Protein transduction domains (PTDs), both naturally occurring and synthetic, have been increasingly employed to deliver biologically active agents to a variety of cell types in vitro and in vivo. In addition to the previously characterized arginine-rich PTDs, including TAT, Antp and PTD-5, we have demonstrated that lysine and ornithine as well as arginine homopolymers are able to mediate transduction of a wide variety. To screen for optimal PTDs, we have used as a therapeutic cargo a peptide derived from IkB Inducible Kinase (IKK) β, able to bind to the IKK regulatory subunit (NEMO), preventing formation of an active kinase complex. This peptide, termed NBD, is able to block activation of NF-kB, but not basal activity. We demonstrate that PTD mediated delivery of NBD using certain PTDs, in particular, 8K, is therapeutic following systemic delivery in murine models of inflammatory bowel disease, diabetes, and muscular dystrophy. In addition, we have developed a peptide phage display library screening method for novel transduction peptides able to facilitate tissue specific internalization of marker protein complexes. Using this approach, we have identified transduction peptides able to facilitate internalization of large protein complexes into tumors, airway epithelia, synovial fibroblasts, cardiac tissue and 293 cells in culture and/or in vivo.