

**Supplementary Figure 1.** Itp-r83A and Nmdar1 genes overlap. The P{PZ}Itp-r83A<sup>05616</sup> insertion maps within both the Itp-r83A and Nmdar1 genes (overlapping genes on opposite strands), while the P{EPgy2}Itp-r83A<sup>EY02522</sup> maps 17 base pairs from the 5' end of Nmdar1.

**Supplementary Figure 2.** Model of DPKQDFMRamide-induced modulation of synaptic function. A. Stimulation of nerve activates voltage-gated calcium channels (blue) in the active zone of the nerve terminal leading to an influx of calcium. Calcium entry initiates both exocytosis of neurotransmitter containing vesicles (turquoise) and the activation of calcium-induced calcium release from ryanodine receptors (yellow) and IP<sub>3</sub> receptors (red). Calcium-induced calcium release likely does not contribute to vesicle exocytosis, but rather, the release Ca<sup>2+</sup> is probably taken up by SERCA (purple). B. Binding of DPKQDFMRamide to its metabotropic receptor activates a second messenger cascade which modulates calcium release from the IP<sub>3</sub>/Ryanodine receptor CICR complex. Release of calcium from endoplasmic reticulum membrane (ER) through the IP<sub>3</sub> receptor enhances ryanodine receptor activity, leading to greater calcium-induced calcium release and subsequent activation of CaMKII. The active CaMKII targets synaptic vesicles leading to the modulation of postsynaptic responses.