macrophages.	(Darfeuille-Michaud et al., 2004)
Microbiota that protect against inflammation diseases				
<i>Prevotella histicola</i>	HLA-DR3.DQ8 transgenic mice	MS	The induction of suppressive macrophages which produced higher IL-10 and lower IL-12, thus induced a decreased capacity of antigen presentation	(Mangalam et al., 2017)

<i>Roseburia</i>	Human	T2DM	Production of butyrate which exert anti-inflammatory role on macrophages	(Liu et al., 2012; Vrieze et al., 2012)
<i>Lactobacillus helveticus</i>	Mice	Asthma	<i>L. gasseri</i> decreased the numbers of alveolar macrophages which produce IL-17	(Jan et al., 2012; Hsieh et al., 2018)

NASH, nonalcoholic steatohepatitis; MS, Multiple sclerosis; RA, rheumatoid arthritis;

T2DM, type 2 diabetes mellitus

References

- Bernard, N.J. (2014). Rheumatoid arthritis: Prevotella copri associated with new-onset untreated RA. *Nat Rev Rheumatol* 10(1), 2. doi: 10.1038/nrrheum.2013.187.
- Carpino, G., Del Ben, M., Pastori, D., Carnevale, R., Baratta, F., Overi, D., et al. (2019). Increased liver localization of lipopolysaccharides in human and experimental non-alcoholic fatty liver disease. *Hepatology*. doi: 10.1002/hep.31056.
- Deng, H., Li, Z., Tan, Y., Guo, Z., Liu, Y., Wang, Y., et al. (2016). A novel strain of Bacteroides fragilis enhances phagocytosis and polarises M1 macrophages. *Sci Rep* 6, 29401. doi: 10.1038/srep29401.
- Hsieh, M.H., Jan, R.L., Wu, L.S., Chen, P.C., Kao, H.F., Kuo, W.S., et al. (2018). Lactobacillus gasseri attenuates allergic airway inflammation through PPARgamma activation in dendritic cells. *J Mol Med (Berl)* 96(1), 39-51. doi: 10.1007/s00109-017-1598-1.
- Jan, R.L., Yeh, K.C., Hsieh, M.H., Lin, Y.L., Kao, H.F., Li, P.H., et al. (2012). Lactobacillus gasseri suppresses Th17 pro-inflammatory response and attenuates allergen-induced airway inflammation in a mouse model of allergic asthma. *Br J Nutr* 108(1), 130-139. doi: 10.1017/S0007114511005265.
- Liu, T., Li, J., Liu, Y., Xiao, N., Suo, H., Xie, K., et al. (2012). Short-chain fatty acids suppress lipopolysaccharide-induced production of nitric oxide and proinflammatory cytokines through inhibition of NF-kappaB pathway in RAW264.7 cells. *Inflammation* 35(5), 1676-1684. doi: 10.1007/s10753-012-9484-z.
- Mangalam, A., Shahi, S.K., Luckey, D., Karau, M., Marietta, E., Luo, N., et al. (2017). Human Gut-Derived Commensal Bacteria Suppress CNS Inflammatory and Demyelinating Disease. *Cell Rep* 20(6), 1269-1277. doi: 10.1016/j.celrep.2017.07.031.
- Paredes-Sabja, D., Cofre-Araneda, G., Brito-Silva, C., Pizarro-Guajardo, M., and Sarker, M.R. (2012). Clostridium difficile spore-macrophage interactions: spore survival. *PLoS One* 7(8), e43635. doi: 10.1371/journal.pone.0043635.
- Salameh, M., Burney, Z., Mhaimed, N., Laswi, I., Yousri, N.A., Bendriss, G., et al. (2020). The role of gut microbiota in atopic asthma and allergy, implications in the understanding of disease pathogenesis. *Scand J Immunol* 91(3), e12855. doi: 10.1111/sji.12855.
- Siouti, E., and Andreakos, E. (2019). The many facets of macrophages in rheumatoid arthritis. *Biochem Pharmacol* 165, 152-169. doi: 10.1016/j.bcp.2019.03.029.
- Sofi, M.H., Johnson, B.M., Gudi, R.R., Jolly, A., Gaudreau, M.C., and Vasu, C. (2019). Polysaccharide A-Dependent Opposing Effects of Mucosal and Systemic Exposures to Human Gut Commensal Bacteroides fragilis in Type 1 Diabetes. *Diabetes* 68(10), 1975-1989. doi: 10.2337/db19-0211.
- Vrieze, A., Van Nood, E., Holleman, F., Salojärvi, J., Kootte, R.S., Bartelsman, J.F., et al. (2012). Transfer of intestinal microbiota from lean donors increases insulin sensitivity in individuals with metabolic syndrome. *Gastroenterology* 143(4), 913-916.e917. doi: 10.1053/j.gastro.2012.06.031.
- Zhu, L., Baker, S.S., Gill, C., Liu, W., Alkhoury, R., Baker, R.D., et al. (2013). Characterization of gut microbiomes in nonalcoholic steatohepatitis (NASH) patients: a connection between endogenous alcohol and NASH. *Hepatology* 57(2), 601-609. doi: 10.1002/hep.26093.