MEDiC Life Sciences
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MEDiC

Improving functional genomics to find novel gene targets and biomarkers

Using three-dimensional tumor models and a next-generation technology platform, MEDiC Life Sciences aims to break boundaries in cancer drug development.

Cancer drug development is being stymied by a lack of two critical elements: novel gene targets and biomarkers for stratifying patients in clinical trials. MEDiC Life Sciences is addressing both gaps. Using a platform that pairs clustered regularly interspaced short palindromic repeats (CRISPR) functional genomics with three-dimensional (3D) tumor models and cancer-immune co-culture systems, the biotech is helping companies including Bristol Myers Squibb to overcome oncology challenges.

Multiple companies have identified functional genomics as the key to finding genes that cause cancer, as opposed to just identifying genes that correlate to cancer. However, functional genomics is yet to fulfill its promise as a tool for discovering causal relationships between genes and tumor development.

Enhancing functional genomics

MEDiC, a spinoff from the Stanford University SPARK translational research program and backed by Illumina Accelerator, identified the reliance of the first wave of functional genomics companies on two-dimensional (2D) monolayer culture systems as a limitation. The companies use the systems to analyze the role of genes in cancer development, but the models are a poor mimic of what happens in vivo.

In the body, tumors develop in three dimensions and are influenced by the immune system. 2D models cannot replicate those critical details; they can only show how genes affect the growth of tumors in two dimensions in the absence of the immune system.

Recognizing the limitations, MEDiC has made massively scalable 3D tumor models optimized for CRISPR screenings and scalable cancer-immune co-culture systems that use human cancer and immune cells. By pairing the models and systems with its advanced CRISPR functional genomics platform, the biotech can find genes that facilitate growth, drive drug resistance and help cancer cells evade the immune system.

The addition of the scalable cancer-immune co-culture system is critical to the success of the platform. In the body, the interaction between cancer cells and the immune system is a key factor in whether tumors grow and spread. Yet, most functional genomics platforms are unable to account for the effects of the immune system. Some companies run screens in cancer-immune co-culture systems that use mouse cells but MEDiC's pairing of human cancer and immune cells with functional genomics sets it apart. MEDiC's proprietary ImBridge is the key to enabling synthetic engagements between allogeneic human cancer cells and immune cells from any sources for such large-scale functional genomics screenings (Fig. 1).

MEDiC is using the platform to address two major blindspots in cancer drug development. The pairing of human samples and cancer models provides both patient correlation and causality information, allowing MEDiC to pinpoint optimal gene targets for solid cancer—incorporating tumor-extrinsic factors such as the immune system—and find biomarkers that identify the people most likely to respond to a therapy.

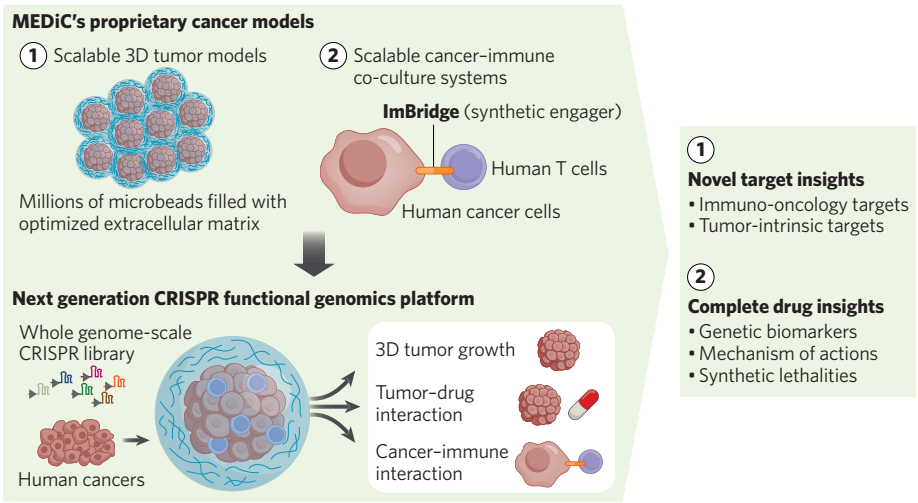

Fig. 1 | MEDiC's CRISPR functional genomics platform for uncovering novel gene targets and biomarkers. This approach combines CRISPR functional genomics with patient-tumor-like cancer models, elevating the precision, reliability, and translational potential of identified targets and biomarkers for solid cancer research.

Validating the platform

The biotech published proof-of-concept work[1] on the platform in *Nature* in 2020. In that project, MEDiC showed that genome-wide CRISPR screens in 3D lung-cancer spheroids found genes that drove tumor growth in vivo but were missed by 2D monolayer models.

Building on the proof-of-concept study, MEDiC performed internal and partnered work that has provided industrial validation of the platform. Bristol Myers Squibb partnered with the biotech in 2023 to use its scalable 3D tumor models to perform CRISPR functional genomics screens in its target solid tumor indications[2].

MEDiC has also used the platform to identify novel gene targets for its internal solid tumor programs. Having discovered novel targets for hepatocellular carcinoma and triple-negative breast cancer, areas of major unmet medical need, the biotech is advancing toward lead optimization while working to expand the pipeline and pursue new indications.

Through a second, undisclosed partnership, the biotech is using its platform to find biomarkers that could identify the patients who are most likely to respond to a cancer candidate in clinical development at a major pharma company.

The second partnership has validated the benefits of using 3D tumor models, rather than traditional 2D monolayers, for the discovery of cancer biomarkers. MEDiC has performed screening using its 3D models and 2D monolayers at the same time. While the 2D monolayers failed to provide meaningful signals, the 3D models have generated biomarkers that could facilitate the stratification of patients in clinical trials.

MEDiC, supported by a growing body of scientific and industrial validation, is now working to expand its network of partners to maximize the benefits of the platform technology. As the internal and partnered programs advance, MEDiC and its collaborators will realize the long-unfulfilled potential of genomics by accurately measuring the causality of variants and advancing life-changing treatments for solid tumors.

1. Han, K. *et al. Nature* **580**, 136–141 (2020).
2. MEDiC Life Sciences Announces Collaboration with Bristol Myers Squibb on Tumor Target Discovery. https://www.businesswire.com/news/home/20230605005591/en/MEDiC-Life-Sciences-Announces-Collaboration-with-Bristol-Myers-Squibb-on-Tumor-Target-Discovery (2023).

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