A novel ligand selectively visualizes and activates chemogenetic receptors in non-human primates

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A chemogenetic technology, Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) affords a means to temporally and remotely control the activity of a target neural population expressing a "designer receptor" by an agonist compound. The combination muscarinic-based DREADDs, hM_3Dq (excitatory) and hM_4Di (inhibitory), and biologically inert compound, clozapine-N-oxide (CNO) has been successfully applied in a variety of *in vitro* and *in vivo* contexts, extending to non-human primate studies to modify behavior. For the application of DREADDs to non-human primates, it is desirable to monitor the DREADD expression *in vivo* because in non-human primates, 1) viral vector-based transgene delivery into target neurons has not been fully established, and 2) the behavioral study is performed for relatively the long-term. In addition, CNO has poor brain permeability and can be metabolized to clozapine, which has potential for causing unwanted off-target actions. We solved these issues by developing a novel ligand, deschloroclozapine (DCZ), which serves a dual purpose in chemogenetics: (1) as a selective compound for visualization of DREADD expression *in vivo* by positron emission tomography (PET) imaging and (2) as a selective agonist for muscarinic-based DREADDs. In this talk, I will introduce the property of DCZ and the role of PET imaging in neuroscience research using non-human primates.