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GENETIC EVIDENCE OF GENE FLOW FROM INDIANS TO MALAYS

Y.S. TENG* and S.G. TAN**

**University of California ICMR, Institute for Medical Research, Kuala Lumpur, Malaysia*
***Department of Biology, Faculty of Science and Environmental Studies, Universiti Pertanian Malaysia, Serdang, Selangor, Malaysia*

Summary Indians appeared in Malaysia early in its history. Sustained contacts often resulted in racial admixture. We have analyzed the biochemical genetic markers phosphohexose isomerase (PHI), lactate dehydrogenase (LDH), adenylate kinase (AK), hemoglobin, rhesus blood group and haptoglobin (Hp) among Malays (the indigenous people of Peninsula Malaysia) and Indians to provide genetic evidence for racial admixture of these two groups. The occurrence of specific rare variants PHI 3-1, LDH Calcutta-1 and Madras-1, and Hb S, as well as the gene frequencies of adenylate kinase and haptoglobin in Malays and Indians confirm the gene flow from Indians to Malays.

INTRODUCTION

Enzyme polymorphisms of common alleles occur in human populations at 25–30% of the loci (Harris and Hopkinson, 1972); rare variants occur at many loci that code for enzyme structure. Harris *et al.* (1973), in a study of European populations, found 56 rare alleles in 22 of 43 loci tested. The average heterozygosity per locus is 1.76 per 1,000. Gene frequencies of polymorphic systems are useful for estimating racial admixture and genetic distances between races based on mathematical formulas like those devised by Bernstein (1931) and Cavalli-Sforza and Bodmer (1971). Rare variants, having geographically uneven distributions, can also be valuable for studies of human migration and racial admixture. For example, Kirk (1975) used the rare variants of SOD, LDH and PMG_1 to demonstrate human migration in various parts of the world.

We have surveyed polymorphic and rare variant genetic markers, which indicate Indians have enriched the Malay gene pool in Malaysia and Singapore. Historical evidence of close contacts between Malays and the peoples of India support this hypothesis. Some Indian immigrants share with Malays the Islamic religion; therefore, these Indian immigrants would have had little problem integrating them-

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selves into the Malay community, gradually influencing the development of Malay religion and culture. A review of genetic evidence in light of the history of Indian-Malay interactions confirms their racial admixture.

Phosphohexose isomerase (PHI) 3-1 variant

Electrophoretic variants of red cell phosphohexose isomerase were first reported by Detter *et al.* (1968). At least nine variants have been found, though the incidence of these variants is usually very low. However, pHI 3-1 has been found in about 1% of Asiatic Indians in London (Detter *et al.*, 1968) and in New Delhi (Blake *et al.*, 1970); Saha *et al.* (1976) reported an incidence of PHI 3-1 in 4–5% of the Muslims and Brahmins in southwest India. In a survey of only 60 Indians in Singapore, Omoto and Blake (1972) found two individuals of the PHI 3-1 phenotype.

In a survey of 579 Malays in Kuala Lumpur, Lie-Injo and Welch (1972) detected one individual with PHI 3-1 while Omoto and Blake (1972) found two PHI 3-1 individuals among 430 Malays living in Singapore. No PHI 3-1 variant was found in a combined sample of 838 Chinese tested in Malaysia and Singapore (Lie-Injo and Welch, 1972; Omoto and Blake, 1972). Therefore, the few PHI 3-1 phenotypes found in Malays may have originated from intermarriage with Indians, given the high incidence of PHI 3-1 among south Indians who as merchant traders had contact with Peninsular Malaysia as early as the fourth and fifth centuries A.D. Fragmentary inscriptions on stone written in Indian characters found in the southern Kedah and Province Wellesley regions of the Malay Peninsula (Arasaratnam, 1970) attest to these early contacts.

