Editorial DOI: http://dx.doi.org/10.18203/issn.2456-3994.IntJMolImmunoOncol20164381

Changing face of genomics in cancer medicine: Which "avatar" to treat?

Radhika A. Vaishnav

Harmony Clinic and Vadodara Stroke Center, Vadodara, Gujarat, India

Correspondence to: Radhika A. Vaishnav,
E-mail: radhikavaishnav@gmail.com

In the years following completion of the sequencing of the human genome, the era of cancer genomics has evolved from hope to reality. However, the simplistic outlook of a decade ago has yielded a more complex and individualized approach that involves carefully choreographed harmony between basic science, computational bioinformatics, and clinical acumen. As it stands today, genomic medicine is an example of translational medicine at its very best. A recent study reported by Morganella *et al*. in nature communications described the sequencing of genomes of cells taken from 560 breast cancers.[1] The genomes of tumor cells were compared to those of healthy cells from the same individual and were observed to contain thousands of mutations. The results suggest that the progression of a cell from healthy to tumor state involves multiple mutations, and they were able to cluster the breast cancers into different types based on their mutation "signatures" and their natural history of tumorigenesis. The authors, led by Serena Nik-Zainal of the Sanger Institute, Cambridge, suggest this approach may make it possible to classify breast tumors into different treatment clusters. This landmark study will help future selection of better individualized treatment and provides a roadmap for similar studies in other cancers.

The single snapshot of a tumor may not be enough, however, as elegantly shown in a collaborative European study by Yates *et al*.[2] All cancers arise from somatic mutations acquired by the DNA over time. However, not all somatic mutations detected in cancer may have been causative to the tumor. Mutations in cancer are generally classified into "driver" and "passenger" mutations; with driver mutations being clonally selected and key to the causative process, while the passenger mutations are considered non-causative.[3] In their prospective study, Yates *et al*. carried out whole genome sequencing and targeted sequencing of multiple samples of breast tumor cells taken from the same patient and applied this approach to 50 patients (27 Estrogen receptor positive [ER+]/HER2−, 3 ER+HER2+, and 20 triple negative [ER−PgR−HER2−]) pre- and post-neoadjuvant treatment. They observed genomic heterogeneity across breast cancers to varying degrees, with subclonal driver mutations observed in several of the samples. They also saw a correlation of degree of heterogeneity with tumor size which they speculated may be due to clonal sweep, which involves the expansion of a fitter subclone of the tumor. In a subset (18) of the cancers, they performed DNA sequencing from diagnostic biopsies and post-chemotherapy residual, invasive disease tissue. Six out of these 18 had subclonal mutations that were present pre- and post-chemotherapy, suggesting subclones that were present that may have been resistant to treatment. On the other hand, five cancers had mutations present in the post-treatment samples that were not there in the pre-treatment tumor, possibly representing mutations that either arose during chemotherapy or those that escaped sampling in the pre-treatment biopsy. The results suggest that multiple sampling and repeated genomic monitoring may be the future of cancer management to address clinical dilemmas such as subclonal genotypes that may be resistant to the chosen chemotherapy.

References

1. Morganella S, Alexandrov LB, Glodzik D, Zou X, Davies H, Staaf J, *et al*. The topography of mutational processes in breast cancer genomes. Nat. Commun 2016;7:11383. Doi: 10.1038/ncomms11383.
2. Yates LR, Gerstung M, Knappskog S, Desmedt C, Gundem G, Van Loo P, *et al.* Subclonal diversification of primary breast cancer revealed by multiregion sequencing. Nat Med 2015;21:751-9.
3. Stratton MR, Campbell PJ, Futreal PA. The cancer genome. Nature 2009;458:719-24.

How to cite this article: Vaishnav RA. Changing face of genomics in cancer medicine: Which "avatar" to treat? Int J Mol Immuno Oncol 2016;1:1-1.

Source of Support: Nil. **Conflict of Interest:** None declared.