Review the Association between Mannose Binding Lectin (MBL) Gene Variations and Infection with Toxoplasma Gondii

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ABSTRACT

Toxoplasma gondii causes toxoplasmosis, an infectious illness. T. A parasite called gondii may infect practically any warm-blooded animal. mammal and is widespread across the world, but The only known definite hosts where it may sexually reproduce are domestic cats.. One of the most widespread parasites in humans is *T. gondii*. industrialized nations that affects people. People who lack mannose-binding lectins are susceptible to upper respiratory infections as well as infections of other bodily systems. People who have this illness run the risk of developing more severe infections including meningitis and pneumonia. The frequency and intensity of an illness's symptoms varies depending on the type of infection. This study aims to review the association between the susceptibility of infection with Toxoplasma and variation in MBL gene.

Keywords: *T. gondii*, MASP, MBL gene, Toxoplasmosis

Introduction

Toxoplasmosis

One of the most prevalent parasites in industrialized nations is *T. gondii*; Despite the fact that infection rates vary greatly from country to country, serological research suggests that 30–50% of the world's population has been exposed to it and may be chronically infected. next. (Jiang et al., 2018). For instance, estimations indicate that as of 2000, France had the greatest proportion of infected people, at 84%. Although infrequently appearing in moderate flu-like symptoms for the first several weeks after exposure *T. gondii* infection has lately been linked to a number of modest unfavorable effects in healthy human adults. (Ravi et al., 2015). Even though it has recently been demonstrated that there is only a slight correlation between behavioral A latent infection is an illness that doesn't cause any symptoms. is caused by *T. gondii*. or pathological behavioral modifications in people (Sathasivam & Ki, 2018).

Infection can result in toxoplasmosis, a dangerous and occasionally deadly condition that can affect babies, people with HIV/AIDS, and other people with weaker immune systems. According to research, *T. gondii* causes infected rodents to behave differently, increasing their vulnerability to felid predators. Towards example, rats with the infection exhibit less disgust for cat pee. Considering that cats are the only hosts in which T (Halonen & Weiss, 2013). Gondi can sexually reproduce to complete It is thought that these behavioral modifications are examples of evolutionary adaptations that increase the parasite's capacity for reproduction and initiate the life cycle. The rats

wouldn't stay away from areas where cats live, and they would find it more difficult to flee if a cat tried to eat them. (2014) Li et al. One of the primary methods by which T cells regulate related behaviors is now understood to be epigenetic modification in neurons. Gondii causes alterations in rodent behavior. For example, it alters epigenetic methylation to create hypomethylation of genes associated to arginine vasopressin in the medial amygdala, which greatly reduces the desire to avoid predators. *T. gondii* employs yet another epigenetic pathway. appears to be widespread histonelysine acetylation in cortical astrocytes. Humans with and without infection show different levels of aversion to cat urine, and there are sex variations between these groups as well. (Njoh et al., 2016).

Infected individuals may experience mild behavioral or psychological changes, according to several studies, and parasite infection has lately been linked to certain neurological illnesses, including schizophrenia and bipolar disorder. Milne and others (2010) According to a regression model with racial and ethnic controls and level of education, a research also discovered that cognitive impairments in adults were connected combined infection with Helicobacter pylori and *T. gondii*. Although a clear connection between latent toxoplasmosis and these neurological abnormalities has not been established, early data suggest that *T. gondii* infection may induce some of the same problems in the human brain as those reported in rats. manifestations has not yet been proven. (Njoh et al., 2016). *Toxoplasma gondii*, a coccidian parasite from the apicomplexa family, is one such nongenetic risk factor. Pregnant women who experience it may have a congenital disease that might include deafness, retinal damage, convulsions, and mental retardation. In immunocompromised individuals, it may result in severe central nervous system (CNS) symptoms.

The incidence of *T.gondii* antibodies in people with schizophrenia was examined in 23 research, and a meta-analysis of those results revealed a combined or of Since then, other investigations have appeared.(Yazar et al., 2003).

Mannose-binding lectin

MBL belongs to the C-type lectin family. superfamily of collectins, and it appears that it serves as by identifying patterns, the pre-immune host's initial line of protection. MBL is able to identify carbohydrate patterns that are present on the surfaces of several harmful microorganisms, such as bacteria, viruses, protozoa, and fungus. The binding of MBL activates the complement system's lectin pathway. to a microbe (Meyrowitsch et al., 2010).

