Elevation of HRPE773 (ZG16B) expression in amnion at term and in human ectocervical cell lines treated with inflammatory mediators is consistent with a function in innate immunity

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Introduction

- Labour is an inflammatory process, mediated via molecules of the innate immune response, including Interleukin-1β (IL-1β).
- Premature activation of these inflammatory pathways, following infection for example, is associated with complications of pregnancy including preterm birth (<37 weeks gestation) (1).
- HRPE773 has been proposed to have an antimicrobial function owing to its localisation to the secretory epithelium of several tissues, including the human female reproductive tract (2).
- We therefore hypothesised that HRPE773 expression may be regulated during human labour by inflammatory stimuli.

Methods

- Tissue samples of term human amnion, chorio-decida, placenta, myometrium & cervix from:
  i. Labour (spontaneous vaginal delivery >40 weeks gestation)
  ii. Non-labour (elective caesarean section 39-43 weeks gestation)
were obtained through the Edinburgh Reproductive Tissue Biobank (ERTBB) with ethical approval of West of Scotland Research Ethics Service.
- Ecotocervical (ECT1/E6E7) & endocervical (END1/E6E7) cell lines were treated (24 hrs) with:
  i. IL-1β
  ii. Lipopolysaccharide (LPS)
  iii. No treatment (control)
- HRPE773 mRNA expression was determined in:
  i. Labour relative to non-labour samples
  ii. Treated cervical cell lines relative to an untreated control using qRT-PCR (2-ΔΔCt method with 18S RNA as internal control).
- The cell specific localisation of HRPE773 protein in human foetal membranes, placenta, myometrium and cervix was determined using immunohistochemistry.

Results

Discussion

- HRPE773 mRNA expression was significantly elevated in labour vs non-labour amnion, but not in other tissues examined (Fig. 1A-D).
- HRPE773 mRNA expression was significantly elevated following treatment with the inflammatory cytokine IL-1β or LPS bacterial endotoxin in ecotocervical, but not endocervical cell lines (Fig. 2A-B).
- HRPE773 protein was largely localised to epithelial surfaces in foetal membranes, placenta and cervix (Figs. 3A-C).

Conclusions

- Elevated HRPE773 mRNA levels in labouring human amnion indicates a role for HRPE773 protein in normal labour.
- Elevated HRPE773 mRNA levels in ecotocervical cell lines treated with inflammatory mediators suggests inflammatory regulation in cervix.
- Epithelial localisation is consistent with an innate immune function.
- Further studies using human cervical tissue are required to determine the role of HRPE773 in the cervix during labour.

References


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