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# Prevalence of HLA-B\*5701 in a Kenyan population with HIV infection

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studies complement research of David Lewis and his team at the Institute of Naval Medicine, where they had previously characterized the influence of some important stressors on immune function and disease susceptibility in Royal Marine training.<sup>11</sup>

The effect of energy deficit on compromised immune function may reflect diversion of restricted energy availability to higher priority survival functions. High intensity training (i.e., elevated metabolic demands) by itself does not seem to be the problem, as demonstrated in this most recent study with asymptomatic, fit, and energy-balanced Royal Marines. Disease resistance does seem to be compromised with some level of energy deficit. New data describe a rich environment of metabolic signals in military training with high energy demands that were not met by energy intake (Norwegian ski patrol).<sup>12</sup> These signals might be important to moderating microbiome composition and behavior and this is what bears further investigation. A pathogenic connection may come clearer from studies of skin and oropharyngeal microbiome responses to host energetics. Most specifically, the interaction between host status and colonizing species and quorum sensing signals should be considered in military field studies such as those that have characterized the variety of species involved in specific pathogenic outcomes.<sup>1,3</sup>

## Acknowledgements

The opinions and assertions in this letter are solely those of the author and do not necessarily represent the official views or policies of the United States Army. No conflicts of interest are reported.

## References

1. Crum NF, Wallace MR, Lamb CR, Conlin AM, Amundson DE, Olson PE, et al. Halting a pneumococcal pneumonia outbreak among United States Marine Corps trainees. *Am J Prev Med* 2003;25: 107–11.
2. Martinez-Lopez LE, Friedl KE, Moore RJ, Kramer TR. A prospective epidemiological study of infection rates and injuries of Ranger students. *Mil Med* 1993;158:433–7.
3. Johnson RC, Ellis MW, Schlett CD, Millar EV, LaBreck PT, Mor D, et al. Bacterial etiology and risk factors associated with cellulitis and purulent skin abscesses in military trainees. *PLoS ONE* 2016;11:e0165491. <http://dx.doi.org/doi:10.1371/journal.pone.0165491>.
4. Friedl KE. Military nutritional immunology. In: Hughes DA, Darlington LG, Bendich A, editors. *Diet and human immune function*. Totowa, New Jersey: Humana Press Inc.; 2003. p. 381–96.
5. Keys A, Brozek J, Henschel A, Mickelsen O, Taylor HL, Simonson E, et al. *The biology of human starvation*; 1950.
6. Bøyum A, Wiik P, Gustavsson E, Veiby OP, Reseland J, Haugen AH, et al. The effect of strenuous exercise, calorie deficiency and sleep deprivation on white blood cells, plasma immunoglobulins and cytokines. *Scand J Immunol* 1996;43:228–35.
7. Kramer TR, Moore RJ, Shippee RL, Friedl KE, Martinez-Lopez L, Chan MM, et al. Effects of food restriction in military training on T-lymphocyte responses. *Int J Sports Med* 1997;18:S84–90.
8. Costello R, Carlson-Newberry S, editors. *Military strategies for sustainment of nutrition and immune function in the field*. Washington DC.: National Academy Press; 1999.

9. Fallowfield JI, Delves SK, Hill NE, Cobley R, Brown P, Lanham-New SA, et al. Energy expenditure, nutritional status, body composition and physical fitness of Royal Marines during a 6-month operational deployment in Afghanistan. *Br J Nutr* 2014;112: 821–9.
10. Moore RJ, Friedl KE, Kramer TR, Martinez-Lopez LE, Hoyt RW, Tulley RE, et al. Changes in soldier nutritional status & immune function during the Ranger training course. Technical Report No. T13-92, September 1992, US Army Research Institute of Environmental Medicine, Natick, MA. 162 pp. AD-A257 437/4; AD-A257678; 1992.
11. Lewis D, Simmons MD, Pethybridge RJ, Wright JM, Chandler HC. The effect of training stress on the immune system of Royal Marine recruits. Technical Report 19/91, Institute of Naval Medicine; 1991.
12. Karl JP, Margolis LM, Murphy NE, Carrigan CT, Castellani JW, Madstien EH, et al. Military training elicits marked increases in plasma metabolomics signatures of energy metabolism, lipolysis, fatty acid oxidation, and ketogenesis. *Physiol Rep* 2017;5: e13407. <http://dx.doi.org/10.14814/phy2.13407>.

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## Prevalence of HLA-B\*5701 in a Kenyan population with HIV infection



Dear Editor,

We read with interest the article published in your Journal entitled “Real-world persistence with antiretroviral therapy for HIV in the United Kingdom: a multicentre retrospective cohort study”<sup>1</sup> which concluded that treatment discontinuation attributable to toxicity profile is not an uncommon event. They also acknowledged lack of data collection on HLA-B\*5701 status, which would heavily influence initial ART regimen and the choice to discontinue medication.

