Abstract: The family of neurotrophins provides one of the best examples of target-derived instructive cues that regulate diverse aspects of nervous system development. We and others have demonstrated that neuronal survival, axon growth and target innervation of peripheral sympathetic neurons is controlled by the target-derived neurotrophin, Nerve Growth Factor (NGF). We also showed that signaling endosomes carrying neurotrophic factors and their receptors are key mediators of neuronal survival in sympathetic neurons. While NGF and its receptor, TrkA, are expressed in several non-neuronal tissues including the pancreas, little is known about their in vivo functions outside of the nervous system. We recently uncovered a new role for neurotrophin signaling in acutely augmenting glucose-stimulated insulin secretion in pancreatic endocrine cells. These studies elucidate a new regulatory pathway that modulates pancreatic beta-cell secretory function, and provides rare insight into physiological roles of neurotrophins that have been classically studied as neuronal growth factors.