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**Microbiology**

## **Inhibition of cyclooxygenase 2 blocks human cytomegalovirus replication**

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Cyclooxygenase 2 (COX-2) mRNA, protein, and activity are transiently induced after infection of human fibroblasts with human cytomegalovirus. Prostaglandin E<sub>2</sub>, the product of COX-2 activity, is transiently increased by a factor of >50 in cultures of virus-infected fibroblasts. Both specific (BMS-279652, 279654, and 279655) and nonspecific (indomethacin) COX-2 inhibitors can abrogate the virus-mediated induction of prostaglandin E<sub>2</sub> accumulation. Levels of COX-2 inhibitors that completely block the induction of COX-2 activity, but do not compromise cell viability, reduce the yield of human cytomegalovirus in human fibroblasts by a factor of >100. Importantly, the yield of infectious virus can be substantially restored by the addition of prostaglandin E<sub>2</sub> together with the inhibitory drug. This finding argues that elevated levels of prostaglandin E<sub>2</sub> are required for efficient replication of human cytomegalovirus in fibroblasts. COX-2 inhibitors block the accumulation of immediate-early 2 mRNA and protein, but have little effect on the levels of immediate-early 1 mRNA and protein. Viral DNA replication and the accumulation of some, but not all, early and late mRNAs are substantially blocked by COX-2 inhibitors. Elevated levels of prostaglandin E<sub>2</sub> apparently facilitate the production of immediate-early 2 protein. The failure to produce normal levels of this critical viral regulatory protein in the presence of COX-2 inhibitors might block normal progression beyond the immediate-early phase of human cytomegalovirus infection.

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