The fact that MBL enhances phagocytes' capacity to take in full, intact apoptotic cells as well as cell detritus by binding senescent and apoptotic cells. is another crucial function of this protein. Three many mechanisms—the alternative route, the lectin pathway, and the classical pathway—can activate the complement system. The mannose-binding lectin protein is one method that the most recent lectin pathway is activated. MBL binds to the three are remnants of D-mannose and L-fructose on the surfaces of several pathogens (Meyrowitsch et al., 2010).

MBL, for instance, has been demonstrated to bind to:

- For example, *Candida albicans*, are yeasts
- Like the influenza virus and the HIV virus A
- A large number of bacteria, such as Salmonella and Streptococci, as well as parasites like Leishmania and toxoplasma

Mannose-binding lectin deficiency

It is an immune system-related disorder. Low levels (deficiency) protein of the immune system lectin that binds to mannose are present in the blood of those who suffer from this illness. It is unclear if this deficit makes those afflicted susceptible to recurring infections (Gorgi et al., 2009).

People who lack mannose-binding lectins are susceptible to upper respiratory infections as well as infections of other bodily systems. People who have this illness run the risk of developing more severe infections including meningitis and pneumonia. The frequency and intensity of an illness's symptoms varies

depending on the type of infection (Meyrowitsch et al., 2010).

However, adults can also experience recurring infections. Mannose-binding lectin deficiency appears to make infants and young children more susceptible to infections than affected adults. Additionally, those with the condition who are receiving chemotherapy or using immune-suppressing medications are more vulnerable to infections than others. (Eisen & Minchinton, 2003).

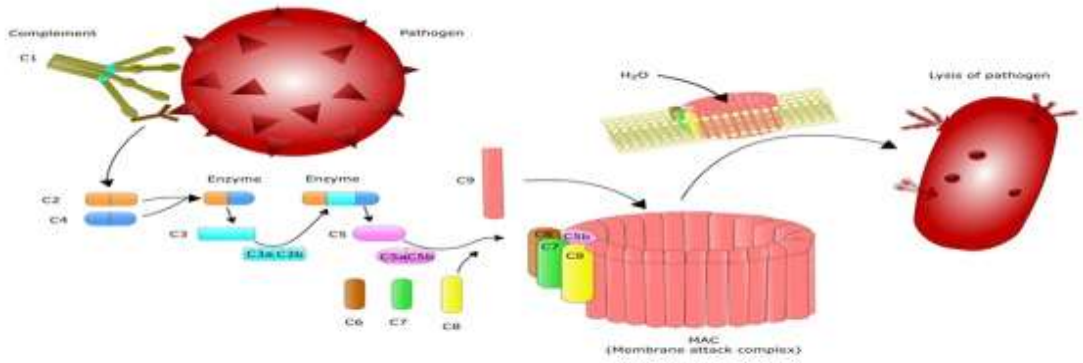

Figure 1: Mannose binding protein structure

Complexes

MASP, a serine protease, and MBL are complexed with (bound to) each other in the blood (serine protease linked with MBL). The three MASPs MASP-1, MASP-2, and MASP-3 all have protease domains.Additionally, there are two other molecules, sMAP (also known MAp44 (also known as MAp19), and other proteins that lack protease domains are most likely MASP regulatory molecules. Additionally, MASPs work with ficolins, which are physically and functionally identical to MBL with the exception that ficolins identify their targets via fibrinogen-like domains as opposed to MBL (Werth et al., 2002).

The MASP protein cleaves the blood protein C4 into C4a and C4b, which then activates the complement system when MBL attaches to its target (for instance, mannose on the surface of a bacterium). The C4b pieces can then attach to the bacterial surface and start the development of a C3-convertase (Werth et al., 2002).

A membrane assault complex is produced by the ensuing complement cascade, which is catalyzed by C3-convertase, and it induces lysis of the pathogen and the changed self when there are necrotic and apoptotic cells present (Sapkota et al., 2010).

Thrombin-like activity is also seen in the MBL/MASP-1 complex Blood clots are started when thrombin clots fibrin. Mice with genetic deficiencies in MBL or MASP-1/3 (but not MASP-2/sMAP) exhibit extended bleeding times in experimental injury scenarios. times, despite these animals appear normal in the absence of a bodily injury (Patel et al., 2017).

