

Missing ethnic information in current BRCA variant databases

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Abstract

BRCA variation is highly ethnic-specific. Our analysis of major BRCA reference databases shows that nearly all databases except BIC do not provide ethnic information for their collected BRCA variants. We consider that inclusion of ethnic information of BRCA variants is necessary as it will benefit the study of human BRCA evolution, understand ethnic-basis of BRCA variation and cancer, and promote ethnic-based clinical applications in diversified ethnic populations.

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To the Editor,

BRCA mutation substantially increases risk of breast and ovarian cancer. Extensive efforts have identified large quantities of human *BRCA1* and *BRCA2* (*BRCA*) variants, and the data have been developed into multiple *BRCA* variant reference databases to guide clinical applications worldwide. Human *BRCA* genes are rapidly evolving (Huttley et al, 2000; Lou et al, 2014). This is reflected by the highly ethnic-specific nature of human *BRCA* variation (Rebbeck et al, 2018; Kwong et al, 2016; Bhaskaran et al, 2019). For example, *BRCA* variation in Africans is substantially different from non-Africans that nearly 90% of *BRCA* variants in Africans were not present in non-Africans (Figure 1) (Shen et al, 2000; John et al, 2007; Churpek et al, 2015; Zheng et al, 2018; Fiebel et al, 2019). Ethnic-specific *BRCA* variation is important for understanding the evolution of human *BRCA*, genetic basis of *BRCA* variation and cancer, and for using ethnic-based variation information for precise diagnosis, prevention and treatment of *BRCA* related cancer in diversified ethnic populations.

To understand current knowledge of ethnic-specific *BRCA* variation, we analyzed the ethnic information in the major *BRCA* databases including BRCA Exchange, ClinVar, ENIGMA, LOVD, BIC, BRCA-share and ARUP. The results show that except BIC, the current *BRCA* databases basically do not provide ethnic information for their collected *BRCA* variants (Figure 1B). The reason for lack of ethnic information in current *BRCA* databases can be that submitters do not provide the ethnic information as considered it unnecessary. This needs to be changed by the increased evidence in ethnic-specific *BRCA* variation and its relevant in cancer application. Another reason can be that ethnic origin is classified as private information being protected by law, therefore, both submitters and database curators don't want to include ethnic information. However, the *BRCA* data in public *BRCA* databases are all anonymous such that ethnic information is not relevant to privacy issue.

We believe that the ethnic information needs to be included in current *BRCA* variant databases to benefit clinical applications.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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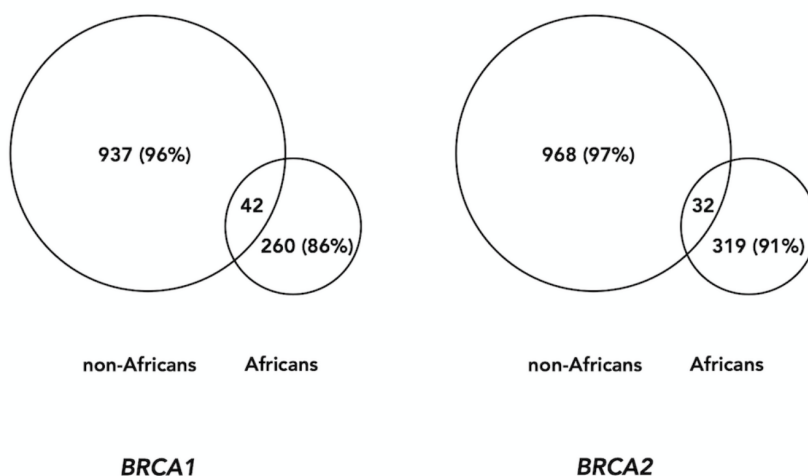
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Figure legends

Figure 1. Ethnic *BRCA* variants. A. Comparison of *BRCA* variants between African and non-African populations. A total of 302 *BRCA1* and 351 *BRCA2* variants originated from Africans were identified from literatures, and compared with the 1,051 *BRCA1* and 2,145 *BRCA2* variants with ethnic information in *BRCA*Exchange Database after removal of its African-derived variants (<https://brcaexchange.org>). The results show that 86% of *BRCA1* variants and 91% of *BRCA2* variants from Africans were not shared with these derived from non-Africans; B. Ethnic information in current major *BRCA* variant databases. It shows the information is not present in most of the databases except in BIC.

A.



B.

Databases	BRCA1		BRCA2		BRCA	
	Total	with ethnic info. (%)	Total	with ethnic info. (%)	Total	with ethnic info. (%)
BRCA share	2495	0	3454	0	5949	0
ARUP	1823	0	2103	0	3926	0
BED	19276	1051 (5)	20068	1094 (5)	39344	2145 (5)
BIC	1702	1051 (62)	1916	1094 (57)	3618	2145 (59)
LOVD	4800	852 (18)	6134	836 (14)	10934	1688 (15)
Clinvar	7787	1036 (13)	11538	1092 (9)	19325	2128 (11)
ENIGMA	3340	569 (17)	4105	530 (13)	7445	1099 (15)