Perspective Article

Personalized Medicine

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Introduction

'Genetics' is a term 'allergic' to most of the physicians, but the day has come that they need to understand and make use of it for better patient management. There are many studies in recent times showing unequivocal association of select genes with hypersensitivity to select drugs. One such widely known in the recent times is the 'Abacavir', an anti-retroviral drug widely used to treat AIDS patients, and patients with HLA-B*57:01 develop severe adverse reactions[1]. Another sister clade of this HLA, viz B*58:01 has on the other hand been shown to cause severe cutaneous adverse reactions (SCAR) with 'allopurinol' treatment of gout patients[2]. Hence in the West, clinics have started testing HLA B*57 and 58 status before prescribing these drugs.

This has great relevance to India in practicing medicine and avoiding such unwarranted outcomes. It is known that HIV infected patients with HLA B*57 normally turn into long term non progressors (LTNP) and in India too these patients show good CD4 count and may stay healthy for long without progressing towards AIDS. Our study on Bangalore cohorts is the tip of the iceberg[3]. HLA B17, particularly its split, B*57 (revised nomenclature HLA B*57) is one of the common alleles in India (Fig 1) to be called as Telugu haplotype by Brian Hamman from Durban, South Africa, as early as 1979[4]. Interestingly this allele and its haplotype HLA A1-B17 is present only in certain populations of India and not all; again not in all demes (populations, castes) of a state.

Fig - 1

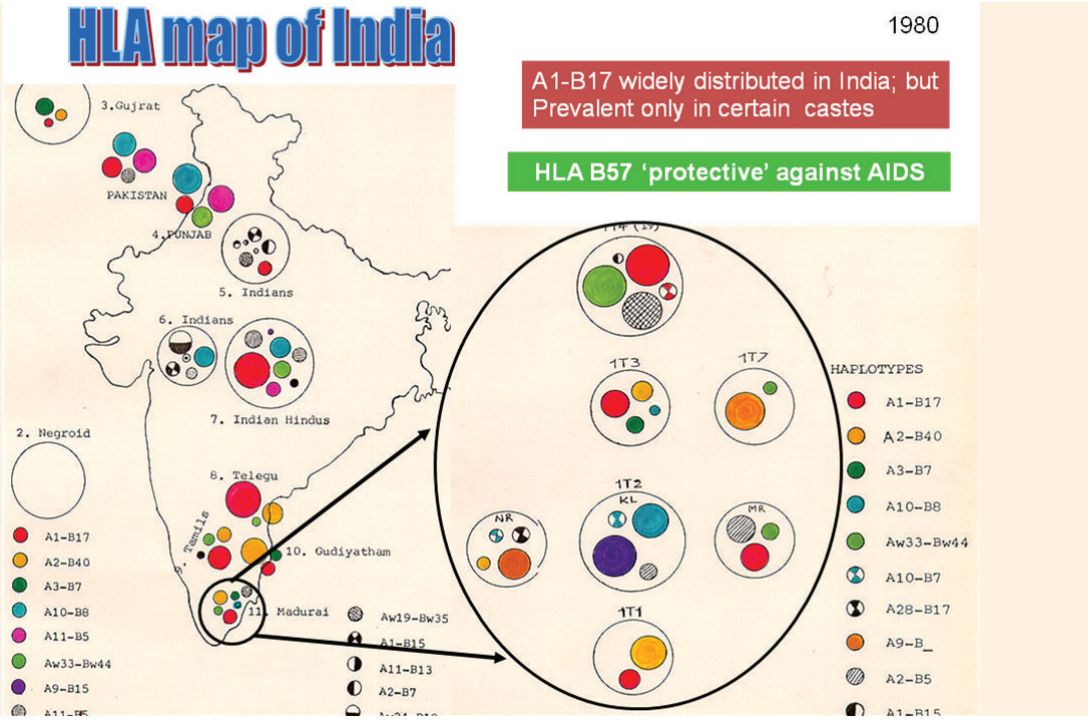

Fig 1 - HLA A-B haplotypes identified in various studies on different populations of India are mapped in the respective regions sampled. Each color represents one haplotype and the relative size, their frequencies. Larger the dot, higher the frequencies. Data were all from literature and from our lab as of 1980.

