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# BridGene BioSciences Develops Chemoproteomic Platform for Drug, Target Discovery

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NEW YORK – Biomedical company BridGene Biosciences is expanding the project pipeline of its chemoproteomic isobaric mass-tagged affinity characterization (IMTAC) discovery platform to discover and develop small molecules for hard-to-drug therapeutic targets, and plans to initiate at least one IND-enabling project in the coming year.

The company also recently entered a collaboration with Takeda Pharmaceutical, involving the use of the IMTAC platform to identify drugs and therapeutic targets for neurodegenerative disease.

The IMTAC platform matches drugs to target molecules via their relative binding affinities through a proprietary computational algorithm. The platform broadly consists of three key elements: a unique covalent small-molecule library, live cell screening, and quantitative mass spectrometry.

Live cells are exposed to a small molecule library, whose components bind to the cells' proteins. Cells are then lysed to pull down the proteins bound to molecules from the library. Those proteins are enriched and digested into peptides of roughly equivalent masses (isobaric) for mass spec analysis, which identifies the proteins and quantifies their relative binding affinities to their corresponding small molecules.

BridGene then evaluates any small molecules that bind to cellular targets of interest for their ability to impact disease phenotypes.

The strategy is similar to other companies applying high-throughput protein analysis technologies to drug discovery, such as Interline Therapeutics, which performs protein pulldown followed by isobaric labeling and mass spec.

Ping Cao, BridGene's cofounder and CEO, explained that IMTAC differs in several ways, key among these being its proprietary small-molecule library, the ability to achieve proteome-wide screening as well as target-focused screening in live cells, and the company's binding affinity analysis algorithm.

The platform can also be used to screen both covalent and non-covalent small molecules.

"Competing platforms focus on just covalent small molecules, to our knowledge," Cao said.

"Our biggest advantage," he added, "is we can identify drugs for traditionally undruggable targets, including targets containing shallow binding pockets."

Ligand binding sites often correspond to large and/or deep clefts found along a protein's surface. A pocket's depth can help to reinforce any binding activity occurring within the pocket by constraining a ligand's movement and locking it geometrically in place. Shallow binding pockets, by comparison, generally require more binding energy to hold a ligand, such as a bioactive compound, in place, making it more challenging to target these sites.

Recently, the company showcased IMTAC's drug and target discovery abilities through five abstracts presented at the 2021 AACR-NCI-EORTC Virtual International Conference on Molecular Targets and Cancer Therapeutics.

The discoveries discussed included small-molecule ligands for hard-to-drug targets such as RhoA, TEAD1, SRSF1, and WDR5, as well as previously unknown non-kinase targets for ibrutinib and sunitinib.

The company is currently in the early stages of developing small molecule inhibitors of TEAD1 to treat mesothelioma, glioblastoma, liposarcoma, and pancreatic cancer, among others. It has also discovered several inhibitors of the epigenetic modulator WDR5, and plans to develop new drugs targeting WDR5-dependent cancers, that are based on the lead hit from this screen, called BGS2597.

Finally, BridGene has identified a covalent ligand of the oncogenic RhoA-Y42C mutation, that inhibits cell growth in the mutation-bearing CCK-81 cell line.

The TEAD1 project is currently the furthest along. The company has planned an IND-enabling study for next year, and hopes to file for an IND in 2023.

Although the company was sparing with the details of other projects, it has a busy pipeline planned.

"We will do lead optimization for three to five projects and will complete [an] *in vivo* study for three projects every two years," said Cao, "and then move one to two projects into the IND [phase], and then we will license out other projects."

Throughout these projects, Cao added that BridGene would continue to improve upon the IMTAC platform and "will introduce more optimization [to] further increase throughput and expand our small molecule library."

BridGene currently uses the IMTAC platform in collaboration with several biotechs and pharmaceuticals. The company recently expanded upon a collaboration with Takeda Pharmaceutical Company, for instance, to discover targets and small molecule drug candidates for neurodegenerative disease.

"Access to BridGene's novel chemoproteomics platform can help us to rapidly identify novel targets and novel drug candidates with the potential to target underlying mechanisms of debilitating neurological disorders," Ceri Davies, head of Takeda's Neuroscience Drug Discovery Unit, said in a statement.

BridGene launched in 2018 and closed a $12 million Series A funding round in May.

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