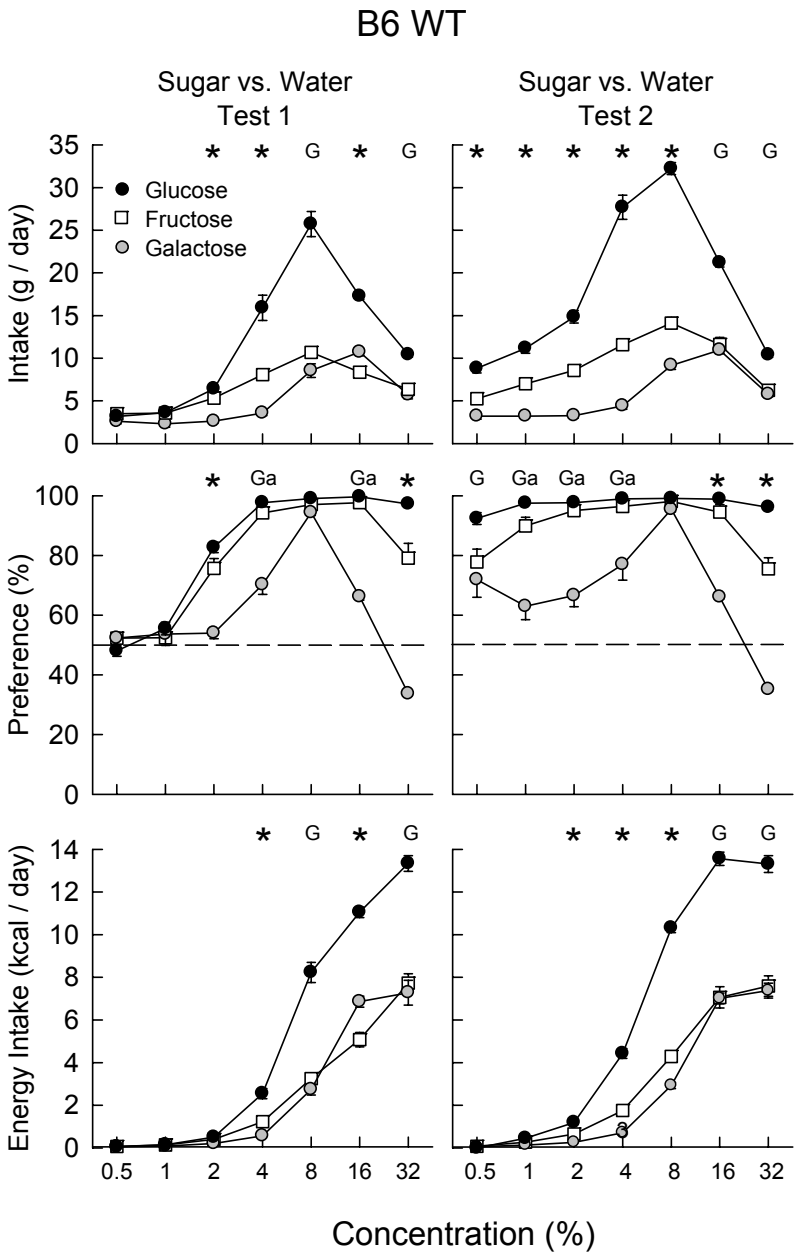
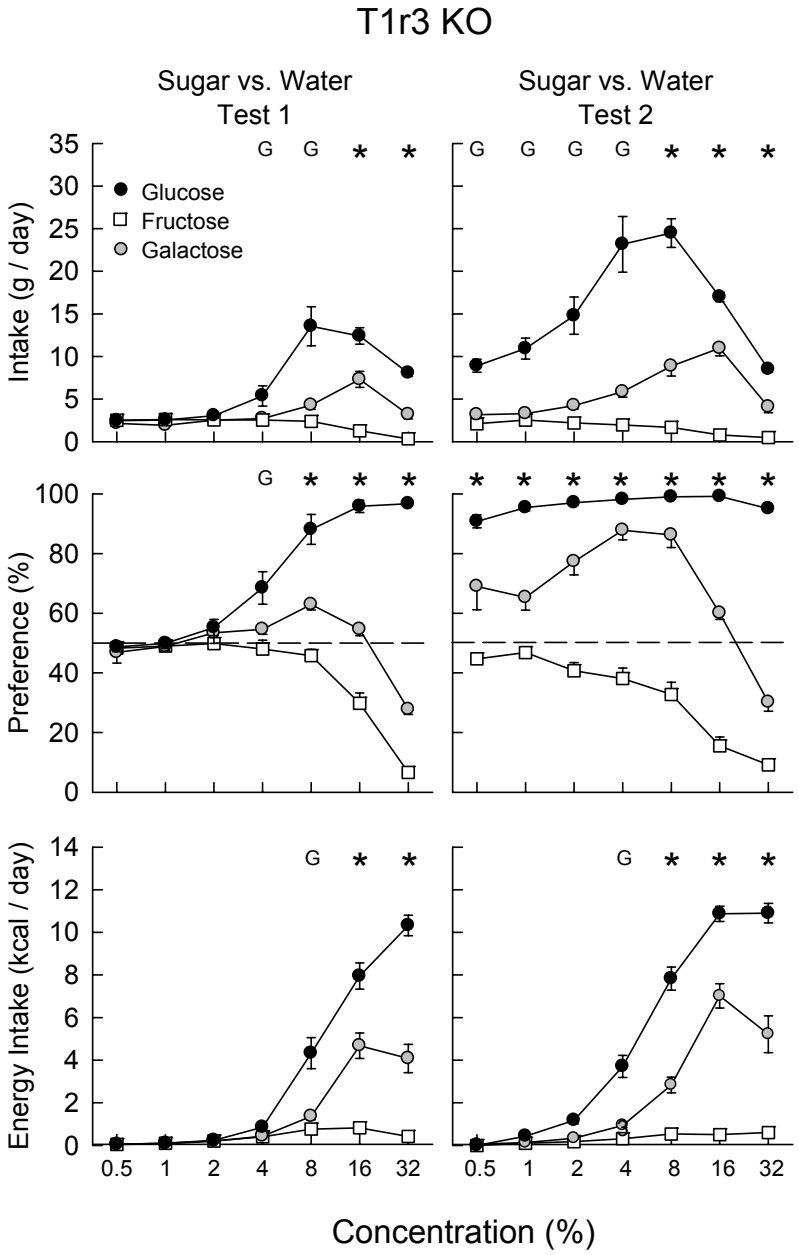
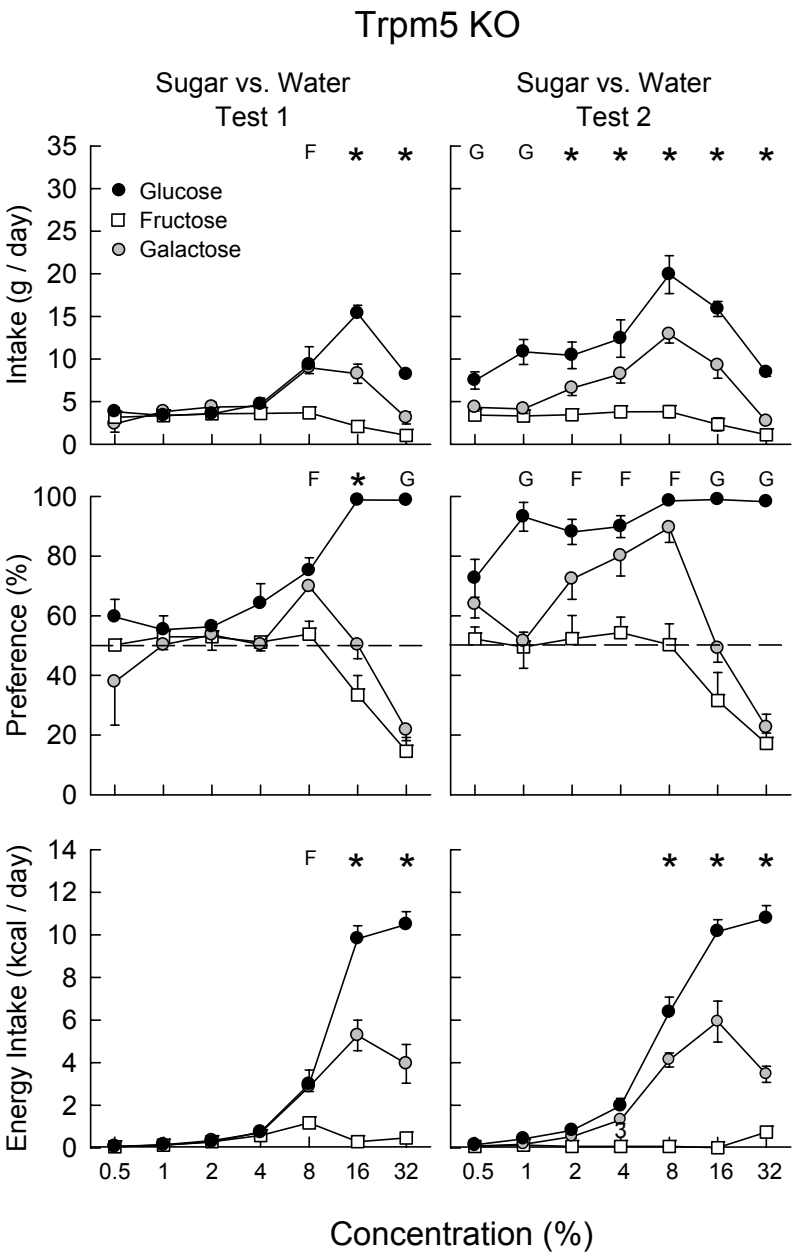


