(*st4529*, *st4547*, *st4532*, *st4545*, and *st3018,* with accession numbers AF060368, AF052426, AF077666, AF077668, and AF077669, respectively). The newly found group A *st4545* sequence was more similar to various group G streptococcal *emm* sequences than to known group A *emm* sequences. One group G isolate had a previously found group G 5' *emm* sequence (*stLG6*, accession number U25741). The nongroupable Streptococcus had an *emm* sequence previously associated with group L Streptococcus (Beall and Facklam, unpub. data). These results demonstrate the usefulness of *emm* typing in areas where specific M-typing antisera are not available.

Identifying 6 (25%) of 24 GAS with new *emm* types provides further evidence of new M serotypes of GAS in Malaysia. The deduced amino acid sequences of the mature hypervariable N termini of ST4529, ST4532, ST4547, and ST3018 ranged from 43% to 82% identity to M proteins of known sequence (data not shown). The M nontypability of these isolates suggests unique serologic specificity. ST4547, ST4532, and ST3018 had 70% to 82% identity over the first 55-variable-region amino acids, with their closest matching known M proteins (M70, M27, and M22, respectively), but whether antibodies against any of these proteins would cross-protect against strains expressing these M proteins is unknown. Even though the M70 protein is 70% identical over its first 50 variable N terminal amino acids to the M33 protein, antibodies against the M70 and M33 proteins do not cross-protect, which suggests that no cross-protection would occur. The new deduced M protein with the lowest similarity to any known M protein was ST4529, whose closest match had a 43% identity over the N-terminal 55 residues of the M5 protein. *st4529* likely encodes a new serospecifically unique M protein.

These findings potentially affect vaccine development. Although new *emm* sequences were identified in a survey in the United States (5), the percentage of new strains with new *emm* sequences was much lower (6%) than was found with these Malaysian isolates. *emm* typing of a larger number of strains from rheumatic fever–and rheumatic heart disease–endemic areas is required to deduce amino acid sequences for the development of a suitable M protein–based vaccine.

Acknowledgments

We thank Sukeri Kasni and Theresa Hoenes for technical assistance.

This work was supported by University Kebangsaan Malaysia sabbatical leave grant and Fulbright Fellowship Award (1997) to Farida Jamal.

Farida Jamal,* Sabiha Pit,* Richard Facklam,† and Bernard Beall†

*University Kebangsaan Malaysia, Jalan Raja Muda Abdul Aziz, Kuala Lumpur, Malaysia; and †Centers for Disease Control and Prevention, Atlanta, Georgia, USA

References

1. Fraser CAM, Colman G. Some provisional M-types among *Streptococcus pyogenes* (Lancefield group A). In: Recent advances in streptococci and streptococcal diseases. Kimura Y, Kotami S, Shiokawa Y, editors. Bracknell (UK): Reedbooks Ltd; 1985. p. 35-6.
2. Musser JM, Kapur V, Kanjilal S, et al. Geographical and temporal distribution and molecular characterization of highly pathogenic clones of *Streptococcus pyogenes* expressing allelic variants of pyogenic exotoxin A (scarlet fever toxin). J Infect Dis 1993;167:337-46.
3. Kaplan EL. Global assessment of rheumatic fever and rheumatic heart disease at the close of the century. Circulation 1993;88:1964-72.
4. Beall B, Facklam R, Thompson T. Screening *emm*-specific PCR products for routine and accurate typing of group A streptococci. J Clin Microbiol 1996;34:953-8.
5. Beall B, Facklam R, Hoenes T, Schwartz B. Survey of *emm* gene sequences and T-antigen types from systemic *Streptococcus pyogenes* infection isolates collected in San Francisco, CA, Atlanta, GA and Connecticut in 1994 and 1995. J Clin Microbiol 1997;35:1231-5.
6. Jamal F, Pit S, Johnson DR, Kaplan EL. Characterization of group A streptococci isolated in Kuala Lumpur. J Trop Med Hyg 1995;98:343-6.
7. Johnson DR, Sramsk J, Kaplan EL, Bicova R, Havlicek J, Havlickova H, et al. Laboratory diagnosis of group A streptococcal infection. Geneva: World Health Organization; 1996.

Mutant Chemokine Receptor (CCR-5) and Its Relevance to HIV Infection in Arabs

To the Editor: Approximately 10% of HIV-infected patients may remain AIDS-free for a long time; moreover, some persons do not become infected with HIV despite multiple high-risk sexual exposures (1,2). Factors responsible for this relative resistance to infection and disease include cytotoxic T cells, neutralizing antibodies, high concentrations of certain chemokines (e.g.,

RANTES, MIP-1), human leukocyte antigen haplotype, mannose-binding protein, and tumor necrosis factor alpha, C4, and TAP polymorphism (2-4). One of the chemokine receptors, CCR-5, which along with CD4 acts as co-receptor for HIV entry into macrophages, provides upon mutation a genetic restriction to HIV infection in homozygous persons and control of disease progression in heterozygous persons (5,6). Thus a 32bp deletion in the open reading frame of the region encoding the second extracellular loop of this receptor causes synthesis of a highly truncated protein that fails to express on the cell surface, leading to loss of HIV-1 co-receptor activity.

