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Star-PAP control of *BIK* expression and apoptosis is regulated by nuclear PIPKI α and PKC δ signaling.

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Summary:

BIK protein is an initiator of mitochondrial apoptosis, and *BIK* expression is induced by proapoptotic signals, including DNA damage. Here, we demonstrate that 3' end processing and expression of *BIK* mRNA are controlled by the nuclear PI4,5P₂-regulated poly(A) polymerase Star-PAP downstream of DNA damage. Nuclear PKC δ is a key mediator of apoptosis, and DNA damage stimulates PKC δ association with the Star-PAP complex where PKC δ is required for Star-PAP-dependent *BIK* expression. PKC δ binds the PI4,5P₂-generating enzyme PIPKI α , which is essential for PKC δ interaction with the Star-PAP complex, and PKC δ activity is directly stimulated by PI4,5P₂. Features in the *BIK* 3' UTR uniquely define Star-PAP specificity and may block canonical PAP activity toward *BIK* mRNA. This reveals a nuclear phosphoinositide signaling nexus where PIPKI α , PI4,5P₂, and PKC δ regulate Star-PAP control of *BIK* expression and induction of apoptosis. This pathway is distinct from the Star-PAP-mediated oxidative stress pathway indicating signal-specific regulation of mRNA 3' end processing.