



## Christine Ann

### Denny PhD

#### Assistant Professor of Psychiatry

During her time as a PhD student at Columbia, Christine Denny developed a transgenic mouse line that allows for an indelible label of neurons that were active during a particular learning experience. She is then able to tag the cells that are active during memory retrieval and compare the overlapping populations. These overlapping populations are what she calls a memory trace. Moreover, these populations can also be manipulated using optogenetics. Now, as a recipient of the NIH Director's Early Independence Award, she has her own lab and will be advancing her study of memory traces using this mouse line.

By labeling the cells in the hippocampus that were active both during a fear conditioning experiment and during retrieval of the fear memory, Dr. Denny has tracked how these memory traces differ in different conditions and how they change over time. Of specific interest are the effects of stress, depression, aging, and Alzheimer's disease on memory encoding and retrieval. Dr. Denny has also received another grant to support work on ketamine's preventative effects on stress and how it impacts these memory traces.

Current procedures, however, have two drawbacks: temporal and spatial limits. Tamoxifen, the drug used to induce the labeling of memory traces at a given time, has a long half-life. Dr. Denny is thus embarking on a project to find a drug that allows for more finely-tuned temporal control of the labeling. Secondly, current techniques restrict any study of these labeled cells to a small area of the brain. To enable the study of memory traces brain-wide, Dr. René Hen, Dr. Denny, and Dr. Mazen Kheirbek, have received a grant to begin CLARITY, a technique of whole brain labeling and viewing.

**Experience Includes:** Previous biochemical work in lipid disorders, such as Tay-Sachs and Sandhoff disease.

**Research focus:** Memory encoding and retrieval in health and disease.

**Resources/expertise:** Double transgenic mouse line for memory labeling; design of novel behavioral tasks for specific aims; immunohistochemistry and confocal imaging.

**Resources wanted:** Drug development collaboration with chemists; collaboration with pharmacologists for ketamine studies; clinical studies in stress prevention.