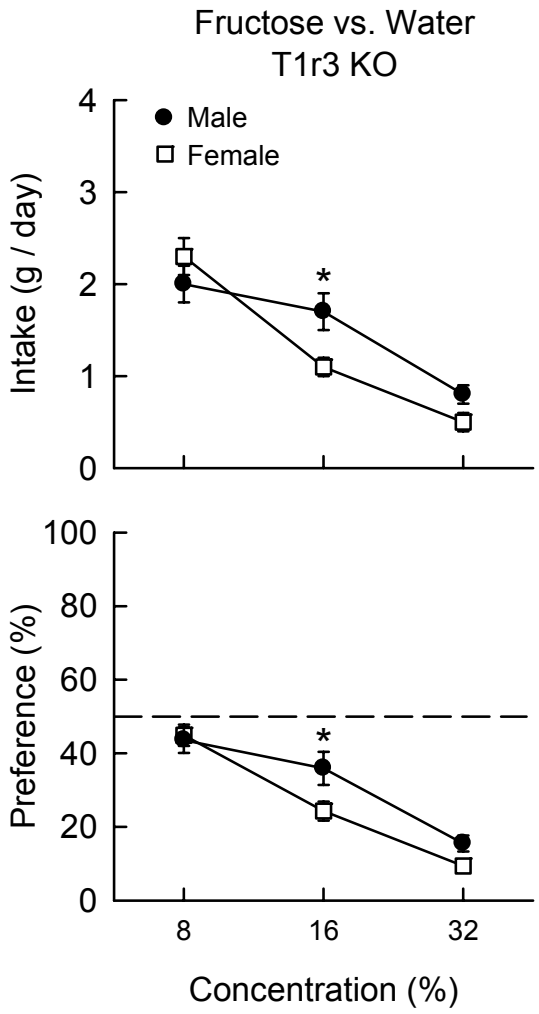
Supplemental Figure 1. Mean (±SE) sugar solution intake (top), percent preference over water (middle) and sugar energy intake (bottom) of B6 WT Glucose, Fructose, and Galactose groups during 24-h two-bottle Tests 1 and 2 with their respective sugar. Water intakes are not shown. Analysis of variance revealed Group x Concentration interactions for solution intake, preference, and energy intake for Tests 1 and 2 [$F(12,162) \geq 16.4$, $P < 0.01$]. Significant ($P < 0.05$) group differences at individual concentrations are denoted by * where all the groups differ from one another, by G where Glucose group differs from both Fructose and Galactose groups, and Ga where Galactose group differs from Glucose and Fructose groups based on simple main effects tests.