Of the 25.6 million living with Human Immunodeficiency Virus (HIV) in Africa, an estimated 1.6 million people live in Kenya.<sup>2</sup> With an HIV prevalence of 5.6%, Kenya has upscaled HIV treatment and care in the past 10 years to cover 80% of those requiring therapy.<sup>2</sup> The current Kenyan guidelines, as in the case of many developing countries, rely on WHO guidelines.<sup>3,4</sup> Abacavir is a nucleoside reverse transcriptase inhibitor (NRTI) used for treating HIV infection and is recommended as both first and second line drug options. A barrier to prescribing of abacavir in Kenya is the fear of Abacavir Hypersensitivity Reaction, and this has been compounded by the lack of availability of testing for HLA-B\*5701 testing. The Kenyan population is heterogeneous, consisting of 42 tribes

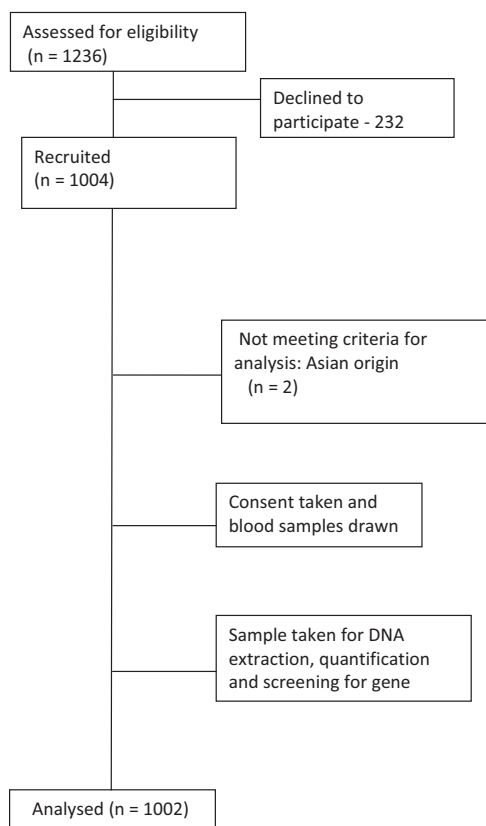


Figure 1 Study flow diagram.

with the main ethnic groups being Bantu, Nilotes and Cushites. In our study, we have determined the prevalence of HLA-B\*5701 in the black HIV positive population in Kenya using a cross sectional epidemiological survey. We recruited 1004 patients from three HIV centers: the Aga Khan University Hospital Nairobi, Mbagathi Hospital and Machakos Hospital in Kenya after ethics approval was sought from the Research Ethics Committee in Aga Khan University and from the ethics boards of Mbagathi and Machakos hospitals.

We included HIV positive individuals who reported both parents as being from the 42 tribes in Kenya, regardless of previous exposure to abacavir. After obtaining written informed consent, 5 ml of venous blood was drawn into EDTA tubes.

DNA extraction was performed using the protocol provided in the PureLink™ kit which was provided by Invitrogen Lab<sup>5</sup> and followed by quantification using the Nano drop 1000 spectrophotometer (Nano Drop Technologies, DE, USA). DNA samples were then stored at -20 °C awaiting HLA-B\*5701 screening, which was performed using the Real™ PCR test provided and produced by Sacace.<sup>6</sup> This was conducted according to the manufacturer’s protocol and then run on the Qiagen Rotor Gene thermal cycler. External validation was performed using positive and negative samples from our lab which were sent to Imperial College, London, UK.

Analysis was conducted using SPSS and Wilson score used to determine the confidence interval.

### Results

Out of a total of 1004 samples, 1002 were included in the analysis, and eight samples tested positive for the HLA-B\*5701 gene amounting to a prevalence of 0.8% (CI 0.41–1.57) (Fig. 1, Table 1).

Our study revealed that the prevalence of HLA B\*5701 gene in this HIV-infected Kenyan population was 0.8%. There is no statistical significance difference in the prevalence between ethnic groups.

Previous studies conducted in African Americans have revealed a lower prevalence of the gene as compared to Caucasians, at 2–3%.<sup>7</sup> Other studies done in Black Africans of Bantu origin revealed a prevalence of 0.52%(8). Furthermore, other genetic mapping studies have been performed among the Luo and the Nandi community (which is a sub-tribe within the greater Kalenjin community), with a prevalence of 0.8% which is consistent with our study.<sup>8,9</sup>

Our study’s prevalence of 0.8% is much lower than that reported in the African American population and is similar to that reported in the Bantu population. This may be an explanation as to why AHR is not a major problem in the Kenyan setting.

Ideally HLA-B\*5701 testing should be performed prior to abacavir use, however where it is not available and abacavir is used the incidence of AHR is likely to be low in a black Kenyan population. Education should be provided to the patient and health care provider regarding the possible side effects and the health care provider should also be vigilant for the possibility of AHR developing.

Table 1 Prevalence of HLA B\*5701 within ethnic groups.

