Journal of Biosciences and Medicines, 2023, 11, 175-183
https://www.scirp.org/journal/jbm
ISSN Online: 2327-509X
ISSN Print: 2327-5081

DC-SIGN (CD209) Promoter −336 A/G Polymorphism Is Not Associated with Dengue Fever at Burkina Faso, West Africa

Fiffou Yougbare[1], Aziz Sidi Aristide Tapsoba[1], Pegdwendé Abel Sorgho[1,2], Bagora Bayala[1,2], Lassina Traore[1], Prosper Bado[1], Bapio Valérie Elvira Jean Télesphore Bazie[3], Abdou Azaque Zoure[3], Esther Mah Alima Traore[3], Théodora Mahoukèdè Zohoncon[4], Sessi Frida Tovo[1], Albert Théophane Yonli[1,2], Alice Kiba[5], Florencia Wendkuuni Djigma[1,2*], Jacques Simpore[1,2]

[1]Laboratoire de Biologie Moléculaire et de Génétique (LABIOGENE), Université Joseph KI-ZERBO, Ouagadougou, Burkina Faso
[2]Centre de Recherche Biomoléculaire Pietro Annigoni (CERBA), Ouagadougou, Burkina Faso
[3]Université Saint Thomas d'Aquin, Ouagadougou, Burkina Faso
[4]Centre National de la Recherche Scientifique et Technologique (CNRST), Ouagadougou, Burkina Faso
[5]Centre National de Transfusion Sanguine (CNTS), Ouagadougou, Burkina Faso
Email: *florencia.djigma@gmail.com

How to cite this paper: Yougbare, F., Tapsoba, A.S.A., Sorgho, P.A., Bayala, B., Traore, L., Bado, P., Bazie, B.V.E.J.T., Zoure, A.A., Traore, E.M.A., Zohoncon, T.M., Tovo, S.F., Yonli, A.T., Kiba, A., Djigma, F.W. and Simpore, J. (2023) DC-SIGN (CD209) Promoter −336 A/G Polymorphism Is Not Associated with Dengue Fever at Burkina Faso, West Africa. *Journal of Biosciences and Medicines*, **11**, 175-183.
https://doi.org/10.4236/jbm.2023.111017

Received: December 5, 2022
Accepted: January 28, 2023
Published: January 31, 2023

Abstract

Objective: The aim of this study was to characterize the polymorphisms of the DC-SIGN (−336 A/G, rs4804803) gene and their association with the immunopathogenicity of dengue fever in Burkina Faso. **Methods:** A total of three hundred forty-one subjects, patients of all ages have been included in the study: 208 persons presenting clinical signs of dengue fever which were confirmed by diagnostic and 133 Healthy Controls. Genotyping for the CD209 variant (−336 A/G, rs4804803) was carried out using TaqMan SNP Genotyping Assays. Haplotype frequencies were inferred and compared between the study groups. **Results:** The percentage of men was 61.88% (211/341) and 38.12% (130/341) for women. The highest frequency of dengue fever (77.42%) was noted in patients with age between 20 to 40 years. Around 1.52% of the study population was positive for HIV, 40.55% were carriers of HBV and 3.83% of HCV. Genotype distribution of the CD209 variant (−336 A/G, rs4804803) was in Hardy-Weinberg equilibrium in both patients and controls. The frequency of allele A was higher than allele G; however, statistical analyses showed that there is no significant difference in genotypes GG, AG and AA in patients and controls. **Conclusion:** This related no significant association with dengue for the variant of −336 A/G in the DC-SIGN gene in an Ouagadougou population. However, our results offered the SNP frequencies in a West African population, which might be useful for the study of ethnic groups.

Keywords

Dengue Virus, CD209 Variant (−336 A/G, rs4804803), Burkina Faso

1. Introduction

Dengue fever is widespread in the tropics and subtropics regions. It is the first public health problem caused by arboviruses. Around 40% - 50% or 3.9 billion people in 128 countries are exposed to the Dengue Virus (DENV). Each year, there are 390 million cases of dengue fever with 96 million presenting symptoms and more than 3000 deaths in the world [1] [2]. Recently, outbreaks of the Dengue Fever (DF) epidemic were reported in many European countries, but also in Africa. In Burkina Faso, 1061 probable cases and 15 deaths were reported in 2016.