Studies in healthy Caucasian Europeans and North Americans show that approximately 1% of the population are homozygous for this deletion (Δ32), whereas 15% to 20% are heterozygous (5-9); surprisingly, a higher percentage (up to 20%) of persons at high risk for HIV but HIV-negative are homozygous for this deletion. However, no such mutation is seen in Japanese, Native Americans, Chinese, Africans, and Tamil Indians, which suggests that in these groups either resistance to HIV infection is not present or factors other than mutated CCR-5 are in operation. African-Americans and Hispanics show a low rate of mutation, possibly because of intermarriage with Caucasians (4). The low frequency of CCR-5 mutation in Arabs with close contacts with Turks in the Eastern Province of Saudi Arabia may also be due to intermarriage. However, certain persons with mutated CCR-5 can become HIV-infected (10); in such cases other chemokine receptors (e.g., CXCR-4, CCR-2, and CCR-3) are believed to facilitate infection.

HIV infection in Saudi Arabia (population 18 million) is uncommon; the World Health Organization has so far (1985 to 1997) documented 334 cases of AIDS in this region (11). We, therefore, studied for the first time the mutation of CCR-5 in Arabs residing in Saudi Arabia. DNA was isolated from the peripheral blood mononuclear cells of 105 male blood donors not infected with HIV and nine HIV-infected patients (seven male and two female). The latter were divided into three groups, according to published criteria (2): four persons whose infection did not progress over the long term and who showed only modest decline of CD4 count after several years of infection, one person whose infection progressed normally, and four persons whose infection progressed rapidly and CD4 count fell below 100/µl within 2 years. Primers flanking 32 nucleotide deletion of CCR-5 were used to generate wild type (W) and deleted (Δ32) fragments of 189 bp and 157 bp, respectively (5). Amplification was done in a Perkin-Elmer thermal cycler 9,600, by a 20 µl reaction mixture that contained 0.25mM of dNTPs, 20 pM of each primer ('5-CAAAAAGAAGGTCTTCATTACACC-3,5-CCTGTGCCTCTTCTTCTCATTTCG-3'), and 0.5 units of Taq polymerase in 1x reaction buffer. All reagents were obtained from Pharmacia (Sweden). The amplified product was separated on 2% agarose at 120 V for 45 min and examined under UV light. Of the uninfected blood donors, 104 (99%) were homozygous for the wild type, and 1 (0.96) was heterozygous for the mutation. None of the HIV-infected patients had the mutation. Thus, the mutation is present, albeit infrequently, in Arabs. A review of 68 HIV-infected patients in our files showed that, as in Caucasians, infection progressed rapidly in 8%, did not progress over the long term in 6%, and progressed normally in 86% (2). Therefore, other hitherto unknown protective factors must be operative in Arabs.

Iman H. Al-Sheikh, Amjad Rahi, and Mohammed Al-Khalifa
King Faisal University and Regional Laboratory, Ministry of Health, Dammam, Saudi Arabia

References

1. Malkovsky M. HLA and natural history of HIV infection. Lancet 1996;348:142-3.
2. Haynes BF, Pantaleo G, Fauci AS. Toward an understanding of the correlates of protective immunity to HIV infection. Science 1996;271:324-8.
3. Cocchi F, DeVico AL, Garzine-Demo A, Arya SK, Gallo RC, Lusso P. Identification of RANTES, MIP-1a and MIP-1b as the major HIV suppressive factors produced by CD8+ T-cells. Science 1995;270:1811-5.
4. McNicholl JM, Smith DK, Qari SH, Hodge T. Host genes and HIV: the role of the chemokine receptor gene CCR-5 and its alleles (32 CCR-5). Emerg Infect Dis 1997:3:261-71.
5. Huang VY, Paxton WA, Wollinsky SM, Neumann AU, Zhang L, He T, et al. The role of mutant CCR-5 allele in HIV-1 transmission and disease progression. Nature Med 1996;2:1240-3.
6. Dean M, Carrington M, Winkler C, Huttley GA, Smith MW, Allikmets R, et al. Genetic resistance of HIV infection and progression to AIDS by deletion of the CKR5 structural gene. Science 1996;273:1856-62.
7. Liu R, Paxton WA, Choe S, Ceradini D, Martin SR, Horuk R, et al. Homozygous defect in HIV co-receptor accounts for resistance of some multiply-exposed individuals to HIV-1 infection. Cell 1996;86:367-77.

8. Samson M, Libert F, Duranz BJ, Rucker J, Liesnard C, Farber CM, et al. Resistance to HIV-1 infection in caucasian individuals bearing mutant alleles of the CCR-5 chemokine receptor gene. Nature 1996;382:722-5.
9. Zimmerman PA, Bucklewhite A, Alkhatib G, Spalding T, Kubofcik J, Combadiere C. Inherited resistance to HIV-1 conferred by an inactivating mutation in CC chemokine receptor 5- studies in populations with quantified risk. Mol Med 1997;3:23-36.
10. O'Brien TR, Winkler C, Dean M, Nelson, JAE, Carrington M, Michael NL, et al. HIV-1 infection in man homozygous for CCR-5 Δ32. Lancet 1997;349:1219-20.
11. World Health Organization. AIDS update: reported AIDS cases in East Mediterranean Region. EMR AIDS News 1997;1:8.