This study was conducted to evaluate the mechanism by which n-3 PUFA regulated the protein degradation in C2C12 myotubes. Compared with the BSA control, EPA at concentrations from 400 to 600 μM decreased total protein degradation ($P < 0.01$). However, the total protein degradation was decreased when the concentrations of DHA ranged from 300 μM to 700 μM ($P < 0.01$). DHA (400 μM, 24 h) more efficiently decreased the I κ B α phosphorylation and increased in the I κ B α protein level than 400 μM EPA ($P < 0.01$). Compared with BSA, 400 μM EPA and DHA resulted in a 47% or 68% induction of the NF κ B DNA binding activity, respectively ($P < 0.01$). Meanwhile, 400 μM EPA and DHA resulted in a 1.3-fold and 2.0-fold induction of the PPAR γ expression, respectively ($P < 0.01$). In C2C12 myotubes for PPAR γ knockdown, neither 400 μM EPA nor DHA affected the levels of p-I κ B α , total I κ B α or NF κ B DNA binding activity compared with BSA ($P > 0.05$). Interestingly, EPA and DHA both still decreased the total protein degradation, although PPAR γ knockdown attenuated the suppressive effects of EPA and DHA on the total protein degradation ($P < 0.01$). These results revealed that DHA inhibits protein degradation more efficiently than EPA by regulating the PPAR γ /NF- κ B pathway in C2C12 myotubes.