Chromosomal variation in lymphoblastoid cell lines

Matthew D. Shirley1, Joseph D. Baugher1, Eric L. Stevens2, Zhenya Tang3, Norman Gerry3, Christine M. Beiswanger3, Dorit S. Berlin3, and Jonathan Pevsner1,2,4,5

1 Program in Biochemistry, Cellular and Molecular Biology, Johns Hopkins School of Medicine, Baltimore, MD 21205
2 Program in Human Genetics, Johns Hopkins School of Medicine, Baltimore, MD 21205
3 Coriell Institute for Medical Research, Camden, NJ 08103
4 Department of Psychiatry and Behavioral Sciences, Johns Hopkins School of Medicine, Baltimore, MD 21205
5 Department of Neurology, Humbourg Research Institute at Kennedy Krieger, Baltimore, MD 21205

Abstract

Tens of thousands of lymphoblastoid cell lines (LCLs) have been established by the research community, providing nearly unlimited source material from samples of interest. LCLs are used to address questions in population genomics, mechanisms of disease, and pharmacogenomics. Thus, it is of fundamental importance to define the extent of chromosomal variation in LCLs. We measured variation in genotype and copy number in multiple LCLs derived from peripheral blood mononuclear cells (PBMCs) of single individuals as well as two comparison groups: (a) three types of differentiated cell lines (DCLs) and (b) triplicate HapMap samples. We then validated and extended our findings using data from a large study consisting of samples from blood or LCLs. We observed high concordances between genotypes and copy number estimates within all sample groups. While the genotypes of LCLs tended to faithfully reflect the genotypes of PBMCs, 3.1% (4 of 29) of immortalized cell lines harbored mosaic regions greater than 20 megabases which were not present in PBMCs, DCLs, or HapMap replicate samples. We created a list of putative LCL-specific changes (affecting regions such as immunoglobin loci) that is available as a community resource.

Conclusions

- Lymphoblastoid cell lines usually faithfully reflect the genotype and copy number of PBMCs from which they are derived.
- Occurrence of large regions of mosaic UPD and aneuploidy in 4/29 (13.7%) LCLs suggests that it is appropriate to characterize LCLs via SNP array genotyping or other methods before performing further studies.
- We have generated a list of putative LCL-specific changes (resulting from analysis of GENEVA SAGE), which may prove useful when utilizing LCLs in genomic studies.
- Studying these same cell lines over multiple passages may allow analysis of the temporal aspect of LCL-specific genomic variation.

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