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Nanobytes

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Precision Immunotherapy Milestone

The US Food and Drug Administration (FDA) recently announced its decision to go ahead with approval of existing immunotherapeutic drug Keytruda to treat cancers based on the genetic profile of a tumor rather than the type of cancer. Such a decision to approve a drug in a "site agnostic" manner is a first, with drugs traditionally approved for specific types of cancer based on location or cell type. The drug has been given the green light for individuals – adults as well as children - who have solid tumors with microsatellite instability or mismatch repair deficiency and that do not respond to other treatment. Both of these genetic changes involve impairment of the cell's gene repair system and lead to increased mutations. Such genetic changes, although rare overall among cancers, are fairly common in colorectal, endometrial, and gastrointestinal cancers. The FDA used accelerated approval based on five clinical trials that studied it in 15 different cancer types. Almost 40% individuals saw shrinkage of tumors after receiving Keytruda. The development is encouragement for other immunotherapies in the pipeline as well - with over 200 immunotherapeutics currently in various stages of clinical trial or approval.

Targeted Fusion Assays

Illumina has announced a comarketing and distribution agreement with ArcherDX. The agreement allows customers outside the United States to be able to access Archer® FusionPlex® products through Illumina distribution. The purpose of the kits is to be able to detect gene fusions using next-generation sequencing (NGS). The assays can detect both known as well as novel gene fusions from only 20 ng nucleic acid derived from formalin-fixed paraffin-embedded samples. The targeted fusion assays will focus on clinical research in various types of cancers including thyroid, lung, sarcomas, acute myeloid leukemia, acute lymphoblastic leukemia, and lymphoma.

Molecular Diagnostics

Agilent Technologies and Agendia entered into an agreement on molecular cancer diagnostics - specifically, to develop an RNA-Seq version of Agendia's existing mamma print and blue print assays. The advantage is that the tests will be decentralized and more accessible to a global patient population and can hence be performed at locations closer to the patient. Agilent Technologies specializes in target enrichment for NGS platforms.

Old Target, New Drug

A South Korean group (Oram therapeutics) has developed an experimental cell-penetrating drug to target Ras, which is alarmingly highly mutated in pancreatic cancers (95%). Colorectal cancers (45%) and lung cancers (35%) and melanomas also commonly show Ras mutations. The new molecule, RT11-I, is a monoclonal antibody that penetrates cells, binds to Ras and blocks its function in tumor signaling.[1]

Gene-environment Interplay

A group in Cambridge, the UK has uncovered a mechanism[2] by which exogenous chemicals (such as formaldehyde) and endogenously produced aldehydes (like acetaldehyde) can induce depletion of BRCA2 in cells containing one mutant copy of BRCA2. As a result, spontaneous mutagenesis is triggered through replication fork instability, and a mechanism called unscheduled R-loop formation, resulting in chromosomal aberrations. Although neither BRCA2 nor aldehydes are new to scientists, the unraveling of the mechanism of toxin-induced mutagenesis in cells containing one mutant BRCA2 copy puts these common chemicals in the limelight again in carcinogenesis, opening up avenues for careful design of therapies that include aldehyde scavenging for prevention of breast cancer.

References

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