Title

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Journal

Molecular Psychiatry, 28(1)

ISSN

1359-4184

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Publication Date

2023

DOI

10.1038/s41380-022-01810-5

NEWS

Meeting report for the 2022 UC Irvine Center for neural circuit mapping conference: linking brain function to cell types and circuits

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Molecular Psychiatry (2023) 28:2–3; https://doi.org/10.1038/s41380-022-01810-5

Emerging evidence suggests that brain circuits can be therapeutically targeted to treat neurological, neuropsychiatric and neurodevelopmental disorders. To develop such therapeutic approaches in the clinic with precision, the targeted cell types and neural circuitry must be characterized with the brain function served. One successful recent approach is to identify cell type-specific circuits using genomic and neural tracing technologies along with experimental tests of their function. Despite remarkable progress on this front, there is still much work to be done. This motivated the program for the 2nd annual Center for Neural Circuit Mapping (CNCM) summer conference held in Irvine, California in August 2022. The meeting considered the strengths and weaknesses of the current state-of-the-art approaches and concepts for linking brain function to structure. The following topics were discussed by twenty-one invited world-class neuroscientists: (1) Cell-type specific analysis of gene regulatory networks in neural circuits, (2) Cortical cell types and circuit function, (3) Local and global neural circuits for navigation and learning, and (4) Linking cell types and circuits to disease. This stimulating CNCM conference series will continue as a productive venue for future neuroscience discussions concerning neural circuit organization and function.

The second annual conference hosted by the UC Irvine Center for Neural Circuit Mapping (CNCM) was held on August 15–16, 2022 at the Beckman Center of the National Academies of Science and Engineering in sunny Irvine, California. The annual summer conference brought together a strong multidisciplinary group of neuroscientists, molecular geneticists, and clinical psychiatrists (Fig. 1), including Julio Licinio, Editor in Chief of *Molecular Psychiatry* and Associate Editor Ma-Li Wong, to address the question "How will we link brain function to cell types and circuits?" The meeting was held in the spirit of the Cajal Club, the joint host of the previous outing of the 2021 summer conference. The Cajal Club was established in 1947 to celebrate the intimate relationship between brain structure and function and to honor the legacy of Santiago Ramón y Cajal, the Spanish neuroscientist who received the Nobel Prize in Physiology or Medicine in 1906. Ramón y Cajal established the "neuron" as the basic unit of nervous structure using the methodology developed the Italian neuroscientist Camillo Golgi [1]. A very large bronze bust of Ramón y Cajal, whose *de facto* caretaker is Professor Larry Swanson of the University of Southern California (USC), watched over the summer conference in 2021 from stage left, constantly reminding attendees of their task to decipher the inner workings of the brain. Keeping with the tradition established last year, Cajal Club Secretary Charles "Chuck" Ribak commenced the conference with the official Cajal Club gavel.

A distinguished and multidisciplinary group of scientists and clinicians met in an air-conditioned and well-caffeinated venue at the National Academies of Sciences Beckman Center, first conceived by Dr. Arnold O. Beckman, the inventor of a pH meter precursor instrument and many other workhorse scientific instruments. Arnold Beckman envisioned a West Coast center comparable to the National Academies of Sciences Conference Center in the District of Columbia (D.C.), where experts would discuss the most pressing matters of science and solve big problems. The roughly one-hundred and twenty attendees participated towards the common goals of the conference including addressing the hurdles of (1) "explainability" for testing cause and effect across different levels of biological organization of the brain [2, 3], and (2) how best to link brain function to cell types and circuits given the current state-of-the-art [4–6].

Leaders in the field spanned expertise in omics, systems neuroscience, behavior, and clinical research. Speaker session topics advanced through increasingly broader biological levels of organization.

