Myotonic dystrophy (DM) is the second most common form of muscular dystrophy and is caused by microsatellite expansions of either CTG or CCTG in the 3’ untranslated region of the DMPK gene on chromosome 19 or in intron 1 of the ZNF9 gene on chromosome 3, respectively. Disease results from expression of RNA containing long tracts of CUG or CCUG repeats from the expanded allele. The expanded repeat RNA accumulates in nuclear foci detectable by in situ hybridization. A major pathogenic event in DM1 is the disruption of the regulation of pre-mRNA alternative splicing in heart, skeletal muscle, and brain. The specific subset of pre-mRNAs that are affected normally undergo postnatal splicing transitions. These splicing events are regulated by two families of splicing regulators: CUG-BP and ETR-3 Like Factors (CELF) and muscleblind-like (MBNL). MBNL is sequestered by expanded repeat RNA resulting in a loss of MBNL function. Our work indicates that in addition to sequestering MBNL, expanded CUG repeat RNA also induces a signaling event by activating protein kinase C (PKC) leading to hyperphosphorylation, stabilization and up-regulation of CUGBP1. Activation of a signalling pathway by a noncoding RNA represents a novel mechanism of disease that is relevant to other microsatellite expansion disorders.