Relation between MBL gene and Toxoplasmosis

MBL, an element of the innate immune system, is a protein that has been previously highlighted, functions as a lectin-mediated complement activator. Lack of MBL and genetic MBL variants may contribute to a number of infection-related issues that might possibly impact pregnancy. And this polymorphism has already been linked to a number of illnesses. Kidney Transplant, for instance, or chronic periodontitis (Zçaka et al., 2010) (Gorgi et al., 2009), Vulvovaginal Candidiasis (B et al., 2014), filariasis (Meyrowitsch et al., 2010), malaria (Jha et al., 2014), leishmaniosis (Asgharzadeh, Mazloumi, Kafil, & Ghazanchaei, 2007) and also a contagious illness. It suggests that MBL deficiency predisposes to life-threatening infection. The polymorphism in the promoter region at position -221 of the 5′ flanking region

of the MBL2 gene encodes the alleles H/L and X/Y, and it influences the MBL level in individuals with wild-type genes and in mice. those who are heterozygous for structural gene alterations. (Eisen & Minchinton, 2003).

Mannose-binding lectin (MBL), a crucial element of the human innate immune system, may bind to a wide range of pathogens, including viruses like influenza A, HIV, herpes simplex 2, and SARS-CoV. MBL deficiency is brought on by single nucleotide polymorphisms (SNPs) in exon 1, and the promoter region of the human MBL2 gene has been linked to a variety of infection susceptibilities. Few studies have, however, examined the connection between MBL and CMV infection, although one led by (Hu, Wu, Tao, & Shang, 2010) HCMV infection in infants may be prevented by MBL, a protein of the innate immune system that recognizes patterns. A significant risk factor for the development of infantile HCMV infection may potentially involve MBL gene abnormalities.. prior research by (Çalkavur et al., 2015) When the relationship between MBL polymorphism and pregnancy health ratio was explored, it was discovered that the frequency of allele B was much greater in the research group moms than it was in the healthy Turkish population. We also discovered a strong correlation between low MBL levels and the prevalence of the MBL variant allele B.

Conclusion

There are a strong relation between the susceptibility of infection with toxoplasma and the structure and variation within MBL gene and its product.

References

1. Asgharzadeh, M., Mazloumi, A., Kafil, H. S., & Ghazanchaei, A. (2007). Mannose-binding lectin gene and promoter polymorphism in visceral leishmaniasis caused by Leishmania infantum. *Pakistan Journal of Biological Sciences*, *10*(11), 1850–1854. https://doi.org/10.3923/pjbs.2007.1850.1854
2. B, N., B, P., E, L., A, R., R, A., M, S., W, R., & S, B. (2014). Mannose-binding Lectin Codon 54 Gene Polymorphism and Vulvovaginal Candidiasis: A Systematic Review and Meta-Analysis. *BioMed Research International*, *2014*. https://doi.org/10.1155/2014/738298
3. Çalkavur, Ş., Erdemir, G., Onay, H., Altun-Köroğlu, Ö., Yalaz, M., Zekioğlu, O., Aksu, G., Özkınay, F., Akercan, F., & Kültürsay, N. (2015). Mannose-binding lectin may affect pregnancy outcome. *Turkish Journal of Pediatrics*, *57*(1), 26–33.
4. Eisen, D. P., & Minchinton, R. M. (2003). Impact of Mannose-Binding Lectin on Susceptibility to Infectious Diseases. *Clinical Infectious Diseases*, *37*(11), 1496–1505. https://doi.org/10.1086/379324
5. Gorgi, Y., Sfar, I., Aouadi, H., Makhlouf, M., Abderrahim, E., JendoubiAyed, S., Bardi, R., Ben Abdallah, T., & Ayed, K. (2009). Mannose Binding Lectin (+54) Exon 1 Gene Polymorphism in Tunisian Kidney Transplant Patients. *Transplantation Proceedings*, *41*(2), 660–662. https://doi.org/10.1016/j.transproceed.2009.01.030
6. Halonen, S. K., & Weiss, L. M. (2013). TOXOPLASMOSIS. *Handbook of Clinical Neurology*, *114*, 125. https://doi.org/10.1016/B978-0-444-53490-3.00008-X
7. Hu, Y., Wu, D., Tao, R., & Shang, S. (2010). Association between mannose-binding lectin gene polymorphism and pediatric cytomegalovirus infection. *Viral Immunology*, *23*(4), 443–447. https://doi.org/10.1089/vim.2009.0109
8. Jha, A. N., Sundaravadivel, P., Singh, V. K., Pati, S. S., Patra, P. K., Kremsner, P. G., Velavan, T. P., Singh, L., & Thangaraj, K. (2014). MBL2 variations and malaria susceptibility in Indian populations. *Infection and Immunity*, *82*(1), 52–61. https://doi.org/10.1128/IAI.01041-13
9. Jiang, L., Wang, Y., Liu, G., Liu, H., Zhu, F., Ji, H., & Li, B. (2018). C-Phycocyanin exerts anti-cancer effects via the MAPK signaling pathway in MDA-MB-231 cells. *Cancer Cell International*, *18*(1).

