UNIVERSITY OF LEEDS

This is a repository copy of *HIGH PREVALENCE OF SUBCLASS-SPECIFIC BINDING AND NEUTRALISING ANTIBODIES AGAINST CLOSTRIDIUM DIFFICILE TOXINS IN ADULT CYSTIC FIBROSIS SERA: POSSIBLE MODE OF PROTECTION AGAINST SYMPTOMATIC CLOSTRIDIUM DIFFICILE INFECTION.*

White Rose Research Online URL for this paper:
<http://eprints.whiterose.ac.uk/143376/>

Version: Accepted Version

Proceedings Paper:

Monaghan, TM, Negm, O, MacKenzie, B et al. (5 more authors) (2017) HIGH PREVALENCE OF SUBCLASS-SPECIFIC BINDING AND NEUTRALISING ANTIBODIES AGAINST CLOSTRIDIUM DIFFICILE TOXINS IN ADULT CYSTIC FIBROSIS SERA: POSSIBLE MODE OF PROTECTION AGAINST SYMPTOMATIC CLOSTRIDIUM DIFFICILE INFECTION. In: Gut. British Society of Gastroenterology Annual General Meeting, 19-22 Jun 2017, Manchester, UK. BMJ Publishing Group , A133-A134.

<https://doi.org/10.1136/gutjnl-2017-314472.262>

© 2017 BMJ Publishing Group Ltd and British Society of Gastroenterology. This is an author accepted version of a conference abstract published in Gut. Uploaded in accordance with the publisher's self-archiving policy.

Reuse

Items deposited in White Rose Research Online are protected by copyright, with all rights reserved unless indicated otherwise. They may be downloaded and/or printed for private study, or other acts as permitted by national copyright laws. The publisher or other rights holders may allow further reproduction and re-use of the full text version. This is indicated by the licence information on the White Rose Research Online record for the item.

Takedown

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.

eprints@whiterose.ac.uk
<https://eprints.whiterose.ac.uk/>

HIGH PREVALENCE OF SUBCLASS-SPECIFIC BINDING AND NEUTRALISING ANTIBODIES AGAINST CLOSTRIDIUM DIFFICILE TOXINS IN ADULT CYSTIC FIBROSIS SERA: POSSIBLE MODE OF PROTECTION AGAINST SYMPTOMATIC CLOSTRIDIUM DIFFICILE INFECTION

¹TM Monaghan*, ²O Negm, ³B MacKenzie, ⁴M Hamed, ⁵CC Shone, ³DP Humphreys, ⁶KR Acharya, ⁷MHWilcox. ¹Nottingham Digestive Diseases Centre; ²Centre of Excellence for Autoimmunity in Cancer (CEAC), UNIVERSITY OF NOTTINGHAM, Nottingham; ³Antibody Biology, UCB-New Medicines, Slough; ⁴School of Medicine, UNIVERSITY OF NOTTINGHAM, Nottingham; ⁵Toxins Group, Public Health England, Porton; ⁶Department of Biology and Chemistry, University of Bath, Bath; ⁷Microbiology, University of Leeds, Leeds, UK

Introduction Despite multiple risk factors and a high rate of colonisation for *Clostridium difficile* (CD), the occurrence of *C. difficile* infection (CDI) in patients with cystic fibrosis (CF) is rare. The aim of this study was to compare the prevalence of CD toxin-specific IgA, IgG and anti-toxin neutralising antibodies (NAb) in the sera of adults with CF, symptomatic CDI (without CF) and healthy controls (HC).

Method Subclass-specific IgA and IgG responses to highly purified whole CD toxins A and B (toxintype 0, strain VPI 10463, ribotype 087; toxin A 200 mg/mL, toxin B 100 mg/mL), toxin B from a CD toxin-B only expressing strain (CCUG 20309, 90 mg/mL) and precursor form of B fragment of binary toxin, pCDTb (200 mg/mL), were determined by a validated protein microarray assay. NAb to CD toxins A and B were evaluated using a Caco-2 cell neutralisation assay. Clinical and demographic information was collected from medical records. All statistical analyses were performed on natural log-transformed data using GraphPad Prism version 6. For grouped multiple comparisons, the Kruskal-Wallis test and the Dunn's post hoc test was applied; $p \leq 0.05$ was statistically significant.

Results Serum IgA anti-toxin A and B levels and NAb against toxin A were significantly higher in adult CF patients ($n=16$; median age, 28 years (range 19–49 years)) compared with HC [$n=17$; 32 years (range 22–89 years)] and patients with symptomatic CDI ($n=16$; 36.5 years (range 19–49 years)); $p \leq 0.05$. The same pattern of response prevailed for IgG, except that there was no difference in anti-toxin A IgG levels between the groups. Systemic IgG anti-toxin B antibody responses predominated and high titre sera did not correlate with high neutralising potential. Compared with HC (toxins A and B) and CDI patients (toxin A), CF sera exhibited significantly stronger protective anti-toxin NAb responses.

Conclusion A superior ability to generate robust humoral immunity to CD toxins in the CF population is likely to confer protection against symptomatic CDI. This protection may be lost in the post-transplantation setting, where symptomatic CDI is a significant complication. Sera-monitoring of anti-CD toxin antibody titres may be of clinical value to identify transplant recipients displaying low levels of specific antitoxin antibodies who may be at risk of developing severe CDI. These individuals could be offered prophylactic passive or (when available) active immunotherapies.

Disclosure of Interest T. Monaghan: None Declared, O Negm: None Declared, B MacKenzie: None Declared, M Hamed: None Declared, C Shone: None Declared, D

Humphreys Conflict with: Owns UCB stock options, KR Acharya: None Declared, M Wilcox Conflict with: Astellas, AstraZeneca, Abbott, Actelion, Alere, Bayer, bioMerieux, Cerexa, Cubist, Da Volterra, Durata, Merck, Nabriva, Pfizer, Qiagen, Roche, Seres, Synthetic Biologics, Conflict with: As per grant/research support