Special Article

Advances in basic research in oncology in 2020: Bridging basic science and clinical care

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Cancer has now become a disease that can be understood and interpreted even at the genetic level, and the advent of massive parallel sequencing has ushered in an era of systematic documentation of these genomic changes encompassing the whole genome. The year 2020 had a dramatic start in this area with the pan-cancer analysis of the whole genome (PCAWG), a consortium of the International Cancer Genome Consortium and The Cancer Genome Atlas providing data of the integrative analysis of 2658 whole cancer genomes across 38 cancer types.[1] While the presence of an average of four to five driver mutations among most cancer types indicates a larger role for translational oncology, the absence of mutations in up to 5% of samples (particularly in pancreatic neuroendocrine tumors and chromophobe renal cell carcinoma) also emphasizes the need to explore these tumors in larger cohorts. The data reflected by the PCAWG and its companion publications is now available as an open resource at http://docs.icgc.org/pcawg [last accessed on 28 December 2020] that allows interactive browsing and download of PCAWG data.

The PCAWG data has also thrown the spotlight on "chromothripsis" as an early event in the evolution of cancers. Chromothripsis is a single "catastrophic" event where a million structural variants arise, preceding the appearance of somatic variations. Though the concept has been around for a while since its first description in chronic lymphocytic leukemia, the occurrence of this event among sarcomas, glioblastomas, lung squamous cell carcinomas, melanomas and breast adenocarcinomas,[1] and its increasing association with whole genome duplications is noteworthy. Further the PCAWG data also highlights the role of other genes and pathways (viz., ATRX and DAXX genes) other than the established TERT gene activation that is associated with replicative immortality. However, despite these unprecedented advances in basic science, the data will only be meaningful if it is integrated with clinical and treatment information. The future hopefully will witness the evolution of such comprehensive knowledge bases that will only enhance precision medicine and its utility.

The year has also seen a tremendous focus on cancer diagnostics in context of circulating tumoral factors. From circulating cell-free DNA to circulating tumor cells to extracellular vesicles and now plasma protein biomarkers, "liquid biopsies" have arrived. While detecting ctDNA in the plasma of patients with nonsmall cell lung adenocarcinomas and quantitating ctDNA burden among postoperative cases of colorectal carcinomas to detect recurrences are more established aspects of clinical care, the possibility of early detection of malignancies and disease monitoring via protein biomarkers is also gathering pace. Though CA-125, CEA, AFP, and similar markers have found limited utility, the secreted proteins trapped in exosomes and other such microvesicles[2] hold great promise and might provide tissue specific markers that can be detected using a liquid biopsy.

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Basic research and understanding the biology of these cancers in context of these molecular changes has gathered significant pace in 2020. Also, a significant level of enthusiasm has been generated by the buzz associated with newer targeted agents including AMG510[3] and Sotorasib[4] in targeting $KRAS^{G12C}$ especially with KRAS inhibitors remaining elusive for over 40 years, since the first description of this mutation in 1982. Alpelisib for PIK3CA mutant, hormone receptor positive advanced breast cancer[5] is still trending in 2020 with several investigators working on various aspects including the release of the final survival data by SOLAR-1. The year has also witnessed a "never-seen-before" expansion in companies that provide genomic and software solutions catering to the all expanding need of precision medicine. In fact, precision medicine-driven software market alone is deemed to reach a staggering $2.8 billion market by 2027. The CEO of Foundation Medicine, Cindy Porettie, believes that "2020 will be a tipping point for advanced cancer patients" and that precision medicine has reached an inflection point. It can only be hoped that the strides made at the bench translate to therapy in the years to come and that more and more patients benefit from the tools, assays, and therapy offered as part of precision medicine.

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