5-HT\textsubscript{1F} Receptors and Migraine: From Cloning to the Clinic

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The 5-HT\textsubscript{1F} (serotonin\textsubscript{1F}) receptor serves as an example of how the cloning of novel receptors, coupled with traditional drug discovery techniques, can provide new ideas for the development of therapeutic agents. This 5-HT receptor subtype was unknown before it was cloned, and even today little is known about its possible physiologic roles. However, when a putative animal model of migraine headache (trigeminal ganglion-stimulated dural extravasation) was examined for the effects of serotonergic agonists, it was found that the pharmacologic effect correlated best with affinity at the 5-HT\textsubscript{1F} receptor. This finding stimulated the idea that 5-HT\textsubscript{1F} receptor agonists might have therapeutic efficacy in migraine headache and stimulated an effort to develop selective 5-HT\textsubscript{1F} receptor agonists. This presentation will review the preclinical data supporting the development of LY334370, a selective serotonin-one-F receptor agonist (SSOFRA), leading to the demonstration of the clinical efficacy of this molecule in the acute treatment of migraine headache.