

## Evidence for the involvement of Gi2 in activation of extracellular signal-regulated kinases in hepatocytes

### ABSTRACT

The present data suggest an important role of Gi2 in PGF2 $\alpha$  -induced ERK1/2 signaling in hepatocytes.

### INTRODUCTION

Introduction The extracellular regulated kinases ERK1 (p44mapk) and ERK2 (p42mapk) are believed to be implicated in regulation of cell growth and differentiation. They are activated in response to stimulation both of heptahelical G protein coupled receptors (GPCRs) and receptor tyrosine kinases (RTKs). Epidermal growth factor (EGF), hepatocyte growth factor (HGF), PGF2 $\alpha$ , norepinephrine, and several other agents activate ERK1/2 in hepatocytes. Furthermore, it was observed in these cells that pretreatment with pertussis toxin (PTX) decreased activation of ERK1/2 in response to various agents acting on RTKs or GPCRs. The data suggest an involvement of Gi protein(s) in the mechanisms of ERK1/2 activation in hepatocytes. However, it is not known which Gi protein(s) that mediate this effect. To approach this issue we have targeted the  $\alpha$  subunit of Gi2 by a catalytic RNA (ribozyme). The effect of the ribozyme on PGF2 $\alpha$  -induced ERK1/2 activation, which is strongly sensitive to PTX, was subsequently assessed.

### CONCLUSION

The present study gives further support to a role of Gi proteins in ERK1/2 activation in hepatocytes and suggests a role of Gi2. On the other hand, the data can not exclude a possible involvement of Gi3 in the mechanisms of ERK1/2 activation in these cells or define the precise contribution of the G protein subunit  $\alpha$ i2. The observation that primary hepatocytes are efficiently transfected with ribozymes may facilitate studies of cell signaling in this model system which represents features of normal cells. Thus, it will be interesting to explore the roles of different heterotrimeric G proteins and their subunits in activation of ERK1/2 as well as other mitogen-activated protein kinases by the nucleic acid enzyme strategy.