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Human Leukocyte Antigens in Forms of Leprosy Among Japanese Patients[1]

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Leprosy is characterized by a spectrum of clinical manifestations, resulting from interactions between the host immune response and the invading *Mycobacterium leprae* ([27]). Although the immunobiology of leprosy has received much attention over the years, individual differences in resistance and response to the bacilli are still unknown. Furthermore, leprosy does not occur in all patients who are infected with *M. leprae,* and contact with infectious cases does not always result in disease transmission. Twin, family and population studies have indicated that in humans host genetic factors are major determinants of susceptibility to leprosy ([1, 3–5, 7, 11–13, 17, 23–26, 29, 30, 32–36]).

Previous studies, including ours, have demonstrated that leprosy is associated strongly with human leukocyte antigens (HLA)-DR2, especially the DRB1*1501 and DRB5*0101 alleles of the DR2 group ([12, 25]). Yet few reports have been published on the relationship between HLA class II genotyping and the forms of leprosy, i.e., the classification of the disease ([17, 25, 31]). To the best of the authors' knowledge, no reports have been published on the relationship between HLA class II genotypes and forms of leprosy in Japanese patients based on the classification of Ridley and Jopling ([27]). To ascertain whether immunogenetic differences exist among the forms of leprosy as defined by the Ridley-Jopling classification, we have analyzed HLA-DRB1, DRB5, DQA1 and DQB1 in Japanese patients with leprosy.

MATERIALS AND METHODS

Subjects. Ninety-three unrelated leprosy patients of Japanese ancestry were enrolled in our study and were partially identical with those patients previously reported on ([12]). All patients had been hospitalized in the National Leprosarium Tama-Zensho-En in Tokyo, Japan. The diagnosis of leprosy was based on clinical manifestations, histological features and bacteriological examinations. According to the Ridley-Jopling criteria, the patients could be classified as 21 lepromatous leprosy (LL), 24 borderline lepromatous (BL), 17 mid-borderline (BB), 26 borderline tuberculoid (BT) and 5 tuberculoid leprosy (TT). We were unable to obtain samples from the TT patients because of the limited number of TT Japanese patients who met the Ridley-Jopling criteria. One-hundred-fourteen control subjects were also included in this study. The control subjects were healthy Japanese blood donors at the Saitama Medical Center and were all unrelated to each other.

All studies were approved by the Ethics Committee of the University of Tokyo. Informed consent was obtained from each subject before enrollment in the study, and the tenets of the Declaration of Helsinki were followed.

HLA serologic and genomic typing. A standard complement dependent microcytotoxicity test was used for typing the HLA-DR and HLA-DQ specificities ([16]). DNA analyses for the HLA-DRB1, DRB5, DQA1 and DQB1 alleles were performed using the polymerase chain reaction (PCR) single-strand conformation polymorphism (SSCP) method and the PCR-restriction fragment length polymorphism (RFLP)

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taron disminuidas después de corregir los valores de p. La distribución de los antígenos HLA-DRB1, -DRB5, -DQA1 y DQB1 fue similar en los pacientes de los cinco subgrupos. Concluimos que los alelos de los antígenos HLA clase II no están asociados con la forma clínica de la lepra. Tal vez otros antígenos HLA, antígenos no HLA o algunos factores ambientales, podrían jugar un papel crítico en las diferentes manifestaciones de la lepra.

RÉSUMÉ

Les allèles des antigènes leukocytaires humains (HLA) de classe II de patients lépreux japonais furent analysés afin de vérifier si il n'existe pas de potentielles différences immuno-génétiques parmi les groupes définis selon la classification de Ridley et Jopling. Quatre vingt treize patients lépreux japonais sans liens familiaux (21 lépromateux, 24 lépromateux borderlines, 17 mid-borderlines, 26 tuberculoïdes borderlines et 5 tuberculoïdes) et 114 sujets contrôles en bonne santé furent examinés. Les fréquences des allèles HLA-DRB1*1501, -DRB5*0101, -DQA1*0102 et -DQB1*0602 étaient toutes significativement augmentées chez tous les patients lépreux japonais. Les fréquences de HLA-DRB1*0405, -DQA1*03 et -DQB1*0401 étaient significativement diminuées chez les patients japonais après correction de la valeur p. En revanche, les distributions des allèles de HLA-DRB1, -DRB5, DQA1 et DQB1 n'étaient pas significativement différentes lorsque les 5 sous-groupes de patients furent comparés. Nous concluons que les allèles des HLA de classe II ne sont pas associées avec les différentes formes de lèpre. D'autres HLA, des gènes autres que HLA et/ou des facteurs environmentaux devraient jouer un rôle critique dans les différentes manifestations de la lèpre.

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