In August 2019, Burkina Faso once again experienced cases of DF. Some clinical cases were observed in different hospitals in the city of Ouagadougou, the capital and its surroundings. In their study, Ouattara *et al.* reported a prevalence of 23.5% in 2016 and 13.3% in 2017 [3]. In 2016, the serotypes DENV-1, DENV-2, DENV-3 and even DENV-4 were incriminated in dengue infections [4].

The onset of the severe form of dengue is due to increased endothelial dysfunction and vascular leakage. It could be explained by an increase in viremia, but also by the phenomenon of antigenic sin linked to the genetics of the host [5]. As the vaccine or effective antiviral therapy is not yet available to everyone to prophylactically or therapeutically treat DENV infection, the incidence of dengue is increasing globally around the world, especially in endemic areas [6].

Dendritic Cell-Specific Intercellular adhesive molecule-3-Grabbing Non-integrin (DC-SIGN), or Cluster of Differentiation CD209 is a C-type lectin receptor found on the surface of macrophages. CD209 plays a major role in the pathogenesis of HIV [7], HCV [8], Ebola [9] and dengue [10]. DC-SIGN also mediates the migration of DCs on the endothelium by interacting with ICAM-2. The binding of ligands to DC-SIGN induces internalization from the cell surface and is targeted to late endosomal or lysosomal compartments for processing and subsequent major histocompatibility complex Class II presentation to T cells. DC-SIGN has an intracellular domain that enables the activation of signal transduction pathways that affects the maturation of DCs. Moreover, ligand binding by DC-SIGN also leads to toll-like receptor signaling and subsequent cytokine responses [11]. The gene coding for DC-SIGN, CD209, is located in chromosome 19p 13.3 and has six exons. Complex alternative splicing events in DC-SIGN pre-mRNA generate an array of transcripts that codes for five major groups of isoforms of DC-SIGN. These isoforms include membrane-associated, soluble and truncated forms of DC-SIGN [12]. The gene has several Single Nucleotide Polymorphisms (SNPs) that affect the expression of DC-SIGN. SNPs at positions −871 (rs735239), −336 (rs4804803) and −139 (rs2287886) in the promoter region of the CD209 gene have been investigated for their association with susceptibility to infectious diseases. However, in Burkina Faso, there are yet no studies in the literature showing the influence of

the interaction of CD209 receptors on the development of dengue fever. Therefore, the aim of this study is to characterize the polymorphisms of the DC-SIGN (−336 A/G, rs4804803) gene and their association with the immunopathogenicity of dengue fever in Ouagadougou.

2. Materials and Methods

2.1. Ethics Statement and Subjects of Study

A total of three hundred forty-one subjects, patients of all ages, including children and blood donors from all professions and social categories. The blood samples were taken in the laboratories of the Saint Camille Hospital in Ouagadougou (HOSCO), the National Blood Transfusion Center (CNTS) and the Pietro-Annigoni Biomolecular Research Center (CERBA). This was a case-control analytical study realized from June to December 2018.

The study was approved by the ethics committee for health research of the Ministry of Health of Burkina Faso under number: 2018-5-052 of May 16, 2018 and a written informed consent was obtained from the study participants before blood collection. All the participants were not related to each other and were living in or around Ouagadougou.

All patients seen for consultations during the sample collection period and presenting at least two signs suggestive of dengue fever were included. In addition, voluntary blood donors received during the collection period were also included with no known history of dengue. Patients with already know another symptomatic pathology were not included in this study.

2.2. Dengue Virus Diagnostic

Serological markers for DENV were detected using Dengue Duo Comb Test Kits (Abon Biopharm Guangzhou, Co., Ltd. China). The AgNS1, IgM and IgG were detected directly from blood samples obtained by taking venous blood from the bend of the elbow. The results were read between 15 and 20 minutes.

2.3. Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) Diagnostic

We used a rapid diagnostic test "Determines HIV1/2" and SD-Bioline using immune-chromatography as a principle. We used a cobas e 411 automatic analyzers for the determination of AgHbs and Anti-HCV from plasma containing stored in EDTA tube. For HCV, the kit consisted of a vial of microparticles lined with streptavidin "M", a vial of R1 containing biotinylated HCV antigen, and R2 consisting of ruthenylated HCV antigen.

