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Address of Correspondence

Executive Editor, TMSS Medical College Journal, TMSS Medical College
Rangpur Road, Thengamara, Bogura, Bangladesh.
Phone: 051-61830, Fax : 051-61830
e-mail: editortmcjournal@gmail.com, Web: www.tmssmedicalcollege.com

Editorial

DNA Sequencing: From Medicine to Personalized Medicine

In near future anyone's genome will be sequenced, in which treatment within hospitals will be fine-tuned according to a patient's genome. This concept is known as personalized medicine also commonly reffered as precision medicine. Until recently we can identify therapeutically "actionable" genetic lesions in some cancers. One classic example is lung cancer, in which we can detect individual mutations and manage the patient in a personalized approach by means of using "targeted therapy." Now we can classify cancer on the basis of their molecular signature which aids "targeted therapy."

Targeted therapy is a type of cancer treatment that uses drugs or other substances to precisely identify and attack certain types of cancer cells. A targeted therapy can be used by itself or in combination with other treatments, such as traditional or standard chemotherapy, surgery, or radiation therapy. Although expensive these targeted therapies are specific for cancer, having less side effects and overall excellent therapeutic outcomes than chemotherapy or radiotherapy. Actually Targeted cancer therapies offer renewed hope for an eventual "cure for cancer".

Cancer is caused by mutation in DNA. To give targeted therapy we have to determine the molecular signature of the cancer. Simply we have to know the mutation/mutations of the cancer. Mutation is a permanent change in the DNA. DNA sequencing represents the gold-standard confirmation of a mutation. In DNA sequencing we can determine the precise sequence of nucleotides in a sample of DNA (usually a PCR-amplified product). This is essential for defining the type of mutations, deletions or insertions in the DNA, and sometimes for characterization of gene fusions/translocations. In the old days, laborious manual methods were used. Nowadays, the procedure is typically performed in an automated DNA sequencer.

DNA sequencing approaches are particularly applicable to tumors such as lung carcinomas, which are genetically diverse and require a "personalized" approach. Another example is detection of microsatellite instability of colorectal cancer that is associated with mismatch repair defects, which is an indication for treatment with immune checkpoint inhibitors, regardless of cancer type. DNA sequencing also helps in therapeutic decision. For example, *TP53* mutations have a very poor prognosis in acute leukemia's, which otherwise might be expected to respond well to chemotherapy.

In the last 15 years, advancement and improvement of new sequencing technology, next-generation sequencing (NGS) has been applied increasingly in cancer genomics research fields. More recently, NGS has been adopted in clinical oncology to advance personalized treatment of cancer. There are a number of exciting possibilities for the implementation of NGS in the clinical oncology and microbiology setting:

1. Familial genetic testing

Some cancers are familial. One classic example is breast cancer caused by BRCA1 and BRCA2 genes. These genetic mutations can be detected by NGS. These genetic screening is helpful for not only diagnose a potential case but also helps in Poly (ADP ribose) polymerase (PARP) inhibitor trials and as an aid to surgical management decisions.[1] Next-generation sequencing also improves thalassemia carrier screening among premarital adults.[2]

2. Identification of Somatic Mutations in Cancers

Recently, a number of targeted therapies have become available for various cancers, most notably melanoma, lung cancer and colorectal cancer. The success of such treatments relies to very large extent on the genetic profile of the individual tumor being treated. Melanoma tumors harboring the p.Val600Glu mutation in the BRAF gene respond dramatically to the treatment with vemurafinib.[3] Whilst non-small cell lung carcinomas respond to treatment with gefitinib or erlotinib if they harbor one of a range of activating mutations in the EGFR gene.[4] Conversely, most exon 12 and 13 mutations in the KRAS gene are predictive of a lack of response to monoclonal antibody therapies, such as cetuximab and panitumumab.[5]

3. Liquid biopsy

Liquid biopsy is a noninvasive diagnostic approach involving the isolation of circulating tumor markers such as cell-free nucleic acids and circulating tumor cells from peripheral blood. Circulating biomarkers including circulating tumor DNA, circulating tumor cells, cell-free RNA, tumor-educated platelets and exosomes. They can serve as noninvasive tests for screening, diagnosis, prognosis, and therapy guidance for many solid tumors. A variety of analysis methods are being developed to detect and characterize these markers including next-generation sequencing.[6,7]

4. Emerging infectious disease research

Next-generation sequencing (NGS) technology combined with bioinformatics has become a powerful tool for detection, identification, and analyses of human pathogens. Its advantages over conventional methods are many, as sequences produced can be used for more accurate detection and characterization of pathogens, screening for presence of resistance mutations/genes, vaccine escape variants, recombination or reassortment, and virulence and pathogenicity factors.[8] The assembly and analyses of pathogen genomes can shed light on pathogen spread, contact tracing, dynamics of epidemics, and even possible sources, times, even the geographic origins of pathogen emergence.[9]

In a nutshell, personalized medicine has the potential to tailor therapy with the best response and highest safety margin to ensure better patient care. By enabling each patient to receive earlier diagnoses, risk assessments, and optimal treatments, personalized medicine holds promise for improving health care while also lowering costs. And next-generation sequencing (NGS) is one of the key pillar of personalized medicine.

1. Dr. DM Arifur Rahman, Assistant Professor, Department of Pathology, TMSS Medical College, Bogura.
2. Dr. Fahim Uddin Ahmad, Assistant Professor, Department of Microbiology. TMSS Medical College, Bogura.
3. Dr. Md Matiur Rahman, Deputy Executive Director-2, TMSS, Bangladesh.

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