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Editorial

Hereditary Big Vessel Disease Genetics.

Takyuki, Yorisaki.

Department of Medical Genetics, National Cerebral and Cardiovascular Center, Osaka, Japan.

The retrovirus known as the human immunodeficiency virus (HIV) has a positive sense single strand RNA genome. Essential regulatory elements (Tat and Rev), auxiliary proteins (Gag, Env, and Pol), and viral structural proteins are all translated from the viral genome.Nef, Vpr, Vif, and Vpu are regulatory proteins [1,2]. During the 1900s, there were theories that HIV originated in nonhuman primates and spread to humans by bodily fluids such blood, semen, vaginal or rectal fluids, and breast milk. Using host receptor proteins, such as CD4 and either CC-chemokine receptor 5 (CCR) or CXC-chemokine receptor 4 (CXCR4), HIV is internalized by host cells. Therefore, HIV primarily targets CD4+ T cells and, by disarming the host immune system, can cause acquired immune deficiency syndrome (AIDS) [3,4].Toll-like receptors (TLRs), RIG-I-like receptors (RLRs), and NOD-like receptors (NLRs) are examples of pattern recognition receptors (PRRs) that identify a pathogen-related pattern of external invaders and trigger the host immune system through downstream regulators, such as nuclear factor kappa-light-chain-enhancer, in order to prevent external infection.of interferon type I, mitogen-activated protein kinase (MAPK), and activated B cells (NF-κB) [5–9]. TLR4 on the cell surface was found to be increased in monocyte-derived macrophages (MDM) in response to HIV-1 infection, according to a prior study. and mononuclear cells of the peripheral blood (PBMC) [10]. Furthermore, HIV-1's Tat protein binds directly to TLR4 and triggers the activation of interleukin-10 (IL-10) and tumor necrosis factor-α (TNF-α) [11]. According to these findings, TLR4 and HIV infection are related. In vitro, TLR4 activation remarkably prevents HIV infection from CD4+ T cells [12]. Furthermore, the rs4986790 single nucleotide polymorphism (SNP) (D299G), a functional variant of TLR4, raises the incidence of HIV-1 infection in the Indian population [13].We gathered three studies that include genetic data on ethnic origins and allele frequencies of the TLR4 gene's rs4986790 SNP from HIV-infected individuals in order to confirm whether the SNP is linked to vulnerability to HIV-1 infection [14–16]. The corresponding white control groups, which included northern and western Europeans from Utah, Tuscans from Italy, and Iberian people from Spain, were utilized for an association study after being acquired from the 1000 Genomes Project [17]. Next, we gathered information from relevant papers and conducted a meta-analysis to assess the relationship between HIV-1 infection susceptibility and the TLR4 gene's rs4986790 SNP.A PubMed literature search was done to find papers that reported the TLR4 gene's rs4986790 SNP. The following keywords were used in the search: "Polymorphism" or "susceptibility" in conjunction with "TLR4", "SNP," and "HIV" (the last search The update was completed on July 18, 2020. Following the initial screening of abstracts and titles, reports that were deemed irrelevant were eliminated. Studies that meet the following inclusion requirements are eligible: (1) looking into the relationship between rs4986790 and HIV-1; (2) a case-control or cohort research; (3) genetic data on rs4986790 of patients infected with HIV-1, (4) in full text; and (5) published in English. The following were the criteria for exclusion: (1) animal research; (2) reviews or case reports; and (3) lacking adequate genetic information.

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***Corresponding Author:** Takyuki, Department of Medical Genetics, National Cerebral and Cardiovascular Center, Osaka, Japa.
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rs4986790 of patients infected with HIV-1, (4) in full text; and (5) published in English. The following were the criteria for exclusion: (1) animal research; (2) reviews or case reports; and (3) lacking adequate genetic information.Crude additive odd ratios and 95% CIs were computed for each research to assess susceptibility to HIV infection. An additive genetic model (A allele vs. G allele) was used to compute the pooled odd ratios. The p-value and I2 were used to determine heterogeneity. worth. The pooled odd ratios were computed using a fixed effect model. Egger's weighted regression and Begg's funnel plot were used to analyze publication bias. Every statistical analysis was carried out using the R program's meta package.3.1. In three Caucasian populations, there is a strong correlation between susceptibility to HIV infection and the TLR4 gene's rs4986790 SNP (D299G).

We used the search phrases "TLR4," "SNP," and "HIV" to go through 20 research publications. paired with "susceptibility" or "polymorphism" (the most recent search update was carried out PubMed, July 18, 2020. Four pertinent studies in all were taken from the databases using our inclusion and exclusion criteria after duplicate articles were eliminated. To determine whether the rs4986790 SNP (D299G) and susceptibility are related We conducted an association analysis between HIV patients and matched Caucasian control populations, including Iberian populations in Spain, Tuscans from Italy, and northern and western Europeans from Utah, derived from the 1000 Genomes Project, in order to determine the ethnic background and allele frequencies of the rs4986790 SNP of the TLR4 gene, which were documented in earlier studies [14–16]. Notably, in every analyzed group, allele frequencies of the TLR4 gene's rs4986790 SNP showed a substantial correlation ($p < 0.05$) with HIV infection susceptibility.Four studies in all that documented a link between the rs4986790 SNP and HIV infection susceptibility were found in the literature and incorporated into our metaanalysis (Figure 1). The meta-analysis comprised 1209 controls and 1028 HIV-positive patients in totale.Comprehensive details on the studies that qualify are provided in last page.TLR4 detects bacterial lipopolysaccharide (LPS) and is found on the cell surface. Thus, prior research has demonstrated a correlation between TLR4 and phenotypes associated with bacteria, such as cirrhosis, ascites, scrub typhus, Crohn's disease, and tuberculosis [18,19].In this regard, the TLR4 gene's rs4986790 SNP (D299G) has also been studied to describe how the risk allele of the rs4986790 SNP explains the variation in disease-related characteristics.Furthermore, variations in the TLR4-MD2-LPS complex's local crystal structure were observed between TLR4 carrying the G299 allele and the wild type allele [20,21]. These results suggest that the rs4986790 SNP of the TLR4 gene is connected to the antibacterial properties of TLR4 because genetic changes result in functional alteration [22–24].

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