2.4. Genotyping of CD209 (−336 A/G, rs4804803)

Genotyping of CD209 rs4804803 SNP Genomic DNA was isolated from EDTA-anticoagulated blood sample using the commercial kit called "QIAamp® DNA Mini Kit" according to the manufacturer's protocol. DNA purity and concentra-

tion were determined using a Biodrop (Isogen Life Science, NV/S.A, Temse, Belgium). Approximatively 100 ng/µl of genomic DNA was used to amplify DC-SIGN gene using the rT-PCR method as previously described [13]. Genotyping for the CD209 variant (−336 A/G, rs4804803) was carried out using Custom TaqMan SNP Genotyping Assays (Applied Biosystems, Foster City, CA, 59-USA). The primer sequences were 3'-GGACAGTGCTTCCAGGAACT-5'-(forward) and 5'-TGTGTTACACCCCCTCCACTAG-3' (reverse). The TaqMan minor groove binder probe sequences were 5'-TACCTGCCTACCCTTG-3'- and 5'CTGCCCACC CTTG-3'. The probes were labeled with the TaqMan fluorescent dyes VIC and FAM, respectively. The PCR was conducted in total volume of 15 µL using the following amplification protocol: denaturation at 95˚C for 10 min, followed by 40 cycles of denaturation at 94˚C for 20 s, 60˚C annealing and extension for one minute [13]. After the PCR, the genotype of each sample was determined by measuring the allele-specific fluorescence in the ABI Prism 7500 Sequence Detection System, using SDS 1.1 software for allele discrimination (both applied biosystems).

2.5. Statistical Analysis

Genotype frequency distributions were tested for their confirmation to Hardy-Weinberg equilibrium using the Chi-square test. Comparison of allele and genotype frequencies between different study groups were carried out using the Chi-square test or Fisher's exact test as appropriate. SPSS program was used to calculate the P-value with Yate's correction and Odds Ratio (OR) with 95% interval Confidence Limits (CIs). Haplotype frequencies were inferred and compared between the study groups.

3. Results

3.1. Study Population

The study population consisted of 341 subjects with 208 patients presenting clinical signs of dengue fever which were confirmed by diagnostic and 133 Healthy Controls. The percentage of men was 61.88% (211/341) and 38.12% (130/341) for women. Among 208 dengue virus patients, women were the less represented (39.90%). The youngest was 4 years old and the majority had an age between 20 to 40 years. A highest frequency of dengue fever (77.42%) was noted in patients with age between 20 to 40 years. 1.03% of the study population was positive for HIV and concerning hepatitis, 06.15% were carriers of HBV and 1.94% HCV (**Table 1**).

3.2. Frequencies of CD209 Genotype in Dengue Cases and Healthy Controls

In this study of polymorphism of DC-SIGN gene, genotype distribution was in Hardy-Weinberg equilibrium in both patients and controls (P-value > 0.05). Genotypes AG were more frequent than genotypes AA and GG in patients

and controls. The genotype frequencies of CD209 gene are presented in Table 2.

3.3. Allele Frequencies of CD209 Gene Polymorphisms in Dengue and Healthy Controls

Table 3 presented frequencies of the DC-SIGN allele at −336 loci in 180 Dengue Fever (DF) patients and 128 controls. The frequency of allele A were higher to allele G, however statistical analyses showed that there is no significant difference between genotypes AG, GG and AA in patients and controls.

4. Discussion

This study investigated the role of host genetics on dengue susceptibility by determining polymorphisms of the gene encoding DC-SIGN among a Burkinabè population representative of the dynamic one. On the serological level, the study population presents a sex ratio (1.62) that is unfavorable to women, which does

Table 1. Serogical characteristic of the study population.

Variables	DENG IgG + *n* (%) 208 (100)	DENG IgG – *n* (%) 133 (100)	Total *n* (%) 341 (100)
Gender			
Male	125 (60.10)	86 (64.66)	211 (61.88)
Female	83 (39.90)	47 (35.34)	130 (38.12)
Age (Years)			
<20	22 (10.58)	21 (15.79)	43 (12.61)
20 - 40	163 (78.36)	101 (75.94)	264 (77.42)
>40	23 (11.06)	11 (08.27)	34 (09.97)
Serological Status			
HIV+	02 (01.03)	03 (02.26)	05 (01.52)
HBV+	12 (06.15)	121 (90.98)	133 (40.55)
HCV+	04 (01.94)	09 (06.77)	13 (03.83)

Table 2. Distribution of the CD 209 - 336 A/G (rs4804803) genotypes frequency in patients with dengue infection and controls the study population.

