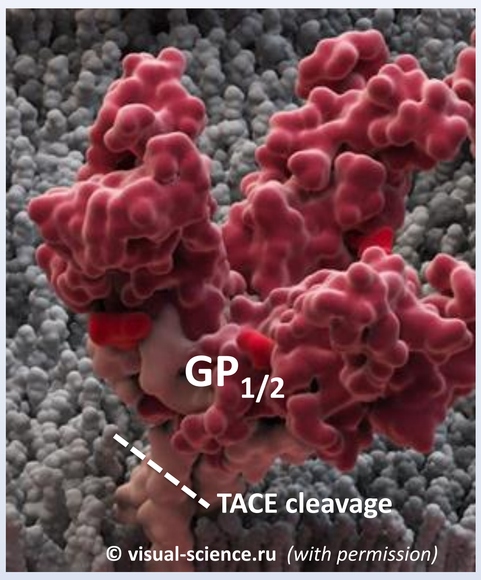

Ebola Shed Glycoproteins and Acute Kidney Injury

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INTRODUCTION AND OBJECTIVES

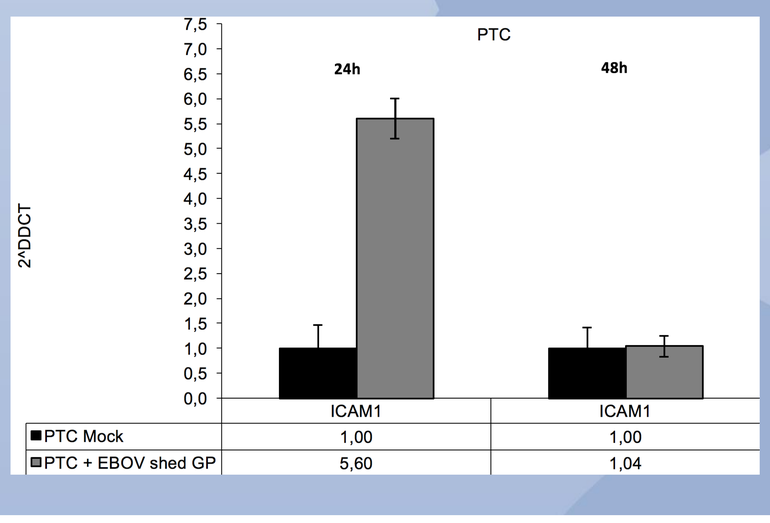
Ebola virus disease (EVD) is an acute febrile illness with a case fatality rate of about 50% (25-90% in past outbreaks, WHO 2016). **Acute kidney injury (AKI) is common in EVD**, arising in about 50% of cases; it is associated with a fatal outcome (Hunt et al.). Also it is known that proteinuric **AKI starts already in EVD stage 1, i.e. without prerenal conditions** (Hunt et al.). **Filoviridae, Coronaviridae and Retroviridae have been shown to shed their glycoproteins** (GP) (Cook et al.). Recent research has shown that Ebola shed GP (GP 1/2 after cleavage by TACE) acts agonistic on **Toll-like receptor 4** (TLR4) on macrophages and dendritic cells, resulting in a wide-scale proinflammatory cytokine release (Escudero-Pérez et al.). **Because TLR4 is also expressed on human renal cells we hypothesize TLR4 mediated kidney injury caused by shed GP.**

METHODS

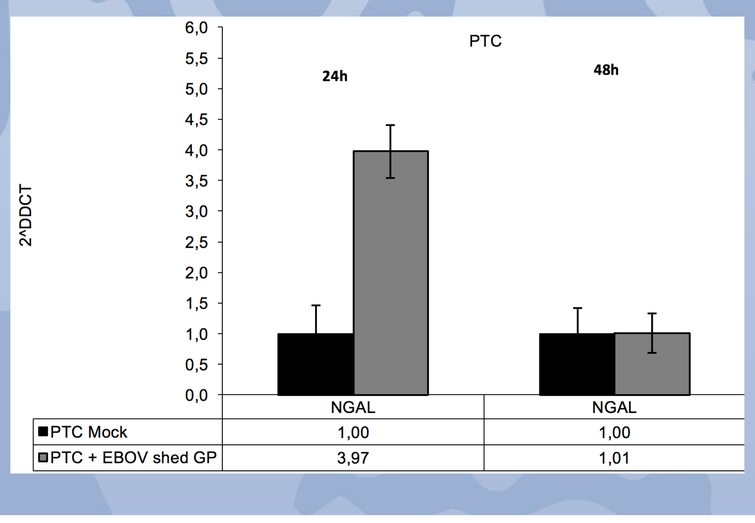
Human **proximal and distal tubular cells** (purified according to Baer et al.) were incubated with **Ebola shed GP** at 400 ng/ml for 24 and 48h (shed GP was purified as published earlier, Escudero-Peréz et al.). Interactions were analyzed by **cytokine and RNA profiling** (IL6 and IL8: ELISA; VCAM1 and ICAM1: quantitative realtime PCR). Ebola shed GP and TLR4 interaction was tested with **TLR4 reporter cells** (HEK-Blue hTLR4, InvivoGen, Toulouse, France).

RESULTS

After 24h of stimulation with Ebola shed GP **NGAL, KIM1 and IL18** as well as **ICAM1 and VCAM1** did show a significant increase. In return on the protein level **IL6** and **IL8** peaked at 48h post stimulation. Incubation of TLR4 reporter cells with Ebola shed GP at 400 ng/ml did show a significant stimulation compared to control.



	ICAM1	ICAM1
PTC Mock	1,00	1,00
PTC + EBOV shed GP	5,60	1,04



	NGAL	NGAL
PTC Mock	1,00	1,00
PTC + EBOV shed GP	3,97	1,01

CONCLUSION

Ebola shed glycoproteins can trigger an inflammatory response of human proximal tubules cells *in vitro.*

Based on existing research and our experiments with TLR4 reporter cells this appears to be caused by TLR4 activation. Because EBOV shed GP can be detected in early phases of disease a contribution to AKI is possible (Hunt et al.).

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