https://doi.org/10.1186/s12935-018-0511-5
10. Li, L.-J., Gong, C., Zhao, M.-H., & Feng, B.-S. (2014). Role of interleukin-22 in inflammatory bowel disease. *World J Gastroenterol*, *20*(48), 18177–18188. https://doi.org/10.3748/wjg.v20.i48.18177
11. Meyrowitsch, D. W., Simonsen, P. E., Garred, P., Dalgaard, M., Magesa, S. M., & Alifrangis, M. (2010). Association between mannose-binding lectin polymorphisms and Wuchereria bancrofti infection in two communities in North-Eastern Tanzania. *American Journal of Tropical Medicine and Hygiene*, *82*(1), 115–120. https://doi.org/10.4269/ajtmh.2010.09-0342
12. Milne, G., Fujimoto, C., Bean, T., Peters, H. J., Hemmington, M., Taylor, C., Fowkes, R. C., Martineau, H. M., Hamilton, C. M., Walker, M., Mitchell, J. A., Léger, E., Priestnall, S. L., & Webster, J. P. (2020). Infectious Causation of Abnormal Host Behavior: Toxoplasma gondii and Its Potential Association With Dopey Fox Syndrome. *Frontiers in Psychiatry*, *11*, 1. https://doi.org/10.3389/FPSYT.2020.513536
13. Njoh, A. A., Njoh, S. N., & Abizou, M. B. (2016). Fetal malformation in maternal toxoplasma and rubella co-infection in Cameroon: a case report. *Journal of Medical Case Reports*, *10*(1), 345. https://doi.org/10.1186/s13256-016-1133-y
14. Özçaka, Ö., Biçakci, N., Nalbantsoy, A., Köse, T., & Berdeli, A. (2010). Association between mannose-binding lectin levels and gene polymorphisms in chronic periodontitis and response to treatment. *Archives of Oral Biology*, *55*(3), 235–241. https://doi.org/10.1016/j.archoralbio.2009.12.006
15. Patel, A. R., Patra, F., Shah, N. P., & Shukla, D. (2017). Biological control of mycotoxins by probiotic lactic acid bacteria. *Dynamism in Dairy Industry and Consumer Demands*, *2015*(February), 2–4. https://doi.org/10.1155/2015
16. Ravi, M., Tentu, S., Baskar, G., Rohan Prasad, S., Raghavan, S., Jayaprakash, P., Jeyakanthan, J., Rayala, S. K., & Venkatraman, G. (2015). Molecular mechanism of anti-cancer activity of phycocyanin in triple-negative breast cancer cells. *BMC Cancer*, *15*(1). https://doi.org/10.1186/s12885-015-1784-x
17. Sapkota, B. R., Macdonald, M., Berrington, W. R., Misch, E. A., Ranjit, C., Siddiqui, M. R., Kaplan, G., & Hawn, T. R. (2010). Association of TNF, MBL, and VDR polymorphisms with leprosy phenotypes. *Human Immunology*, *71*(10), 992–998. https://doi.org/10.1016/j.humimm.2010.07.001
18. Sathasivam, R., & Ki, J. S. (2018). A review of the biological activities of microalgal carotenoids and their potential use in healthcare and cosmetic industries. In *Marine Drugs* (Vol. 16, Issue 1). MDPI AG. https://doi.org/10.3390/md16010026
19. Werth, V. P., Berlin, J. A., Callen, J. P., Mick, R., & Sullivan, K. E. (2002). Mannose binding lectin (MBL) polymorphisms associated with low MBL production in patients with dermatomyositis. *Journal of Investigative Dermatology*, *119*(6), 1394–1399. https://doi.org/10.1046/j.1523-1747.2002.19608.x
20. Yazar, S., Kilic, E., Saraymen, R., & Sahin, I. (2003). Serum Malondialdehyde Levels in *Toxoplasma* Seropositive Patients. *Annals of Saudi Medicine*, *23*(6), 413–415. https://doi.org/10.5144/0256-4947.2003.413