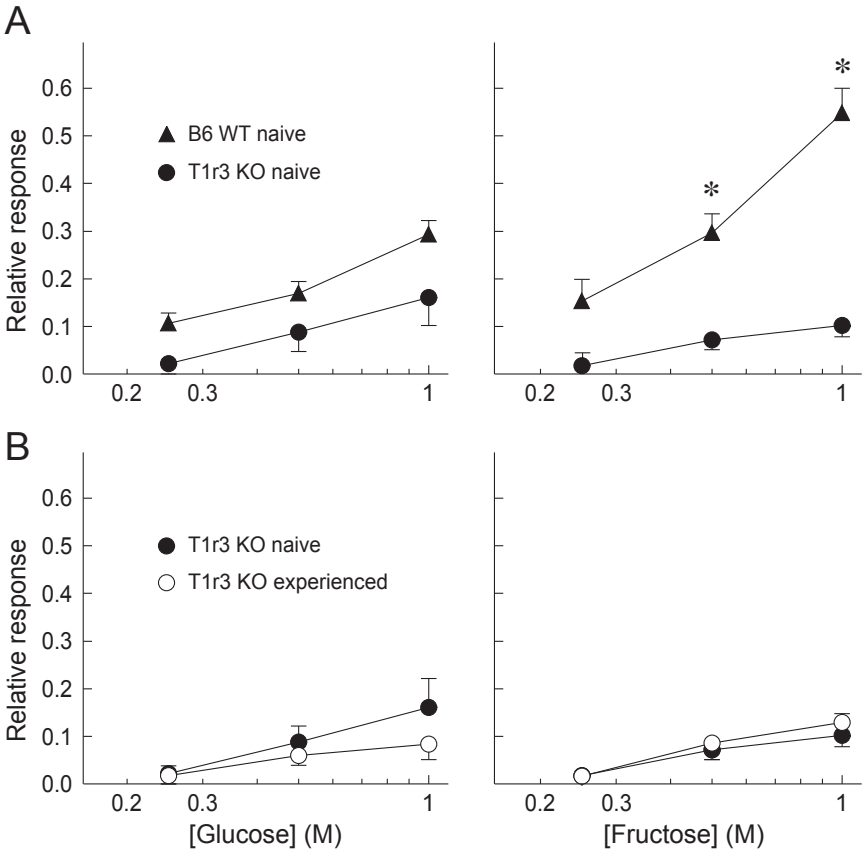
Supplemental Figure 2. Mean (±SE) sugar solution intake (top), percent preference over water (middle) and sugar energy intake (bottom) of T1r3 KO Glucose, Fructose, and Galactose groups during 24-h two-bottle Tests 1 and 2 with their respective sugar. Water intakes are not shown. Analysis of variance revealed Group x Concentration interactions for solution intake, preference, and energy intake for Tests 1 and 2 [$F(12,162) \geq 18.1$, $P < 0.01$]. Significant ($P < 0.05$) group differences at individual concentrations are denoted by * where all the groups differ from one another, and by G where Glucose group differs from both Fructose and Galactose groups based on simple main effects tests.