Lactate dehydrogenase (LDH) Calcutta-1 and Madras-1

Variants of LDH are reported only sporadically in most populations. Among Caucasians, only seven persons had A variants and one person a B variant in over 4,000 randomly sampled individuals (Vesell, 1965; Mourant *et al.*, 1968). Das *et al.* (1970) first reported Calcutta-1 (Cal-1), an LDH variant at the A locus. Later it was discovered in 1–4% of the population of India (Das *et al.*, 1970; Blake *et al.*, 1970; Ananthakrishnan *et al.*, 1970). Madras-1, an LDH variant at the B locus has been found only in Madras city. In a survey of 696 Tamil Hindus in Madras, Das *et al.* (1970) found two individuals with the Madras-1 variant. The Indians in Malaysia have both LDH variants. In a survey of 1,171 Indians in Kuala Lumpur, Lie-Injo *et al.* (1973) found 12 individuals with the Cal-1 and five with the Madras-1 variant, giving a combined frequency of about 1.5%; among 1,026 Malays of the same survey, they detected two individuals with the Cal-1 and one with the Madras-1 variant. In a study of 259 Malays in Singapore, Blake *et al.* (1973) found one LDH variant which was indistinguishable from Cal-1; however, in a screening of over 1,000 Chinese from Kuala Lumpur and 264 Bataks from Sumatra, Indonesia, not a single Cal-1 or Madras-1 variant was detected (Lie-Injo *et al.*, 1973, 1974).

Since Calcutta-1 is widespread among the populations of India, but not in other

populations, it is likely that Indiants transmitted the Cal-1 and the Madras-1 LDH variants found in Malays of Malaysia and Singapore through genetic admixture.

Adenylate kinase (AK^2) allele

Fildes and Harris first reported the genetic polymorphism of adenylate kinase (1966). Two common alleles, AK^1 and AK^2, are found in most populations; Nigerians and American Indians, however, do not have the AK^2 allele. Only one individual in a combined sample of over 1,000 Chinese had the AK 2-1 phenotype (Shih and Hsia, 1969; Shih *et al.*, 1968; Welch *et al.*, 1971; Blake *et al.*, 1973; Mondovano and Gaensslen, 1975). The frequency of the AK^2 allele is very low among Orientals. The gene frequencies of AK^2 for Orientals in Seattle, USA, Japan and Vietnam are 0, 0 and 0.3%, respectively (Giblett and Scott, 1969; Omoto and Harada, 1970; Bowman *et al.*, 1971).

In Indians, AK^2 frequencies range from 8% in Brahmins in Madras city (Ananthakrishnan and Kirk, 1969) to 12% in Muslims of southwest India (Saha *et al.*, 1976), In Malaysia, the AK^2 frequency in Indians is 8.4% (Welch *et al.*, 1971), slightly lower than that of 9.8% found among Indians in England (Rapley *et al.*, 1967). Malays in Malaysia (Chan, 1971; Welch *et al.*, 1971) and Singapore (Blake *et al.*, 1973) have an AK^2 frequency of less than 2%. Since Indians have the highest frequency for the AK^2 allele, it is conceivable that all or some of the AK^2 genes in the Malay population of Malaysia and Singapore may derive from racial admixture with Indians.

Hemoglobin S

High frequencies of the sicke-cell gene have been found in tribal populations from various localities in India, but in the caste populations only sporadic instances of sickle-cell anemia occur, probably because of occasional mixture of tribal and caste populations (Saha and Banerjee, 1973). Vella and Hart (1959) reported the first sickle-cell anemia case in a Malaysian Indian in 1959. Lopez (1966) investigated 240 referral cases for abnormal hemoglobin in 1966 and found four Malaysians of Indian ancestry to have Hb S/β-thalassemia. Lopez and Lie-Injo (1969), in studying 243 patients who had hemolytic anemia, found three patients (all Indians) who had sickle-cell anemia.

In 1974 Ganesan reported four cases of Hb S/β-thalassemia; three in Indians and one in a Malay boy. Since then a few more cases of the Hb S trait have been found in Malays (Ganesan, 1976) but no Hb S has been found in Chinese of Malaysia and Singapore (Lopez and Lie-Injo, 1969; Blake *et al.*, 1973). It is plausible that the few Hb S genes found in Malays may have been acquired from the Indians.

Red cell antigen. Rhesus negative gene

The gene frequencies for Rh(−)*d* in Indians range from 17.3% in Calcutta Bengalis (Sen *et al.*, 1959) to 24.5% in Christian Indians in Bombay (Sanghvi, 1954).

The *d* gene is not present in several populations of southern China, notably the Hakka and Taiwanese (Dewey and Mann, 1967), in Indonesian Chinese (Maruna, 1959) or Calcutta Chinese (mainly Cantonese) (Chaudhuri *et al.*, 1967); neither is it found in Indonesians (Sutarman, 1951; Maruna, 1959) nor Javanese (Simmons and Graydon, 1951).

