Micro(mi)RNA-based post-transcriptional regulatory mechanisms have been broadly implicated in the assembly and modulation of synaptic connections required to shape neural circuits, however, relatively few specific miRNAs have been identified that control synapse formation. Using a conditional transgenic toolkit for competitive inhibition of miRNA function in Drosophila, we performed an unbiased screen for novel regulators of synapse morphogenesis at the larval neuromuscular junction. We identified ten novel validated regulators of NMJ growth. Characterization of miR-34 mutants revealed significant synaptic phenotypes and cell type-specific functions suggesting distinct downstream mechanisms in the presynaptic and postsynaptic compartments. A search for human conserved downstream targets for miR-34 identified the junctional receptor CNTNAP4/Neurexin-IV (Nrx-IV) and the membrane cytoskeletal effector Adducin/Hu-li tai shao (Hts) as proteins whose synaptic expression is restricted by miR-34. Interestingly, manipulation of miR-34, Nrx-IV or Hts function in motor neurons or muscle supports a model where presynaptic miR-34 inhibits Nrx-IV to control active zone formation, whereas, postsynaptic miR-34 inhibits Hts to enable structural growth of presynaptic terminals. miR-34 was also identified to regulate synaptic growth in response to neuronal activity. This work highlights a novel role for miR-34 in both development and plasticity of synaptic connections.