

# Middlesex University Research Repository

An open access repository of  
Middlesex University research

<http://eprints.mdx.ac.uk>

Owen, Helen C., Torrance, H. D. T., Barnes, M. R., Brohi, K., Knight, J. C., Hinds, C. J. and O'Dwyer, M. J. (2015) The role of micrnas in the development of hospital acquired infection in polytrauma patients. Intensive Care Medicine Experimental 2015 3(Suppl 1). In: ESICM LIVES 2015: 28th Annual Congress of European Society of Intensive Care Medicine, 03-07 October 2015, Berlin, Germany. . ISSN 2197-425X [Conference or Workshop Item] (doi:10.1186/2197-425X-3-S1-A35)

Published version (with publisher's formatting)

This version is available at: <https://eprints.mdx.ac.uk/20020/>

## Copyright:

Middlesex University Research Repository makes the University's research available electronically.

Copyright and moral rights to this work are retained by the author and/or other copyright owners unless otherwise stated. The work is supplied on the understanding that any use for commercial gain is strictly forbidden. A copy may be downloaded for personal, non-commercial, research or study without prior permission and without charge.

Works, including theses and research projects, may not be reproduced in any format or medium, or extensive quotations taken from them, or their content changed in any way, without first obtaining permission in writing from the copyright holder(s). They may not be sold or exploited commercially in any format or medium without the prior written permission of the copyright holder(s).

Full bibliographic details must be given when referring to, or quoting from full items including the author's name, the title of the work, publication details where relevant (place, publisher, date), pagination, and for theses or dissertations the awarding institution, the degree type awarded, and the date of the award.

If you believe that any material held in the repository infringes copyright law, please contact the Repository Team at Middlesex University via the following email address:

[eprints@mdx.ac.uk](mailto:eprints@mdx.ac.uk)

The item will be removed from the repository while any claim is being investigated.

See also repository copyright: re-use policy: <http://eprints.mdx.ac.uk/policies.html#copy>

ORAL PRESENTATION

Open Access

# The role of micrnas in the development of hospital acquired infection in polytrauma patients

HC Owen<sup>1\*</sup>, HDT Torrance<sup>1,2,3</sup>, MR Barnes<sup>4</sup>, K Brohi<sup>3</sup>, JC Knight<sup>5</sup>, CJ Hinds<sup>2,4</sup>, MJ O'Dwyer<sup>2,4</sup>

From ESICM LIVES 2015

Berlin, Germany. 3-7 October 2015

## Introduction

Traumatic injury is associated with immunosuppression and an increased risk of developing nosocomial infections. However, the immune regulatory mechanisms involved remain unclear.

## Objectives

1) To describe genome-wide alterations in micro RNA (miRNA) expression following severe trauma.

2) To explore the potential role of miRNAs in mediating the post-traumatic immunosuppressive phenotype and their potential role in enhancing the risk of nosocomial infections.

## Methods

Patients requiring ICU care following traumatic injury were recruited. Whole blood was collected within 2 hours of injury and 24 hours later. Total RNA (containing miRNAs) was isolated utilising PAX Gene and RNA extraction kits (Qiagen). miRNA-sequencing was performed with the Illumina HiSeq2500, and sequences were aligned to the human GRCh37 reference genome. Data analysis was carried out using the DESEQ2 package in R, and miRNAs were considered significantly altered with an adjusted p value of < 0.05. Functional enrichment analysis was performed using Ingenuity Pathway Analysis (IPA) on all miRNAs reaching an adjusted p value of < 0.1. mRNA targets of interest were identified using miRBase and TargetScan (<http://www.mirbase.org>, <http://www.targetscan.org>).

## Results

49 patients were recruited and 25 patients developed nosocomial infections. Expression of 139 miRNAs was

significantly altered between 2 hours and 24 hours following injury, with miR-146b, a key inhibitor of pro-inflammatory pathways<sup>[1]</sup>, upregulated to the greatest degree. Figure 1 presents miRNAs that differ between those patients who developed nosocomial infections and those who did not. miR-144-5p was significantly different between the two groups at both time points. A large percentage of mRNA targets for miR-144 are involved the Cell-mediated Immune Response (Figure 2), including the B-cell receptor complex, p38MAPK, GATA3, IgG, BCL6 and the T-cell receptor. In addition, we have previously shown that the miR-374 family of miRNAs is linked to increased IL-10 expression in trauma patients<sup>[2]</sup>. IPA highlights Cancer, Haematological Disease, Immunological and Inflammatory Disease and Organismal Injury and Abnormalities as important pathways altered between infected and non-infected patients.

## Conclusions

These data provide a miRNA signature of severely injured trauma patients who develop hospital acquired infection compared to those who do not, and identify the miR-144 and miR-374b families as being of particular interest for future studies of trauma-induced immune dysfunction.

## Grant Acknowledgment

This work was funded by a Barts and the London Charity Grant.