In 437 Malays of Malaysia, Lopez (1971) found two Rh(−) individuals. Durasaimy (cited in Hawkins, 1974) detected 16 Rh(−) in 5,282 persons tested, an incidence of about 0.3%. The Rh(−) gene in these individuals may have been obtained from the Indians. Interestingly, Mya-Tu *et al.* (1971) also postulated that the high frequency of *cde* in the Burmese population of Mandalay and the Mons of Moulmein had been introduced by the Indians.

Haptoglobin gene frequencies

The haptoglobin system has been extensively studied in India and throughout the world. Most studies characterize the populations of south India by low frequencies of the Hp^1 allele, ranging from 5.9% to 16.9%, except in the Todas whose frequency is 35% (Kirk *et al.*, 1962). The Indians of Malaysia have Hp^1 frequences of 9.2% and 10.1% (Steinberg *et al.*, 1961; Kirk *et al.*, 1960), similar to those of the south Indian populations.

The Hp^1 frequencies for Malays and Indonesians are almost identical, about 30% in both populations (Kirk *et al.*, 1960; Lie-Injo *et al.*, 1968); the Chinese of Malaysia have Hp^1 frequencies of 27% and 29% (Kirk *et al.*, 1960; Steinberg *et al.*, 1961). However, in a survey of Malays from Perlis, a northern state of Peninsular Malaysia, Kirk *et al.* (1960) found a lower Hp^1 frequency of 20% for Malays. In the same survey, they found Indians in Perlis have a Hp^1 frequency of about 9%. Thais show an Hp^1 frequency of about 24% (Kirk and Lai, 1962; Blackwell and Thephusdin, 1963).

Since the beginning of the eithteenth century, Indian Muslims from the Coromandel Coast of India, known as Chulias in Malaysia, settled in Kedah and later on Penang Island and in Perlis. South Indian Muslims, famed for their skill as merchants, gained admittance into Malay kampongs (villages) and established businesses because they shared the Islamic religion with the Malays. By the end of the nineteenth century, the Malay community had absorbed the Indian Muslim settlers, though they still constituted a separate group called Jawi Pekan (Arasaratnam, 1970). The low Hp^1 gene frequency of Malays from Perlis State, which differs significantly from that of the Malay populations in other parts of the country, very likely resulted from Malay-Indian intermarriage, because the Thais, the only other population with whom northern Malays are known to intermarry have an Hp^1 frequency of about 24%.

DISCUSSION

The Indians made their appearance and influence felt in Malaysia early in its history. Indian Muslim merchants played a role in the politics of the Malacca Sultanate (1403–1511) and furthered its development and prosperity. There is evidence that Tamil Muslim families from the Coromandel Coast occupied high positions at the court, intermarried with the royal family and influenced political events. Indian trade with Malacca expanded considerably from the fifteenth century onward; the close commercial and political connections with Malacca resulted in the founding of an Indian settlement there. The Tamil Muslim element was strengthened by continuous immigration from the Coromandel Coast (Arasaratnam, 1970).

Later other Indians settled further to the north in Kedah. There the early contacts between Indians and Malays did not bring about large scale Indian immigration but instead transmitted the Indian language, culture and religion to the Malays. Intermarriage and integration of the immigrant Indians into the Malay community was common.

Around 1840, a large scale Indian migration to and settlement on the Malay Peninsula started with the recruitment of Indian laborers to the Straits settlements for work on the sugar and coffee plantations. The Tamil speaking areas of India supplied most of Malaysia's labor needs because Malaysian recruiters were permitted to secure workers in Madras state. In 1870, the Indian population in Malaysia was about 30,000; by 1901, it had quadrupled. Most Indians lived in Perak, Selangor, and Negri Sembilan. Indians immigrated in increasing numbers because of the tremendous demand for laborers on the rubber and, later, the oil palm plantations. Today, the Indians of Peninsular Malaysia number 10,385,000, 10.6% of the population.

A great number of biochemical genetic markers are available to illustrate the gene flow from Indians to Malays. We chose only a few to demonstrate marked differences between Indians and Malays. The examples of Calcutta-1 LDH and PHI 3-1 variants are the most convincing as they are both considered Indian traits. The example of Hp^1 frequency we cited is unique because Perlis is a rather small and isolated community and because Indians have characteristically low Hp^1 frequency.

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Please send reprint requests to: Dr. Y.S. Teng, c/o Editor, G.W. Hooper Foundation, 1699 HSW, University of California, San Francisco, CA 94143, U.S.A.