Supplemental Figure 3. Mean (±SE) sugar solution intake (top), percent preference over water (middle) and sugar energy intake (bottom) of Trpm5 KO Glucose, Fructose, and Galactose groups during 24-h two-bottle Tests 1 and 2 with their respective sugar. Water intakes are not shown. Analysis of variance revealed Group x Concentration interactions for solution intake, preference, and energy intake for Tests 1 and 2 [$F(12,132) \geq 9.2$, $P < 0.01$]. Significant ($P < 0.05$) group differences at individual concentrations are denoted by * where all the groups differ from one another, by G where Glucose group differs from both Fructose and Galactose groups, and F where Fructose group differs from Glucose and Galactose groups based on simple main effects tests.



Supplemental Figure 4. Mean (±SE) fructose solution intake (top) and percent fructose preference over water (bottom) of male (n=9) and female (n=10) T1r3 KO mice during 24-h two-bottle fructose vs. water. Water intakes are not shown. The naïve mice (11-12 weeks old) were given two-bottle fructose vs. water tests (2 days each) with 8%, 16% and 32% fructose solutions presented in an ascending order. The mice decreased their fructose intake as concentration increased [$F(2,34) = 10.7$, $P < 0.001$] and the male mice consumed more ($P < 0.05$) 16% fructose than the female mice [Sex x Concentration interaction, $F(2,34) = 3.9$, $P < 0.05$]. Percent fructose intake also declined with concentration [$F(2,34) = 91.5$, $P < 0.001$] and the 16% fructose preference of mice mice exceeded ($P < 0.05$) that of female mice [Sex x Concentration interaction, $F(2,34) = 3.8$, $P < 0.05$].



Supplemental Figure 5. A. Chorda tympani (CT) nerve responses (presented as relative response) of sugar-naïve B6 (n = 8) and T1r3 KO (n = 6) female mice to 2.5, 5, and 1 M glucose and fructose (see Zukerman et al., *Am. J. Physiol*., 2009, 296, R866-R876) for methods). For glucose, there were significant group [$F(1,24) = 7.9$; $P < 0.05$] and concentration [($F(2,24) = 20.9$; $P < 0.0001$) effects, but no significant interaction. For fructose, there were significant group [$F(1,24) = 45.5$; $P < 0.0001$], concentration [$F(2,24) = 24.9$; $P < 0.0001$], and group x concentration interaction [$F(2,24) = 11.1$; $P < 0.0005$] effects. Bonferroni-corrected post hoc comparisons revealed significant strain differences at the 0.5 and 1 M fructose concentrations ($P < 0.05$).

B. CT nerve responses of glucose-naïve (n = 6) and glucose-experienced (n = 5) T1r3 KO female mice to 2.5, 5, and 1 M glucose and fructose. For glucose, there was a significant concentration effect [$F(2,18) = 9.2$; $P < 0.0001$) but no group or group x interaction effects. For fructose, there was a significant concentration effect [$F(2,18) = 22.1$; $P < 0.0001$] but no group or group x interaction effects. The glucose-experienced T1r3 KO mice were initially indifferent to 0.5% glucose and water in a 2-day choice test but after 2 days of one-bottle exposure to 8% glucose they preferred 0.5% glucose to water (91%). They also preferred 32% glucose (95%) and 0.5% glucose to water (98%) in additional 2-day choice tests. CT nerve recordings occurred 1-2 days after the last glucose choice test.

This experiment was performed at Barnard College, Columbia University and the experimental protocol was approved by the Institutional Animal Care and Use Committee at Columbia University.