## Authors' details

<sup>1</sup>Barts & the London School of Medicine, QMUL, Centre for Translational Medicine and Therapeutics, William Harvey Research Institute, London, United Kingdom. <sup>2</sup>Barts Health NHS Trust, Adult Critical Care Unit, Royal London Hospital, London, United Kingdom. <sup>3</sup>Barts & the London School of Medicine, QMUL, Centre for Trauma Sciences, Blizard Institute, London, United Kingdom. <sup>4</sup>Barts & the London School of Medicine, QMUL, William Harvey Research Institute, London, United Kingdom. <sup>5</sup>University of Oxford, Wellcome Trust Centre for Human Genetics, Oxford, United Kingdom.

<sup>1</sup>Barts & the London School of Medicine, QMUL, Centre for Translational Medicine and Therapeutics, William Harvey Research Institute, London, United Kingdom

Full list of author information is available at the end of the article

Time after injury	miR	Log <sup>2</sup> Fold Change	Adjusted p-value	Top pathways	Top mRNA targets of interest
2 hours	hsa-miR-144-3p	-1.80	0.006*	Cancer; Organismal Injury/Abnormalities; Reproductive System; Haematological Disease; Immunological Disease	MAPK6, IGIP, MAP3K8, TNFSF11, IL15, CXCL11, RFX3, IL7, NOS1, GATA3, HSP90AA1, TAB3, CD53, FADD, IFNA1, IL10, IRF6, MMD, C6orf25, IL17F, PIAS2, HBP1, IFNA4, TNFRSF11A
	hsa-miR-144-5p	-1.64	0.020*		
	hsa-miR-374a-3p	-3.59	0.020*		
	hsa-miR-142-5p	-0.75	0.067		
	hsa-miR-126-3p	-1.36	0.067		
	hsa-miR-16-5p	-1.31	0.067		
	hsa-miR-101-3p	-1.12	0.073		
	hsa-let-7a-5p	-0.88	0.085		
24 hours	hsa-miR-144-5p	-1.59	0.029*	Cancer; Haematological Disease; Immunological Disease; Organismal Injury/Abnormalities; Reproductive System	IRF6, MMD, C6orf25, IL17F, PIAS2, HBP1, IFNA4, TNFRSF11A
	hsa-miR-7977	0.52	0.029*		
	hsa-miR-1307-5p	0.53	0.056		
	hsa-miR-4664-3p	0.54	0.056		
	hsa-miR-16-5p	-1.21	0.061		
	hsa-miR-20b-5p	-0.99	0.061		
	hsa-miR-3609	1.07	0.061		
	hsa-miR-433-3p	0.80	0.061		

Most significantly changed miRNAs between trauma patients who develop hospital-acquired infections compared to those who do not, at 2 hours and 24 hours following injury. Top pathways were identified with Ingenuity Pathway Analysis, and top mRNA targets were identified with miRBase. (\*considered statistically significant; - indicates down-regulation).

Figure 1

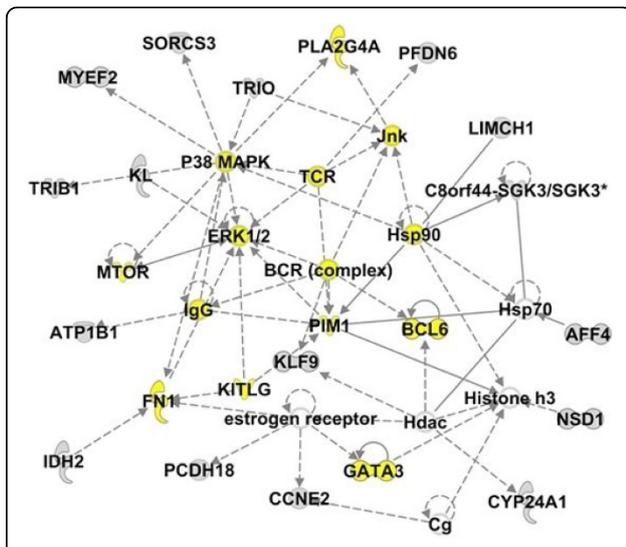


Figure 2 miR-144 mRNA targets create networks linked to the cell-mediated immune response. Genes linked to the immune response are highlighted in yellow.

doi:10.1186/2197-425X-3-S1-A35

Cite this article as: Owen et al.: The role of micrnas in the development of hospital acquired infection in polytrauma patients. *Intensive Care Medicine Experimental* 2015 **3**(Suppl 1):A35.

Submit your manuscript to a SpringerOpen journal and benefit from:

- Convenient online submission
- Rigorous peer review
- Immediate publication on acceptance
- Open access: articles freely available online
- High visibility within the field
- Retaining the copyright to your article

Submit your next manuscript at ► [springeropen.com](http://springeropen.com)

Published: 1 October 2015

References

1. Cheng HS, et al: *EMBO Mol Med* 2013, **5**(7):949-66.
2. Owen HC, et al: *Intensive Care Medicine Experimental* 2014, **2**(Suppl 1).