EMERGING COMPANY PROFILE

LIGHT-SPEED ELECTROPHYSIOLOGY

By Selina Koch, Staff Writer

The inability of standard electrophysiological methods to detect high resolution signals in a large number of cells simultaneously has hampered the development of new therapies for neurological and cardiac diseases. Q-State Biosciences Inc.'s high throughput Optopatch platform solves that problem by applying optogenetic tools to large populations of neurons or cardiomyocytes, enabling the CRO to efficiently assess disease phenotypes and screen compounds.

Optopatch uses patient-derived induced pluripotent stem (iPS) cells engineered to express an actuator that triggers cellular activity in response to light pulses, and a voltage indicator that emits light as a visual readout when cells are electrically active. Q-State's activators include variants of *Scherffelia dubia* channelrhodopsin modified to respond to shorter wavelengths and lower intensities of light than routinely used actuators. The indicators are based on archaerhodopsin 3, a protein derived from a Dead Sea microorganism that ordinarily converts infrared light from the sun into electrical energy.

"We found a way to run this reaction in reverse" and increase the protein's response time, brightness and trafficking to the cell surface compared with the natural protein, co-founder Adam Cohen told BioCentury.

The actuators and indicators operate at two different wavelengths of light — blue and infrared — to avoid the cross talk between input and output pulses that limits the utility of existing GFP-based indicators. Q-State developed each actuator and indicator for use in different cell types and experiments.

The company has protocols for differentiating patient-derived iPS cells into a variety of neuronal subtypes or cardiomyocytes, but can also utilize iPS cells provided by clients or obtained from third parties.

Cohen, who is also a professor of chemistry and chemical biology and physics at Harvard University, said Optopatch can gather information from stimulated cells on a scale that existing electrophysiological methods cannot match.

He noted that the gold standard patch-clamp technique provides robust signals but can only record electrical activity in one cell at a time, whereas microelectrode arrays can simultaneously record signals from tens to hundreds of cells but are substantially less sensitive. "You can't measure the waveform of the action potential" with arrays, he said.

"Our system is more like a million simultaneous patch clamps," he said. "We can now image activity with sub-millisecond temporal resolution and on spatial scales, from events in single dendritic spines to activity across thousands of neurons" or cardiomyocytes.

Q-State has replicated the results of conventional methods showing that hyperexcitability in motor neurons derived from patients with amyotrophic lateral sclerosis (ALS) resulted from low potassium currents and that a potassium channel Kv7 activator reduced the phenotype. Q-State and its academic collaborators published those data in *Cell Reports* last year.

According to Co-founder David Margulies, Q-State's CRO services include demonstrating Optopatch can create assays for a specific disease phenotype, and using those assays to screen compounds, study a lead compound and stratify patients for clinical trials. He added that Q-State can also function as a full development partner.

GlaxoSmithKline plc is a Q-State client for a cardiomyocyte-based project, and Q-State is a development partner on multiple projects with other undisclosed companies, Margulies said.

The company has begun its own drug discovery efforts and is raising a series A round to fund those programs and increase its capacity as a CRO. Cohen and Margulies declined to disclose details about the programs and funding round.

Q-STATE BIOSCIENCES INC., Cambridge, Mass.
Technology: Optical electrophysiology platform for assessing neuronal and cardiac cell function in iPS cell-derived disease models
Disease focus: Supply/service, neurology, cardiovascular
Clinical status: Research
Founded: 2013 by Adam Cohen, Kevin Eggan, David Margulies and Joel Kralj
University collaborators: Harvard University
Corporate partners: Undisclosed
Number of employees: 15
Funds raised: Undisclosed
Investors: Fidelity Biosciences, undisclosed angels
CEO: None
Patents: Undisclosed issued patents covering multiple aspects of the Optopatch platform and its applications

COMPANIES AND INSTITUTIONS MENTIONED

GlaxoSmithKline plc (LSE:GSK; NYSE:GSK), London, U.K.
Harvard University, Cambridge, Mass.
Q-State Biosciences Inc., Cambridge, Mass.

REFERENCES

Wainger, B., et al. "Intrinsic membrane hyperexcitability of amyotrophic lateral sclerosis patient-derived motor neurons." *Cell Reports* **(2014)**