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Version. Artas SAM 6.1 License Key Offline
Installer Offline. Depression of serotonin (5-HT)
function has been linked to depression,
obsessive compulsive disorder, and other mood
and anxiety disorders. The loss of 5-HT function
is thought to be due to over-stimulation of the
5-HT-1A receptor (5-HT1AR) by 5-HT. We
recently developed a novel selective 5-HT1AR
antagonist, WAY-100635 (WAY), that prevents a
loss of 5-HT function when given to conscious
mice. Remarkably, WAY does not cross the
blood brain barrier (BBB) in the intact mouse.
We have been able to devise a novel brain
delivery system (Lenti-DREADD) that enables
use of this drug in intact animals and study its
mechanisms of action in vivo. The proposed
experiments will test a model of 5-HT1AR-
induced angiogenic responses in mice and test
how WAY prevents these responses. Other
experiments will examine the mechanism of
action of WAY. We will test whether WAY works
by facilitating the presynaptic release of 5-HT
using selectively inhibiting the 5-HT transporter
(SERT) or inhibiting the 5-HT metabolizing
enzyme monoamine oxidase A (MAO-A). We will
test whether WAY works by blocking presynaptic

or postsynaptic 5-HT1AR function. We will also test whether WAY works by preventing 5-HT1AR- mediated changes in an inhibitor of phosphodiesterases (PDE) that increases cyclic AMP (cAMP) and/or by increasing levels of the inhibitory neurotransmitter GABA. Experiments will test whether WAY works by blocking 5-HT1AR- mediated changes in levels of extracellular signal-related kinase (ERK), an important intracellular signal for 5-HT1AR function. These experiments will provide novel insights into the effects of selective 5-HT1AR antagonists on mood and anxiety-like behavior. Results will have a large impact on drug discovery for the treatment of mental illnesses such as depression and anxiety. PUBLIC HEALTH RELEVANCE: Mood and anxiety disorders are very prevalent in society and consume a large amount of health care resources. Our proposal studies a novel drug that has a high affinity for the 5-HT1A receptor. We will study

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