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GlyT2/5HT2A Antagonist VVZ-149

National Cancer Institute

Source

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An antagonist of both glycine transporter type 2 (GlyT2) and serotonin receptor 2A (5HT2A), with potential anti-nociceptive activity. Upon administration, GlyT2/5HT2A antagonist VVZ-149 binds to and blocks both GlyT2 and 5HT2A. Blockage of GlyT2 prevents the re-uptake of the inhibitory neurotransmitter glycine in the synaptic cleft, thereby potentiating glycine-mediated inhibitory signaling, and inhibiting the firing of neurons, which suppresses the transmission of pain signals to the brain and induces analgesia. Blockage of 5HT2A prevents both the binding of its ligand serotonin and 5HT/5HT2A-mediated signaling. This also suppresses pain signaling and induces analgesia. GlyT2 and 5HT2A play key roles in the induction and transmission of pain signals. GlyT2, a glycine plasma membrane transporter, modulates glycine-mediated inhibition of synaptic transmission in the spinal cord and mediates pain signal transmission to the brain; inhibition of GlyT2 potentiates glycinergic mediated pain signaling. Serotonin and its 5HT2A receptor are involved in both serotonin receptor-mediated signaling and the perception of pain.