Callaway's Keynote Lecture set the tone for the rest of the conference. The first session on Monday morning, entitled "Cortical cell types and circuit functions", included the talks from Ed Lein of the Allen Institute, Bernardo Rudy of New York University (NYU), Lisa Giocomo of Stanford, and Wei Xu of University of Texas Southwestern (UTSW). Monday's afternoon session entitled "Cell-type specific analysis of gene regulatory networks in neural circuits" included the talks from Bing Ren of University of California, San Diego (UCSD), Joe Ecker of the Salk Institute, Xin Jin of Scripps, Xiang-Dong Fu of UCSD, and Timothy L. Downing of UCI. Tuesday August 16th began with a morning session entitled "Local and global neural circuits for navigation and learning", including the talks from Douglas Nitz of UCSD, Sung Soo Kim of the University of California, Santa Barbara (UCSB), Omar Ahmed of the University of Michigan (UMich), Elizabeth Chrastil of UCI, Kei Igarashi of UCI, and Gord Fishell of Harvard University. The final session of the conference, entitled

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Published online: 5 October 2022

Fig. 1 UCI Center for Neural Circuit Mapping 2022 Conference Group Photograph. Speaker, organizers, and guests from left to right, including (1) Vivek Swarup, (2) Elizabeth Chrastil, (3) Omar J. Ahmed, (4) Ma-Li Wong, (5) Julio Licinio, (6) Jospeh R. Ecker, (7) Edward Callaway, (8) Xin Jin, (9) Patricia Cogram, (10) Bing Ren, (11) Kim N. Green, (12) Bert L. Semler, (13) Xiangmin Xu, (14) Charles "Chuck" Ribak, (15) Lisa Giocomo, (16) Alec J. Davidson, (17) Gordon Fishell, (18) Kei M. Igarashi, (19) Shane A. Liddelow, (20) Daozhan Yu, (21) Wei Xu, (22) Xiang-Dong Fu, (23) Bernardo Rudy, and (24) Todd C. Holmes. Speakers not in photograph: Ed Lein, Timothy L. Downing, Douglas A. Nitz, Sung Soo Kim, Catherine Kaczorowski, Autumn Ivy. Photographed by Ryan Raasch.

"Linking cell types and circuits to disease", heard talks from Kim Green of UCI, Shane Liddelow of NYU, Catherine Kaczorowski of Jackson Laboratories (JAX), Vivek Swarup of UCI, and Autumn Ivy of UCI. Details on the topics covered by each speaker can be found by opening the link https://cncm.som.uci.edu/2022-cncm-conference/.

Next year's 3rd annual CNCM summer conference entitled "Structure, Function, and Development of Neural Circuits" is currently being organized. The Keynote speaker for this conference in 2023 will be Hongkui Zeng of the Allen Institute. We are expecting this to be another stimulating conference with participation from speakers with many diverse expertise and interests.

Edward Callaway, a pioneer in the in the field of neural circuits commenced the conference by delivering its Keynote Lecture. Dr. Callaway presented the premise that in order to comprehend the brain, neuroscientists need to rethink how they define circuits. One of the most successful approaches for identifying circuits has been monosynaptic circuit tracing with rabies virus (glycoprotein-deleted). This method was initially developed by the Callaway laboratory and colleagues, and published in *Neuron* in 2007 [7]. The rabies virus tracing approach has been complimented by single cell genomics to atlas the circuitry of the brain by cell type-specificity [8]. One of the central messages conveyed in Callaway's address is that cell type-specificity alone does not always establish a circuit [9] - circuit logic is also important [10–12]. For example, a fundamental circuit logic rule proposed by Francis Crick and Christof Koch, is called the "no strong loops hypothesis" [13]. This rule posits that the presence of strong recurrent loops would lead to uncontrollable oscillations. It is not yet clear how circuit logic is established, as it may depend on a combination of both genetic and environment processes, but as more circuits (including invertebrate circuits composed of fewer neurons) are mapped along with functional data, the rules will emerge [14].

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ACKNOWLEDGEMENTS

We acknowledge and thank the conference organizers, Edward Callaway, TCH, Kim Green, Douglas A. Nitz, Bing Ren, Bert Semler and XX and our Center Staff Michelle Wu and Ginny Wu.

AUTHOR CONTRIBUTIONS

SFG, TCH, and XX prepared the figure and wrote the report.

COMPETING INTERESTS

This conference received partial corporate support from sponsors AAVnerGene and Vizgen.

ADDITIONAL INFORMATION

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