**NF-κB** (**nuclear factor kappa-light-chain-enhancer of activated B cells**) is a protein complex that controls the [transcription](http://en.wikipedia.org/wiki/Transcription_factor) of [DNA](http://en.wikipedia.org/wiki/DNA). NF-κB is found in almost all animal cell types and is involved in cellular responses to stimuli such as stress, [cytokines](http://en.wikipedia.org/wiki/Cytokine), [free radicals](http://en.wikipedia.org/wiki/Free_radical), [ultraviolet irradiation](http://en.wikipedia.org/wiki/Ultraviolet_irradiation), oxidized [LDL](http://en.wikipedia.org/wiki/LDL), and bacterial or viral [antigens](http://en.wikipedia.org/wiki/Antigen).[[1]](http://en.wikipedia.org/wiki/I%CE%BAB#cite_note-pmid17072321-0)[[2]](http://en.wikipedia.org/wiki/I%CE%BAB#cite_note-pmid17303919-1)[[3]](http://en.wikipedia.org/wiki/I%CE%BAB#cite_note-pmid17183360-2)[[4]](http://en.wikipedia.org/wiki/I%CE%BAB#cite_note-pmid10602459-3)[[5]](http://en.wikipedia.org/wiki/I%CE%BAB#cite_note-pmid12795416-4) NF-κB plays a key role in regulating the immune response to infection. Conversely, incorrect regulation of NF-κB has been linked to cancer, inflammatory and [autoimmune diseases](http://en.wikipedia.org/wiki/Autoimmune_diseases), [septic shock](http://en.wikipedia.org/wiki/Septic_shock), viral infection, and improper immune development. NF-κB has also been implicated in processes of synaptic plasticity and memory.[[6]](http://en.wikipedia.org/wiki/I%CE%BAB#cite_note-pmid10611641-5)

Inhibition

In unstimulated cells, the NF-κB dimers are sequestered in the [cytoplasm](http://en.wikipedia.org/wiki/Cytoplasm) by a family of inhibitors, called IκBs (Inhibitor of κB), which are proteins that contain multiple copies of a sequence called ankyrin repeats. By virtue of their ankyrin repeat domains, the IκB proteins mask the [nuclear localization signals](http://en.wikipedia.org/wiki/Nuclear_localization_signal) (NLS) of NF-κB proteins and keep them sequestered in an inactive state in the cytoplasm.[[18]](http://en.wikipedia.org/wiki/I%CE%BAB#cite_note-pmid9865693-17)

**IκBs** are a family of related proteins that have an N-terminal regulatory domain, followed by six or more ankyrin repeats and a [PEST domain](http://en.wikipedia.org/wiki/PEST_sequence) near their C terminus. Although the IκB family consists of [IκBα](http://en.wikipedia.org/wiki/I%CE%BAB%CE%B1), [IκBβ](http://en.wikipedia.org/wiki/NFKBIB), IκBγ [IκBε](http://en.wikipedia.org/wiki/NFKBIE), and [Bcl-3](http://en.wikipedia.org/wiki/BCL3), the best-studied and major IκB protein is IκBα. Due to the presence of ankyrin repeats in their C-terminal halves, p105 and p100 also function as IκB proteins. Of all the IκB members, IκBγ is unique in that it is synthesized from the *nF-kb1* gene using an internal promoter, thereby resulting in a protein that is identical to the C-terminal half of p105.[[19]](http://en.wikipedia.org/wiki/I%CE%BAB#cite_note-pmid1339305-18) The c-terminal half of p100, that is often referred to as IκBδ, also functions as an inhibitor.[[20]](http://en.wikipedia.org/wiki/I%CE%BAB#cite_note-PMID:_17254973-19)[[21]](http://en.wikipedia.org/wiki/I%CE%BAB#cite_note-pmid7898917-20) IκBδ degradation in response to developmental stimuli, such as those transduced through [LTβR](http://en.wikipedia.org/wiki/Lymphotoxin_beta_receptor), potentiate NF-κB dimer activation in a NIK dependent non-canonical pathway.[[20]](http://en.wikipedia.org/wiki/I%CE%BAB#cite_note-PMID:_17254973-19)[[22]](http://en.wikipedia.org/wiki/I%CE%BAB#cite_note-pmid16195333-21)

Activation of the NF-κB is initiated by the signal-induced degradation of IκB proteins. This occurs primarily via activation of a kinase called the [IκB kinase](http://en.wikipedia.org/wiki/I%CE%BAB_kinase) (IKK). IKK is composed of a heterodimer of the catalytic IKK alpha and IKK beta subunits and a "master" regulatory protein termed [NEMO](http://en.wikipedia.org/wiki/IKBKG) (NF-κB essential modulator) or IKK gamma. When activated by signals, usually coming from the outside of the cell, the IκB kinase phosphorylates two serine residues located in an IκB regulatory domain. When phosphorylated on these serines (e.g., serines 32 and 36 in human IκBα), the IκB inhibitor molecules are modified by a process called [ubiquitination](http://en.wikipedia.org/wiki/Ubiquitination#Ubiquitination_.28Ubiquitylation.29), which then leads them to be degraded by a cell structure called the proteasome.

With the degradation of the IκB inhibitor, the NF-κB complex is then freed to enter the nucleus where it can 'turn on' the expression of specific genes that have DNA-binding sites for NF-κB nearby. The activation of these genes by NF-κB then leads to the given physiological response, for example, an inflammatory or immune response, a cell survival response, or cellular proliferation. NF-κB turns on expression of its own repressor, IκBα. The newly synthesized IκBα then re-inhibits NF-κB and, thus, forms an auto feedback loop, which results in oscillating levels of NF-κB activity.[[23]](http://en.wikipedia.org/wiki/I%CE%BAB#cite_note-pmid15499023-22) In addition, several viruses, including the AIDS virus HIV, have binding sites for NF-κB that controls the expression of viral genes, which in turn contribute to viral replication or viral pathogenicity. In the case of HIV-1, activation of NF-κB may, at least in part, be involved in activation of the virus from a latent, inactive state.[[24]](http://en.wikipedia.org/wiki/I%CE%BAB#cite_note-pmid11160127-23) YopJ is a factor secreted by [Yersinia](http://en.wikipedia.org/wiki/Yersinia) pestis, the causative agent of plague, that prevents the ubiquitination of IκB. This causes this pathogen to effectively inhibit the NF-κB pathway and thus block the immune response of a human infected with Yersinia.[[25]](http://en.wikipedia.org/wiki/I%CE%BAB#cite_note-pmid18201977-24)