SNP	Genotypes	Cases and Controls *n* (%) *n* = 308 (100)	Cases *n* (%) *n* = 180 (100)	Controls *n* (%) *n* = 128 (100)
−336 rs4804803	AA	100 (32.47)	60 (33.33)	40 (31.25)
	AG	148 (48.05)	81 (45.00)	67 (52.34)
	GG	60 (19.48)	39 (21.67)	21 (16.41)
	HWE p-value	0.89	0.52	0.76

Table 3. Association between polymorphisms and risk of dengue.

SNPs	Genotypes and Alleles	Cases n (%) 180 (100)	Controls n (%) 128 (100)	OR	CI (95%)	*p*-value
−336 (Rs4804803)	**AA *versus* AG and GG *n* (%)**	60 (33.33)	40 (31.25)	1.11	0.67 - 1.78	0.71
	AG and AA *versus* GG *n* (%)	141 (78.3)	107 (83.59)	0.70	0.39 - 1.27	0.30
	A (%)	201 (55.83)	147 (57.42)		Reference	
	G (%)	159 (44.17)	109 (42.58)	0.93	0.68 - 1.29	0.74

not contradict the CNTS statistics [14] [15]. With a maximum rate of DENV infection in the 20 - 40 age group, our data are not seen as a contradiction because it is the most active part of the population and therefore the most exposed to DENV. Also the serological analysis linked to HIV, HBV and HCV presents us with rates relatively close to those national with a rate of co-infection of HBV which peaks at 6.15% [16].

Although no DC-SIGN −336 (rs4804803) genotype is significantly associated with the development of dengue, we are able to note that the frequency of the heterozygote is lower in dengue cases than in controls (45.00%/52.34%) which is not the case in the Thai population where it is the GG and AG genotype frequencies which are low and associated with an increased risk of dengue [17] [18]. While another study had, it showed that it is rather homozygous AA that would be associated with protection against the development of dengue On the other hand, in the same scope as the present study; a Brazilian study proposed that polymorphisms in the CD209 gene were not associated with dengue fever [13]. The difference in results between different studies could be due environment interactions, ethnicity-specific effects, and differences in circulating genotypes of different serotypes of DENV.

Dendritic Cells (DCs) are known to be the most powerful antigen presenting cells so far. It could not only initiate primary immune response, but down-regulate immune reaction as well [15]. DCs play an important role in maintaining immune homeostasis for their distinguished immune regulatory capability. Also, DCs are initial factors in auto-immune diseases, and play a key role in immune escape of pathogens and tumors. It is known that immune regulatory capability of DCs is closely related to pattern recognition and immune regulation of the receptors on DC surface [5] [15]. DC-SIGN recognizes several pathogens, such virus like as HIV, Dengue, West Nile virus [10] [13] [19] [20] [21] [22], tuberculosis [19]. Thus in the case of Ebola virus infection, a highly contagious and deadly virus, DC-SIGN on the surface of dendritic cells is able to function as a trans-receptor, binding to Ebola virus pseudo typed lentiviral particles and transmitting infection to susceptible cells [9]. Dendritic cells play a major role in HIV

pathogenesis. Epithelial dendritic cells seem be one of the first infected cells after sexual transmission and transfer of the virus to CD4 lymphocytes, simultaneously activating these cells to produce high levels of HIV replication [7].

In the present study, no association was found between the CD209 and DF gene polymorphisms. It was suggested earlier that in DF, DENV might use receptors other than DC-SIGN, the receptors that are known to promote antibody-dependent enhancement [13]. The present study also has a medium sample size, in particular, for DF cases and may have limited power in detecting minors the associations revealed for DF also explore the association between these polymorphisms and DHF cases could also provide valuable information in the knowledge of dengue pathogenicity. To our knowledge, this is the first study to report an association between CD209 gene variants and dengue fever in a Burkinabè population. Further studies with larger numbers of samples, especially DHF cases, are needed in the population.

In another study concerning dengue in the Taiwanese population, the authors show that the SNP rs4804803 in the CD209 promoter contributed to the susceptibility to dengue infection and complication of DHF. This SNP with the AG genotype affects the expression of cell surface DC-SIGN related to the immune system increase and less viral replication [13]. *Tassaneetrithep and al* thinks that DC-SIGN can be considered as a new target for the design of therapies that block dengue infection [10].

