Jones et al. Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine 2015, 23(Suppl 2):O5
http://www.sjtrem.com/content/23/S2/O5

SCANDINAVIAN JOURNAL OF
trauma, resuscitation & emergency medicine

ORAL PRESENTATION Open Access

MicroRNA-mediated regulation of IL-10, IL-12 and TNFα gene expression in severely injured trauma patients

Timothy F Jones[1,2*], Helen C Owen[1], Hew DT Torrance[1,2,3], Negar Pirmadjid[1], Karim Brohi[2], Charles J Hinds[1,3], Michael J O'Dwyer[1,3]

From London Trauma Conference 2014
London, UK. 9-12 December 2014

Background

Severe trauma induces a blunted immune response associated with an enhanced susceptibility to nosocomial infections [1]. Within 2 hours of injury, expression of the prototypical anti-inflammatory cytokine, IL-10, increases whilst expression of the pro-inflammatory cytokines, TNFα and IL-12, decreases [1]. We hypothesise that microRNAs (miRs) may exacerbate this immunosuppressive gene expression pattern.

Methods

Following ethical approval and consent, 30 ICU patients admitted following trauma and 16 healthy age and sex-matched controls were recruited. Blood samples were obtained within 2 hours of injury and at 24 hours. miRs were isolated using PAXGene (Qiagen). miRs were selected on the basis of their miRBase target prediction scores for the promoters of IL-10, IL-12 and TNFα. Six miRs selected for analysis were miR374b, -202 and 125a3p (IL-10), -410 and -21 (IL-12) and -454 (TNFα). qPCR was used to quantify candidate miRs and the results were normalised relative to small nucleolar RNAs U6/RNU44. Infections were assessed using predefined criteria [2].

Results

Twenty three patients (77%) developed an infection, 15 (50%) were shocked (base deficit ≥ 6 mEq/L) on admission and 6 (20%) died. Within 2 hours, expressions of miR-202, -125a3p, -21 and -454 were reduced (all $p<0.03$) in patients compared to healthy controls. This reduction was maintained (all $p<0.01$) 24 hours after injury. At 24 hours, miR-202 was down-regulated (2.4-fold, $p=0.01$) in shocked compared to non-shocked patients. Decreased miR-374b expression on admission was associated with subsequent development of pneumonia ($p=0.009$).

Conclusion

Expression of miRs complementary to cytokine promoters varies significantly following severe traumatic injury and is associated with clinical outcomes. Reduction in inhibitory miRs could partly explain increased IL-10 expression and provide a mechanistic link between severe trauma, the observed immunosuppressive phenotype and an increased incidence of nosocomial infections. In vitro studies are now needed to invoke causation.

Authors' details
[1]Centre for Translational Medicine and Therapeutics, William Harvey Research Institute, Barts and the London School of Medicine and Dentistry, London, UK. [2]Centre for Trauma Sciences, Blizard Institute, Barts and the London School of Medicine and Dentistry, London, UK. [3]Adult Critical Care Unit, Royal London Hospital, Barts Health NHS Trust, London, UK.

Published: 11 September 2015

References

1. Torrance HD, Brohi K, Pearse RM, Mein CA, Wozniak E, Prowle J, Hinds CJ, O&Dwyer MJ: **Association between gene expression biomarkers of immunosuppression and blood transfusion in severely injured polytrauma patients.** *Ann Surg* , in press.
2. Horan TC, Andrus M, Dudeck MA: **CDC surveillance definition of healthcare-associated infection and criteria for specific types of**

* Correspondence: t.jones@smd11.qmul.ac.uk
[1]Centre for Translational Medicine and Therapeutics, William Harvey Research Institute, Barts and the London School of Medicine and Dentistry, London, UK
Full list of author information is available at the end of the article

infections in the acute care setting. *Am J Infect Control* 2008, **36**:309-332.

doi:10.1186/1757-7241-23-S2-O5
Cite this article as: Jones *et al.*: MicroRNA-mediated regulation of IL-10, IL-12 and TNFα gene expression in severely injured trauma patients. *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine* 2015 **23**(Suppl 2):O5.