From DNA to precision medicine, researchers discuss breakthroughs in cancer research

By Samantha Black, PhD, ScienceBoard.net Editor in Chief

The Science Advisory Board

See Original Article

June 22, 2020 -- From the use of novel technologies such as machine learning and CRISPR, to gaining a deeper understanding of the genetic and molecular drivers of cancer, researchers from around the globe shared their progress with the cancer research community on June 22 at the opening plenary session of the American Association for Cancer Research (AACR) 2020 virtual annual meeting II.

The session discussed topics on the cutting edge of cancer research, as indicated in the session's title, "Turning Science into Lifesaving Care." With an introduction from Dr. Antoni Ribas, PhD, president of the AACR, this jam-packed session highlighted advancements in diverse fields of basic and clinical science with implications in cancer therapies.

Circular extrachromosomal DNA promotes cancer growth

First up, Dr. Howard Y. Chang, PhD, from Stanford University shared how his team is investigating how epigenetic changes in chromatin impact cancer genomics. They found that circular extrachromosomal DNA (ecDNA), which are circular DNA fragments that lack telomeres and centromeres and can be thought of as oncogene plasmids, are much more prevalent than previously thought.

The lack of chromatin structure of circular ecDNA makes it more accessible, and further supports transcription of cancer oncogenes. These serve to amplify expression of oncogenes that provide an advantage for replication and are linked to genetic susceptibility to various cancers.

With the ability to identify and track the chromatin structure of single-cell phenotypes, Chang suggests that the paradigm for cancer treatment could shift toward reeducating the immune system to treat tumors as nonself entities. For example, CRISPR technology can be used to "reboot" T cells with an exhausted phenotype to again target cancer cells after treatment.

CRISPR improves T-cell therapies

In a similar but unique approach, Dr. Alex Marson, PhD, from the Gladstone-University of California, San Francisco Institute of Genomic Immunology discussed how CRISPR genome engineering can be used to understand how specific sequences can control T-cell behavior and potentially modify T cells to make them more effective for treating cancer or other diseases.

Among the techniques discussed, Marson explained how a patient's primary T cells can be isolated from a blood sample and target sequences can be knocked-in with a nonviral homology-directed repair template library using the CRISPR-Cas9 ribonucleoprotein. This creates a barcoded modified T-cell library that can identify which immune cell therapy may be most effective for a particular patient.

Predicting precision medicine with artificial intelligence

The idea of precision medicine was also discussed in the plenary session. Olivier Elemento, PhD, from Weill Cornell Medicine provided insights on how he and his colleagues are working toward artificial intelligence-driven precision medicine for cancer patients.

Advances in whole-genome sequences and artificial intelligence have enabled researchers to map genotypes to phenotypes, and apply them to individual cancer patients and predictions. For instance, Elemento described two cases where whole-genome sequencing was leveraged to determine that human epidermal growth factor receptor 2 (HER2) was significantly amplified in a patient with metastatic bladder cancer and recurrent uterine cancer.

The knowledge of this mutation, not traditionally associated with these cancers, was translated to provide therapeutic options that were previously unknown. This cancer- and tissue-agnostic approach relies on targeting mutations.

Moreover, artificial intelligence can be used to predict targets of molecules without a known mechanism of action, which could accelerate drug discovery. Here, machine learning uses gene expression data, cell line viability, known side effects, and structural information to predict targets. Researchers found that the more data you have, the more you are able to predict, with over 90% accuracy, once enough data have been included.

With over 50,000 expected attendees, AACR's virtual meeting will showcase the best in cancer research with the focus of how new molecular and genetic drivers can accelerate the development of therapies and rapidly bring them to the clinic.