DC-SIGN polymorphisms and dengue susceptibility have been described in numerous studies, with a positive association in the Taiwanese population [12], and those from other countries [17] [20]. This does not turn out to be the case in the Burkina population. Indeed, we dare to think that the genetic inheritance of the host could be an explanation for this divergence. However, in the present study, the −336A allele had a frequency of 55.83% whereas this SNP with the AG genotype affects the expression of DC-SIGN at the cell surface related to immune augmentation and replication less viral [12].

5. Conclusion

This related no significant association with dengue for the variant of −336A/G in the DC-SIGN gene in an Ouagadougou population. However, our results offered the SNP frequencies in a West African population (Ouagadougou), which might be useful for the study of ethnic groups.

Acknowledgements

We would like to thank the World Academy of Sciences and the Swedish International Development Cooperation Agency (Sida) for funding this research through grant No. 17-403 RG/BIO/AF/AC_I-FR3240297757. We are also grateful to the staff of Saint Camille Hospital, the Biomolecular Research Center Pietro Annigoni and the National Blood Sanguine Transfusion center for their collaboration.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Bhatt, S., Gething, P.W., Brady, O.J., *et al.* (2013) The Global Distribution and Burden of Dengue. *Nature*, **496**, 504-507 https://doi.org/10.1038/nature12060

[2] Brady, O.J., Gething, P.W., Bhatt. S., Messina, J.P., Brownstein, J.S., Hoen, A.G., *et al.* (2012) Refining the Global Spatial Limits of Dengue Virus Transmission by Evidence-Based Consensus. *PLOS Neglected Tropical Diseases*, **6**, e1760. https://doi.org/10.1371/journal.pntd.0001760

[3] Ouattara, K., Nadembega, C., Diarra, B., Yonli, A., Obiri-yeboah, D., Belemgnegre, M., *et al.* (2018) Serological Diagnosis in Suspected Dengue Cases at Saint Camille Hospital of Ouagadougou: High Prevalence of Infection among Ouagadougou: High Prevalence of Infection among Young Adults Aged 15 to 30 Years. *International Journal of Recent Advances in Multidisciplinary Research*, **4**, Article No. 2.

[4] Eldin, C., *et al.* (2016) Identification of Dengue Type 2 Virus in Febrile Travellers Returning from Burkina Faso to France, Related to an Ongoing Outbreak, October to November 2016. *Eurosurveillance*, **21**, 18-20. https://doi.org/10.2807/1560-7917.ES.2016.21.50.30425

[5] Zhou, T., Chen, Y., Hao, L. and Zhang, Y. (2006) DC-SIGN and Immunoregulation. *Cellular & Molecular Immunology*, **3**, 279-283.

[6] Taylor-Robinson, A.W. (2016) A Putative Fifth Serotype of Dengue-Potential Implications for Diagnosis, Therapy and Vaccine Design. *International Journal of Clinical & Medical Microbiology*, **1**, Article No. 101. https://doi.org/10.15344/2456-4028/2016/101

[7] Turville, S., Wilkinson, J., Cameron, P., Dable, J. and Cunningham, A.L. (2003) The Role of Dendritic Cell C-Type Lectin Receptors in HIV Pathogenesis. *Journal of Leukocyte Biology*, **74**, 710-718. https://doi.org/10.1189/jlb.0503208

[8] Pöhlmann, S., Zhang, J., Baribaud, F., Chen, Z., Leslie, G.J. and Lin, G., *et al.* (2003) Hepatitis C Virus Glycoproteins Interact with DC-SIGN and DC-SIGNR. *Journal of Virology*, **77**, 4070-4080. https://doi.org/10.1128/JVI.77.7.4070-4080.2003

[9] Alvarez, C.P., Lasala, F., Carrillo, J., Muñiz, O., Corbí, A.L. and Delgado, R. (2002) C-Type Lectins DC-SIGN and L-SIGN Mediate Cellular Entry by Ebola Virus in Cis and in Trans. *Journal of Virology*, **76**, 6841-6844. https://doi.org/10.1128/JVI.76.13.6841-6844.2002

[10] Tassaneetrithep, B., Burgess, T.H., Granelli-Piperno, A., Trumpfheller, C., Finke, J., Sun, W., *et al.* (2003) DC-SIGN (CD209) Mediates Dengue Virus Infection of Human Dendritic Cells. *Journal of Experimental Medicine*, **197**, 823-829. https://doi.org/10.1084/jem.20021840

