Characterization of genomic variations in SNPs of PE_PGRS genes reveals deletions and insertions in extensively drug resistant (XDR) M. tuberculosis strains from Pakistan

Akbar Kanji a, Zahra Hasan a,*, Asho Ali a, Ruth McNerney b, Kim Mallard b, Francesc Coll b, Grant Hill-Cawthorne c, Arnab Pain c, Mridul Nair c, Taane G. Clark b, Ambreen Zaver a, Sana Jafri a, Rumina Hasan a

a Aga Khan University, Karachi, Pakistan
b London School of Hygiene & Tropical Medicine (LSHTM), United Kingdom
c Pathogen Genomics Laboratory, King Abdullah University of Science and Technology (KAUST), Thuwal, Saudi Arabia
d Sydney Emerging Infections and Biosecurity Institute and School of Public Health, Sydney Medical School, University of Sydney, NSW 2006, Australia

ABSTRACT

Background: Mycobacterium tuberculosis (MTB) PE_PGRS genes belong to the PE multi-gene family. Although the function of the members of the PE_PGRS multi-gene family is not yet known, it is hypothesized that the PE_PGRS genes may be associated with genetic variability.

Material and methods: Whole genome sequencing analysis was performed on (n = 37) extensively drug resistant (XDR) MTB strains from Pakistan which included Central Asian (n = 23), East African Indian (n = 2), X3 (n = 1), T group (n = 3) and Orphan (n = 8) MTB strains.

Results: By analyzing 42 PE_PGRS genes, 111 SNPs were identified, of which 13 were non-synonymous SNPs (nsSNPs). The nsSNPs identified in the PE_PGRS genes were as follows: 6, 9, 10 and 55 present in each of the CAS1, CAS2, EAI3 and Orphan XDR MTB strains studied. Deletions in PE_PGRS genes: 19, 21 and 23 were observed in 7 (35.0%) CAS1 and 3 (37.5%) in Orphan XDR MTB strains, while deletions in the PE_PGRS genes: 49 and 50 were observed in 36 (95.0%) CAS1 and all CAS, CAS2 and Orphan XDR MTB strains. An insertion in PE_PGRS6 gene was observed in all CAS, EAI3 and Orphan, while insertions in the PE_PGRS genes 19 and 33 were observed in 19 (95%) CAS1 and all CAS, CAS2, EAI3 and Orphan XDR MTB strains.

Conclusion: Genetic diversity in PE_PGRS genes contributes to antigenic variability and may result in increased immunogenicity of strains. This is the first study identifying variations in nsSNPs, Insertions and Deletions in the PE_PGRS genes of XDR-TB strains from Pakistan. It highlights common genetic variations which may contribute to persistence.

© 2014 Asian-African Society for Mycobacteriology. Published by Elsevier Ltd. All rights reserved.

* Corresponding author at: Department of Pathology and Microbiology, The Aga Khan University, Karachi, Pakistan. Tel.: +92 21 3486 4527.
E-mail address: zahra.hasan@aku.edu (Z. Hasan).
http://dx.doi.org/10.1016/j.ijmyco.2014.10.051
2212-5531/© 2014 Asian-African Society for Mycobacteriology. Published by Elsevier Ltd. All rights reserved.