Immunogenetics: Open Access

Almal and Padh, Immunogenet open access 2016, 1:2

Commentary Open Access

Frequency Distribution of Autoimmunity Associated *FCGR3B* Gene Copy Number in Indian Population

Suhani Almal[1] **and Harish Padh**[2*]

[1]*Department of Cell and Molecular Biology, B. V. Patel Pharmaceutical Education and Research Development (PERD) Centre, Thaltej, Ahmedabad, Gujarat, India*

[2]*Vice Chancellor, Sardar Patel University, Vallabh Vidyanagar, Gujarat, India*

***Correspondence author:** Harish Padh, Vice Chancellor, Sardar Patel University, Vallabh Vidyanagar, Gujarat, India, Tel: +91-2692 226812; Fax: +91-2692 237258; E-mail: hpadh@yahoo.com

Received date: May 19, 2016; **Accepted date:** June 15, 2016; **Published date:** June 20, 2016

Commentary

The availability of technologies to detect genetic variation like Single Nucleotide Polymorphism (SNP), Copy Number Variation (CNV), Insertion and Deletion (INDEL) and others has generated unprecedented opportunities for defining the genetic basis of susceptibility to complex diseases traits [1]. A spectrum of common diseases like neuropsychiatric disorders, infections, autoimmunity, cancer, cardiovascular and metabolic diseases have been analyzed to establish the association between genetic variant (CNV) and health-diseases including drug responses [2].

As drug metabolizing enzymes (DMEs) are linked to genetic variability in drug response, several genes involved in immunity have been strongly associated with susceptibility to several complex diseases which characterized human leukocyte surface antigens constitute the most striking immunity related loci associated with and involved in development of many diseases. Mapping and analysis of the human genome has paved the way to identify and investigate other genes linked to susceptibility to many autoimmune and infectious diseases [3].

The population based studies highlighting the role of copy number variable genes related to health, disease and drug metabolism has provided a new angle and depth to population genomics. Unlike SNP, CNV is relatively new entrant in our conceptual framework of understanding of health and diseases, and therefore CNV variation database is not as exhaustive as SNP database. Although the extensive presence of CNV spread throughout human genome and affecting about 7000 genetic loci and about 3000 genes initially was unexpected surprise which later on became a challenge to understand their physio-pathological roles in health and diseases [2,4]. While considering CNV, one needs to remember that there might be multiple alleles of a gene. Consideration of only copy number without reference to allele is likely to be misleading as same copy number of different alleles might have variable phenotype. Therefore, ideally a genotype should indicate copy number of a specific allele. In case of *FCGR3B*, there are three alleles: FCGR3B*1, FCGR3B*2 and FCGR3B*3, presumably with different phenotypes [5]. Published literature on CNV of *FCGR3B*, including Almal & Padh [6] is silent on the identification of allele.

Among several *FCGR3B*, which maps on human chromosome 1q23 encoding for the low affinity Fcγreceptor, Fcγ-RIIIb (CD16b),being exclusively expressed on surface of human neutrophils that recognizes IgG-antigen complexes, are thought to play a crucial role in immunity, as well as in the pathogenesis of several autoimmune diseases [7]. The variability in terms of copy number variation of *FCGR3B* is found to be involved in the impaired clearance of immune complexes, which significantly contributes to the pathogenesis of several autoimmune diseases such as Systemic Lupus Erythematosus (SLE), Anti-Neutrophil Cytoplasmic Antibody (ANCA) - associated vasculitis, Rheumatoid Arthritis (RA), type-1 diabetes and others [8]. However, the frequency distribution of *FCGR3B* gene copy number differs in various populations. It may also be noted that association of CNV of *FCGR3B* with respective diseases varies from population to population in the reported studies perhaps an indication of a need for even larger studies of case-control groups or consideration of possible significant involvement of other variants at distant loci.

Till date several population based association studies have been reported. The association of the Fc gamma receptor 3B (*FCGR3B*) gene copy number in autoimmunity in various population is well summarized [9]. In a recent report [6], researchers examined frequency distribution of *FCGR3B* gene copy number among healthy individuals in Western Indian population, and compared to available reports from various populations throughout the world. The key finding highlighted the average gene dose of two copies in Indian population (77%); while 21% of population had only one copy and 2% had >2 copies. Worldwide comparative analysis of the frequency distribution of *FCGR3B* gene copy number revealed fairly even distribution of *FCGR3B* copy number (<2) in most parts of world except countries near equator region. The reason may be deflection from the human migratory pattern, and subsequent adaption/evolution of the genomic loci related to immunity. Also contribution of epigenetic, environmental and demographic influences needs to be factored in.

This research article by Almal and Padh (2015) is a clear illustration of the worldwide frequency distribution of *FCGR3B* gene copy number and comparison with frequency reported for Indians. It is good to know frequency distribution of CNV for any gene, in this case *FCGR3B*, but the larger objective is to decipher impact of CNV of *FCGR3B* in health and diseases. Additional factor to be remembered is that *FCGR3B* has three alleles and copy number of which allele is unknown and that can't be overlooked as it will affect the phenotype.

It is conceivable that complex diseases like autoimmunity and infections may not reveal a clear correlation with any single genetic locus; as the process may be influenced by a combination of several unrelated distinct genetic loci involving SNPs, CNV and INDELS, where epigenetic and environmental influence will have to be factored in. The article by Almal and Padh, is a good beginning, but a lot has to be done before the pathophysiological effect of CNV of *FCGR3B* in health and diseases are completely unveiled.

References

1. Goldstein DB (2009) Common genetic variation and human traits. N Engl J Med 360: 1696-1698.
2. Almal SH, Padh H (2012) Implications of gene copy-number variation in health and diseases. J Hum Genet 57: 6–13.
3. Hill AV (2001) Immunogenetics and Genomics. Lancet 357: 2037–2041.
4. Redon R, Ishikawa S, Fitch KR, Feuk L, Perry GH, et al. (2006) Global Variation in Copy Number in the Human Genome. Nature 444: 444-454.
5. Ory PA, Clark MR, Kwoh EE, Clarkson SB, Goldstein IM, et al. (1989) Sequences of complementary DNA that encodes the NA1 and NA2 forms of Fc receptor III on human neutrophils. J Clin Invest 84:1688-1691.
6. Almal SH, Padh H (2015) Frequency distribution of autoimmunity associated FCGR3B gene copy number in Indian population. Int J Immunogenet 42: 26–30.
7. Bournazos S, Bournazou I, Murchison JT, Wallace WA, McFarlane P, et al. (2011) Copy Number Variation of Fcgr3b Is Associated with Susceptibility to Idiopathic Pulmonary Fibrosis. Respiration 81:142-149.
8. Schaschl H, Aitman TJ, Vyse TJ (2009) Copy number variation in the human genome and its implication in autoimmunity. Clin Exp Immunol 156:12-16.
9. Mamtani M, Anaya JM, He W, Ahuja SK (2010) Association of copy number variation in the FCGR3B gene with risk of autoimmune diseases. Genes Immun11: 155-160.