[11] Švajger, U., Anderluh, M., Jeras, M. and Obermajer, N. (2010) C-Type Lectin DC-SIGN: An Adhesion, Signalling and Antigen-Uptake Molecule that Guides Dendritic Cells in Immunity. *Cellular Signalling*, **22**, 1397-1405. https://doi.org/10.1016/j.cellsig.2010.03.018

[12] Mummidi, S., Catano, G., Lam, L.A., Hoefle, A., Telles, V., Begum, K., *et al.* (2001) Extensive Repertoire of Membrane-Bound and Soluble Dendritic Cell-Specific ICAM-3-Grabbing Nonintegrin 1 (DC-SIGN1) and DC-SIGN2 Isoforms: Inter-Individual Varia-

tion in Expression of DC-Sign Transcripts. *Journal of Biological Chemistry*, **276**, 33196-33212. https://doi.org/10.1074/jbc.M009807200

[13] Wang, L., Chen, R.-F., Liu, J.-W., Lee, I.-K., Lee, C.P., Kuo, H.C., *et al.* (2011) DC-SIGN (CD209) Promoter-336 A/G Polymorphism Is Associated with Dengue Hemorrhagic Fever and Correlated to DC-SIGN Expression and Immune Augmentation. *PLOS Neglected Tropical Diseases*, **5**, e934. https://doi.org/10.1371/journal.pntd.0000934

[14] CNTS (2019) Annuaire Statistique de la Transfusion Sanguine 2018. https://www.cnts.bf/en/node/133

[15] Banchereau, J., Briere, F., Caux, C., Davoust, J., Lebecque, S., Liu, Y., *et al.* (2000) Immunobiology of Dendritic Cells. *Annual Review of Immunology*, **18**, 767-811. http://www.annualreviews.org/doi/10.1146/annurev.immunol.18.1.767 https://doi.org/10.1146/annurev.immunol.18.1.767

[16] Sorgho, A.P., Martinson, J.J., Djigma, F.W., Yonli, A.T., Nagalo, B.M., Compaore, T.R., *et al.* (2018) Insights into the Interplay between KIR Gene Frequencies and Chronic HBV Infection in Burkina Faso. *Mediterranean Journal of Hematology and Infectious Diseases*, **10**, 1-11. https://doi.org/10.4084/mjhid.2018.060

[17] Sakuntabhai, A., Turbpaiboon, C., Casadémont, I., Chuansumrit, A., Lowhnoo, T., Kajaste-Rudnitski, A., *et al.* (2005) A Variant in the CD209 Promoter Is Associated with Severity of Dengue Disease. *Nature Genetics*, **37**, 507-513. https://doi.org/10.1038/ng1550

[18] Coffey, L.L., Mertens, E., Brehin, A.C., Fernandez-Garcia, M.D., Amara, A., Després, P., *et al.* (2009) Human Genetic Determinants of Dengue Virus Susceptibility. *Microbes and Infection*, **11**, 143-156. https://doi.org/10.1016/j.micinf.2008.12.006

[19] Zheng, R., Zhou, Y., Qin, L., Jin, R., Wang, J., Lu, J., *et al.* (2011) Relationship between Polymorphism of DC-SIGN (CD209) Gene and the Susceptibility to Pulmonary Tuberculosis in an Eastern Chinese Population. *Human Immunology*, **72**, 183-186. https://doi.org/10.1016/j.humimm.2010.11.004

[20] Rappocciolo, G., Jenkins, F.J., Hensler, H.R., Piazza, P., Jais, M., Borowski, L., *et al.* (2006) DC-SIGN Is a Receptor for Human Herpesvirus 8 on Dendritic Cells and Macrophages. *The Journal of Immunology*, **176**, 1741-1749. https://doi.org/10.4049/jimmunol.176.3.1741

[21] Tomo, S., Sindhujadevi, M., Kumar, V., Sevathy, S., Daisy, M.S., Agieshkumar, B.P., *et al.* (2021) Differential Platelet Receptor Expression for Viral Capture (DC-SIGN) and Plasma Leakage in Patients with Dengue Infection. *Journal of Clinical Virology Plus*, **1**, Article ID: 100039. https://doi.org/10.1016/j.jcvp.2021.100039

[22] Whitehorn J. and Simmons, C.P. (2011) The Pathogenesis of Dengue. *Vaccine*, **29**, 7221-7228. https://doi.org/10.1016/j.vaccine.2011.07.022