Note that while some colors are strewn all over, not all are distributed widely. The samples from Madurai, ~540, in 1980 were stratified based on social ladder, major population groups / castes (inset). Observe how distinct and disparate they are from one another. Note particularly the red dots: it is HLA A1-B17 haplotype. HLA B17 has two splits 57 and 58, of which 57 is prevalent in Indian populations studied so far. Thus B17 though present in many populations considered, they differ iIn their frequencies and not present in many other populations.

HLA B17(57) positive HIV seropositives possess normal CD4 count (>400) and they do not progress towards AIDS faster. Hence they will survive in population for longer, thus infecting more partners. This epidemiological scenario warrants to understand the immunognetic basis of LTNP (<10,000 viral count) and elite controllers (<50 viral count) in India and to undertake appropriate strategy in HIV control.

(Nostalgic memories: The HLA A-B haplotype India color map, was made by Pitchappan in 1980 for Prof. Dausset, the Nobel laureate, discoverer of the HLA system for his presentation, during one of his (Pitchappan) visits to France.: At that time, the significance of HLA B17 was not known to anybody!)

Alas, no systematic study on Immunogentic profiling of Indian populations has been carried out, sans the piece meal publications by a handful of groups in India. Hence time is ripe that a systematic study on 'immunogenome' of Indian population is underataken and further, this kind of gene diagnostic tools[5] are put to use in India for better patient management.

It is disturbing to note that 'Penicillin, called the wonder drug that saved tens of thousands (12-15%) of patients in World War II, shunned in India by medical practitioners. About 6% of Caucasians administered with this drug developed serious symptoms that required attention of an allergologist, while Asians are not susceptible to this allergy (Albin & Agarwal, 2014)[6]. In a genome wide fine mapping analysis, HLA-DRA rs7192 and rs8084 have been shown to be associated with allergy to penicillins and amoxicillin but not to cephalosporins (Guent et al 2015)[7]. In resource poor countries such as India, one has to look at cost benefit ratio of the available drugs and use the meager resources more effectively to alleviate the sufferings of the poor. Whether to use a broom stick or a nuclear missile to kill a cockroach at home is the question. One has to practice evidence based and pragmatic medicine, and spare the sophisticated antibiotics for emergencies. Time is ripe in India for practitioners and policy makers to think and act in the right direction, and to practice appropriate, evidence based, predictive medicine.

References

1) Sousa-Pinto B, Pinto-Ramos J, Correia C, Gonçalves-Costa G, Gomes L, Gil-Mata S, Araújo L . Pharmacogenetics of abacavir hypersensitivity: A systematic review and meta-analysis of the association with HLA-B*57:01. J Allergy Clin Immunol. 2015 Apr 28; S0091-6749(15): 00422-4. doi: 10.1016/j.jaci.2015.03.019.

2) Scarsi M, Bosio C, Coccoli S, Barucco A, Tavelli G, AirÃ P. Flow cytometry test to screen for HLA-B*58:01-associated allopurinol hypersensitivity. Clin Rheumatol. 2014 Jun;33(6):873-5

3) Jagannathan L, Chaturvedi M, Satish B, Satish KS, Desai A, Subbakrishna DK, Satishchandra P, Pitchappan R, Balakrishnan K, Kondaiah P, Ravi V. HLA-B57 and gender influence the occurrence of tuberculosis in HIV infected people of south India. Clin Dev Immunol. 2011:549023.

4) Hammond MG, Appadoo B, Brain P. HLA and cancer in South African Indians. Tissue Antigens 1979; 14: 296-302

5) Cargnin S, Jommi C, Canonico PL, Genazzani AA, Terrazzino S. Diagnostic accuracy of HLA-B*57:01 screening for the prediction ofabacavir hypersensitivity and clinical utility of the test: a meta-analytic review. Pharmacogenomics. 2014 May;15(7):963-76. doi: 10.2217/pgs.14.52.

6) Albin S, Agarwal S. Prevalence and characteristics of reported penicillin allergy in an urban outpatient adult population. Allergy Asthma Proc. 2014 Nov-Dec;35(6):489-94.

7) Guéant JL, Romano A, Cornejo-Garcia JA, et al. HLA-DRA variants predict penicillin allergy in genome-wide fine-mapping genotyping. J Allergy Clin Immunol. 2015 Jan;135(1):253-9. doi: 10.1016/j.jaci.2014.07.047.