

**P002** Epidermal growth factor inhibits apoptosis induced by ibuprofen in gastric epithelial cells  
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Epidermal growth factor (EGF) can activate cell survival pathways involving signalling through p44/42 mitogen-activated protein (MAP) kinase, p38 MAP kinase, phosphatidylinositol 3-kinase (PI 3-kinase) and NF- $\kappa$ B. The aim of the present work was to determine whether EGF could inhibit apoptosis induced by the non-steroidal antiinflammatory drug (NSAID) ibuprofen in primary cultures of guinea-pig gastric surface epithelial cells. Apoptosis was assessed by measurement of caspase 3-like activity, and by counting the proportion of condensed and fragmented nuclei stained with H33258.

Inhibition of pathways involving p44/42 MAP kinase by PD 98059 (30  $\mu$ M), p38 MAP kinase by SB 203580 (10  $\mu$ M) or PI 3-kinase by wortmannin (100 nM) did not prevent inhibition of ibuprofen (250  $\mu$ M) induced apoptosis by EGF (20 ng/ml). However, the inhibitor of NF- $\kappa$ B activation, MG132 (5  $\mu$ M), prevented EGF action against ibuprofen-induced apoptosis. EGF increased Bcl- $x_L$  (immunoblotting), both in the presence and absence of ibuprofen. This effect was blocked by MG132. In conclusion, EGF inhibits apoptosis induced by ibuprofen possibly by increasing Bcl- $x_L$  by a pathway involving NF- $\kappa$ B. Such a pathway may be beneficial in normal gastric cells, but in transformed cells it could interfere with a component of the anti-cancer activity of NSAIDs.