4 mechanisms for anti-inflammatory benefits of fatty acids, particularly fish oil

1. **competitive inhibition**: Back in the old days, we thought that EPA and DHA from fish oil reduced prostaglandin formation by competitively inhibiting cyclooxygenase-catalysed conversion of arachidonic acid into inflammatory prostaglandins. According to this model, EPA and DHA were "anti-inflammatory" only because they jammed-up the formation of prostaglandins from arachidonate. This is still true, but there is more to the story.
2. **PPAR-alpha activation**: EPA from fish oil interacts with the fatty acid receptor PPAR-alpha, which then exerts and anti-inflammatory benefit by inhibiting NF-kappaB. This is an important distiction from the competitive inhibition model described above because it indicates that dietary fish oil acts at a nutrigenomic/pretranscriptional level and not merely at a metabolic/posttranscriptional level.
3. **docosatrienes and resolvins**: DHA from fish oil is metabolised by COX and LIPOX into docosatrienes and resolvins which then interact with DNA to produce a net antiinflammatory effect, mostly by inhibiting cytokine production.
4. **Inhibition of Toll-like receptors**: Scientists now recognize at least 11 different Toll-like receptors (TLRs). TLRs are the pro-inflammatory receptors for microbial molecules. When activated, they stimuate an intense pro-inflammatory response. I suppose we could almost think of Toll-like receptors as microbial-specific NF-kappaB receptors. When Toll-like receptors are activated, they stimulate inflammation by both/either an NFKB-dependent or NFKB-independent pathway. Thus, this is an example of a major inflammatory pathway that is at least partially immune to NFKB inhibitors (ie, KappArest). TLRs are activated by saturated fats while their activation is inhibited by n-3 PUFA such as EPA and DHA--fish oil

In summary, fish oil fatty acids exert anti-inflammatory actions by at least 4 different pathways.