

UBIQUITIN CHAINS IN ACTION

Present in every tissue of the body, ubiquitin appears to be involved in a dizzying array of functions, from cell cycle and division to organelle and ribosome biogenesis, as well as the response to viral infection. The protein plays at least two roles in turning on signals that destroy virally infected cells from within.

DOUBLE ACTION

TNF- α is an inflammatory cytokine that can induce cell death or apoptosis in a virus-infected cell. When the cytokine's receptor detects TNF- α , it initiates a signaling cascade in which a ubiquitin chain linked via lysine-63, which may either be free floating or bound to a substrate **1**, activates a kinase **2**. This kinase converts ATP to ADP, and phosphorylates I- κ B **3**, which keeps NF- κ B inactive as long as the two are bound together. The phosphorylation activates ligases that build a Lys-48-linked chain on I- κ B **4**, marking it for proteasomal degradation **5**, and leaving NF- κ B free to enter the nucleus and turn on a program of gene transcription that can result in apoptosis **6**.

