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Oral presentation

Ritonavir Inhibits NF-AT Activation Through Effects on the PI-3 Kinase/Akt Pathway

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The HIV protease inhibitor ritonavir has been reported to have activities unrelated to inhibition of HIV protease, including anti-tumor activity *in vivo* and *in vitro*, induction of lipodystrophy *in vivo*, inhibition of the 20S proteasome, and inhibition of NFkB activation. Here we show that ritonavir also inhibits activation of NF-AT by PMA plus ionomycin and by the HHV-8 vGPCR. Inhibition of NF-AT activation occurs through the PI-3 kinase/Akt/GSK-3 pathway, since ritonavir treatment leads to decreased Akt phosphorylation and a resultant decrease in GSK-3 phosphorylation. Treatment with ritonavir also inhibits the expression of NF-AT-dependent pro-inflammatory factors. Inhibition of multiple signaling pathways may help to explain the anti-tumor and other effects of ritonavir that are unrelated to its anti-retroviral activity.