Ethnic group	N	HLA B*5701 Status		Positive HLA B*5701 status		P value <sup>a</sup>
		Positive	Negative	%	95% CI	
Bantu	646	6	640	0.92	0.42–2	0.891
Nilotes	226	2	224	0.88	0.24–3	
Cushites	6	0	6			
Others	124	0	124			
Overall	1002	8	994	0.8	0.41–1.57	

<sup>a</sup> P value of difference between the different ethnic groups.

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## References

- Lewis JM, Smith C, Torkington A, Davies C, Ahmad S, Tomkins A, et al. Real-world persistence with antiretroviral therapy for HIV in the United Kingdom: a multicentre retrospective cohort study. *J Infect* 2017;74(4):401–7. <http://dx.doi.org/10.1016/j.jinf.2017.01.012>.
- De Cock KM, Rutherford GW, Akhwale W. Kenya AIDS Indicator Survey 2012. *J Acquir Immune Defic Syndr* 2014;66(Suppl 1):S1–2. Available from: [http://journals.lww.com/jaids/Fulltext/2014/05011/Kenya\\_AIDS\\_Indicator\\_Survey\\_2012.1.aspx%5Cn,http://www.ncbi.nlm.nih.gov/pubmed/24732819](http://journals.lww.com/jaids/Fulltext/2014/05011/Kenya_AIDS_Indicator_Survey_2012.1.aspx%5Cn,http://www.ncbi.nlm.nih.gov/pubmed/24732819).
- National AIDS and STI Control Programme. Guidelines on use of antiretroviral drugs for treating and preventing HIV infection. 2016.
- On CG. The use of antiretroviral drugs for treating and preventing HIV infection. 2013.
- Life Technologies. PureLink® Genomic DNA Kits: for purification of genomic DNA. Document Part Number 25-1012. 2013.
- Professional F, Only U. For professional use only HLA B\* 5701 Real-TM handbook. 2011.
- Mallal S, Phillips E, Carosi G. HLA-B\* 5701 screening for hypersensitivity to abacavir. *N Engl J Med* 2008;358(6):568–79. Available from: <http://www.nejm.org/doi/full/10.1056/NEJMoa0706135>.
- Orkin C, Sadiq ST, Rice L, Jackson F. Prospective epidemiological study of the prevalence of human leukocyte antigen (HLA)-B5701 in HIV-1-infected UK subjects. *HIV Med* 2010;11(3):187–92.
- Cao K, Moormann AM, Lyke KE, Masaberg C, Sumba OP, Doumbo OK, et al. Differentiation between African populations is evidenced by the diversity of alleles and haplotypes of HLA class I loci. *Tissue Antigens* 2004;63(4):293–325.

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## Cost effectiveness of screening for dengue infection in a UK teaching hospital



### KEYWORDS

Dengue;  
Screening;  
Serology;  
PCR;  
Cost-effectiveness

Dear Editor,

We note with interest the recent Letter from our Singaporean colleagues describing dengue and Zika virus co-infections.<sup>1</sup> In the UK, such infections are mostly imported,<sup>2</sup> and our local testing involves sending samples to a national reference laboratory, where the possibility of co-infections are covered by a panel of tests covering various viruses where infection presents with similar clinical features, such as dengue, chikungunya and Zika virus.

We analysed the admission clinical and laboratory parameters that were most closely associated with a positive diagnosis of acute dengue infection, in returning travellers in a UK teaching hospital over a 3-year period (2014–2016 inclusively), including the data from 173 patients (i.e. 2014: 43; 2015: 68; 2016: 62 patients).

The UK is not a dengue-endemic area so certain case criteria are required to prompt a consideration of acute dengue infection. These include: return from a country where dengue is endemic, clinical features compatible with dengue appearing within 3–10 days (more typically an incubation period of 4–7 days), i.e. fever, rash, headache, malaise, retro-orbital pain, myalgia and arthralgia.<sup>3</sup> The more severe haemorrhagic manifestations of dengue are not seen in this patient cohort and the traditional tourniquet test is not usually performed during the routine clinical examination of these patients.

Along with a compatible travel history and clinical features we examined the admission haematology and biochemical laboratory parameters and performed correlation statistics to investigate which of these variables either singly or in combination were most accurately associated with a diagnosis of acute dengue infection. This was defined as the detection of dengue RNA by PCR, the presence of dengue-specific IgM or documented dengue IgG seroconversion. In addition, we included the requesting team (general practitioners – GPs, general medicine, or infectious diseases) as an additional parameter to include in the correlation analysis.

The dengue virus testing was performed at the Rare and Imported Pathogens Laboratory (RIPL) (Porton Down, Salisbury, UK). The main test options at the PHE RIPL reference laboratory are either dengue IgG and IgM serology (if presenting more than 5 days after symptom onset) and/or dengue reverse-transcription polymerase chain reaction (RT-PCR, if presenting within 5 days of symptom onset) – NS1 antigen testing is not routinely offered. This test is a routine geographical panel (including serology and PCR as appropriate,