of samples of cord blood serum containing IgM anti-TT antibodies (*2*). The observations that samples of the corresponding maternal serum did not contain IgE anti-TT antibodies further suggested that a T_H2-like response had been induced in the fetus. This result may be explained by (i) the type of adjuvant present in the preparation of TT vaccine (that is, aluminum salts), which is commonly used to induce T_H2 response in experimental animals, and (ii) the T_H2 deviation of the immune response during pregnancy (*3*). The concentrations of cord blood IgE antibodies were very low and not clinically relevant. These observations thus extend to the human system the concept that neonatal and even fetal T cells are fully immunocompetent. The findings that immunization during the last trimester of pregnancy induces active protective immunity in both the mother and the fetus should be considered in vaccination programs, particularly in areas of the world where infectious diseases are a leading cause of perinatal mortality.

Marika Sarfati
Guy Delespesse
Louis-Charles Simard Research Center, University of Montreal, Montreal, Quebec H2L 4M1, Canada

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■

Peopling the Americas

We appreciate that Peter Parham and Tomoko Ohta have taken our map to outline their superb findings in their report "Population biology of antigen presentation by MHC class I molecules" (5 Apr., p. 67). Our contribution, however, would seem to go further than that because we have pointed out that transpacific routes from Asia, and more specifically from Japonesia, toward South America could be important in understanding the differences between North American and South American Natives (SAN) (*1*).

People with the so-called "new" (according to Parham and Ohta) allele, such as the Cayapa or Chachi from Ecuador, also display an aldehyde dehydrogenase deficiency that is molecularly similar to that found in Southeast Asian and Japanese people, but absent in Northeast Asians (*2*). In Japan, Ryukyu and Ainu populations, considered the original Japanese, included a higher percentage of slow acetylators than the "modern" Japanese (*2*) and also showed the highest prevalence of human T lymphotropic virus type I (HTLV-I) infection (*2*, *3*). Curiously, HTLV-I strains from Japan are related in their molecular structure to those found in South America (for example, Chile, Colombia, and Brazil), and HTLV-II present in SAN and in some Japanese groups is also absent in the far eastern part of Siberia (*3*).

On the other hand, the α-globin gene haplotype distributed in SAN—similar to that observed in Southeast Asian and Pacific Island populations—does not have α-globin gene deletions, and this suggests that malaria was not present in the ancient SAN (*4*). Further similarities in major histocompatibility complex type I (MHC-I), as well as type II, haplotypes and in mitochondrial DNA are observed in Japanese, Pacific (for example, Polynesians), and SAN (for example, Mapuches) populations, but are absent in the far eastern part of Siberia (*5*). These similarities add strength to the proposal that ancient voyagers could follow the Pacific sea currents that join Japan to South America, as well as other routes (*1*).

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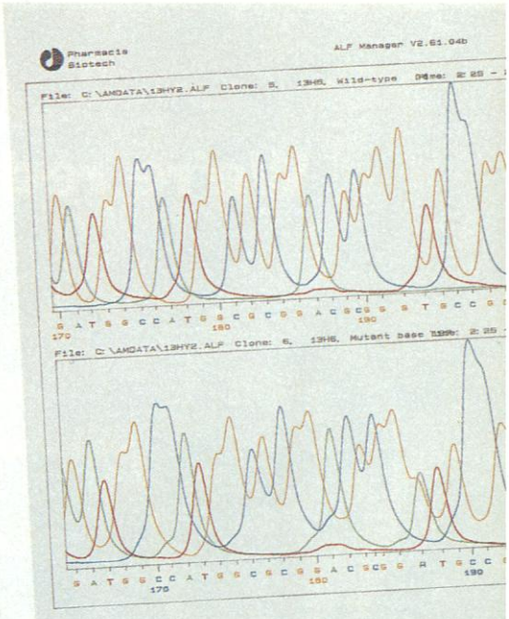

The *p53* gene from 316 breast cancer patients was sequenced using ALF automated sequencing technology. (Bergh J., Norberg, T., Sjögren, S., Lindgren A., Holmberg, L. "Complete Sequencing of the *p53* Gene ..." *Nature Medicine* 1995; 10:1029-1034.)

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Therefore, the similarities among Japanese, Pacific islanders, and SAN might be helpful not only in charting the peopling of the Americas, studying parasites, and selecting clinical treatments, but also in developing preventive measures for the deleterious effects of xenobiotics (for example, mycotoxins) (6) present in these geographical areas.

Fidias E. Leon-S.
Department of Neurology, University of Alabama, Birmingham, AL 35294, USA
Amparo Ariza-Deleon
Martha E. Leon-S.
Colombian Institute for Restorative Medicine, Bucaramanga, Colombia
Adriana Ariza-C.
Universidad Autónoma de Bucaramanga, Bucaramanga, Colombia

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7. We thank N. Gaffga for helpful comments. F.E.L.-S. was supported in part by a grant from the Ministry of Health of Colombia.

Response: The theory of transpacific contacts expounded by Leon-S. and his colleagues (*1*, *2*) holds that genetic differences observed between North and South American Natives may in part stem from an ancient admixture of the SAN with sea voyagers from the south of Japan. In the course of examining the HLA class I data, we have periodically confronted this possibility. For example. A*0211, which was first discovered in a Southeast Asian individual (*3*) and then found in the Guarani Amerindians of Brazil (*4*), initially provided a candidate for an allele that had arrived in South America by transpacific contact. However, in a recent DNA typing analysis of 553 healthy, unrelated individuals from southern Japan, A*0211 was not observed (*5*), although other "new" subtypes of A*02, A*24, and A*26 were discovered. Population studies discussed at the recent 12th International Histocompatibility Workshop and Conference produced no evidence for A*0211 in Japanese, Chinese, Koreans, or Mongolians, although the allele is present at high frequency in some Asian Indian populations (*6*).

Another recombinant allele, B*4003, which was first discovered in the Guarani (*4*) and was described by us (*7*) as being specific to South America, has now been found in Koreans, Japanese, and Mongolians (*8*). Whether Asian Indians possess a B*4003 allele is not yet known. In the Guarani population, A*0211 and B*4003 were found on the same haplotype (with Cw*0304), and to our knowledge neither of these alleles has been found in any other North or South American Native population (*9*). Given this insight, the HLA class-I haplotype B*4003, Cw*0304, A*0211 becomes a candidate for having found its way to South America by a route not involving passage through North America. India and Brazil have both been sites of Portuguese influence during the last 500 years, and because the Guarani live on the Atlantic side of the Andes, the B*4003, Cw*03034, A*0211 haplotype might more likely have been brought to South America in the course of recent

transatlantic trade rather than by an ancient transpacific contact.

A theme recurring in many presentations made at the 12th International Histocompatibility Workshop and Conference was the discovery of more and more new recombinant HLA-B alleles in the indigenous and mestizo populations of Latin America. On the order of one quarter of the known HLA-B alleles appear specific to this region, and the simplest interpretation remains that they are for the most part "new," having been formed in America since its first colonization by humans 10,000 to 35,000 years ago. Although we acknowledge the possibility that individual HLA alleles and haplotypes found in modern South Amerindian populations may have been brought to South America by a transpacific route before the European voyages of discovery, their contribution to the overall picture of HLA in SAN is likely to be minor. At present, the HLA class I and II data are remarkably consistent with North and South American Indians sharing a common origin (*2*, *6*, *8*, *10*), including the finding that the new HLA-B alleles found in South America could have been derived by recombination from those in North America.

The potential for recombination between HLA class I alleles and genes makes it likely, perhaps inevitable, that certain recombinant alleles have been formed independently in different populations. In such instances, the sharing of an allele would be the result of convergent evolution and not shared descent.

Given the increasingly rapid development of trade and associated human movements during the last 1000 years, isolated cases of HLA alleles appearing in unusual places cannot be considered as evidence for ancient contacts. For example, HLA-B*4601, a characteristic allele of the Far East, has cropped up in caucasoid populations at the western end of the Silk Road (*11*). The many linked, highly polymorphic genes of the HLA complex provide the potential for resolving the issues of time and place of population admixture that go well beyond simple observations of allele sharing.

Peter Parham
Department of Structural Biology, Stanford University School of Medicine, Fairchild Center, Stanford, CA 94305–5400, USA

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