1252. CD4+ T Cells Specific for C. difficile Toxins are a Marker of Patients with Active Relapsing Disease

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Session: 148. C. difficile: From the Bench to Bedside

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Background. The bacterial pathogen *Clostridium difficile* is the leading cause of nosocomial infectious diarrhea. Although *C. difficile* infection (CDI) can be treated with antibiotics, approximately 25% of patients relapse after treatment. The pathogenicity of CDI requires the activities of its toxins, TcdA and TcdB, but T cell-mediated responses to these toxins remain uncharacterized.

Methods. We enrolled two cohorts of patients, one with newly acquired CDI (n = 14) and the other with relapsing CDI (n = 25); and healthy volunteers with no history of CDI (n = 12). We measured peripheral blood $CD4^+$ T cell responses to the toxins using a whole blood flow cytometry assay that identifies antigen-specific $CD4^+$ T cells by co-expression of CD25 and OX40 following 44h incubation with antigen (**Fig 1**).

Results. We found that in patients with recurring CDI, T cell responses to TcdB were significantly higher than in healthy controls (median 1.04% vs. 0.18%; P = 0.003, **Fig 2**). In contrast, TcdA T cell responses and anti-TcdA/TcdB IgG titres were not different between recurring patients and controls. TcdB, but not TcdA, T cell responses were significantly higher in recurring CDI compared with newly acquired CDI (median 1.04% vs. 0.44%; P = 0.032). In both patient cohorts TcdB-specific CD4+ T cells were functionally heterogeneous, on average: 25% expressed the gut homing marker integrin β7; there was a 1:1 ratio of Tregs to T effectors; and T effectors contained Th1, Th2 and Th17 cells at a 1.5:1:3 ratio. The proportion of Th1 and Th17 cells within TcdB-specific CD4+ T cells was also significantly reduced in recurring, compared with newly acquired, CDI (**Fig 3**). Analysis of sorted TcdB-specific CD25+OX40+ cells confirmed specificity for TcdB and polarization towards Th17 cells, which are important for intestinal anti-pathogen immunity.

Conclusion. This is the first investigation of T cell immunity to *C. difficile* toxins. Our data show that anti-TcdB $CD4^+$ T cell responses are a more specific marker of disease than IgG titres. Tracking how toxin-specific $CD4^+$ T cell responses change following treatment and/or vaccination not only has the potential to predict relapse, but also to deliver insight into how $CD4^+$ T cell memory develops in response to this prevalent pathogen.

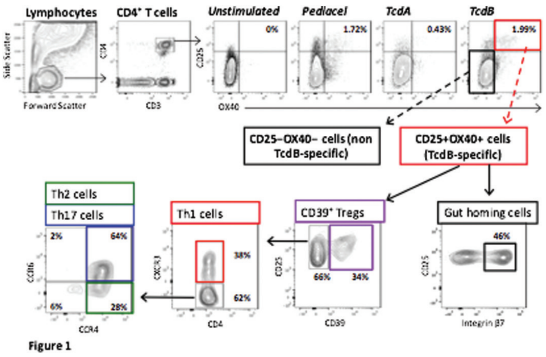

Figure 1

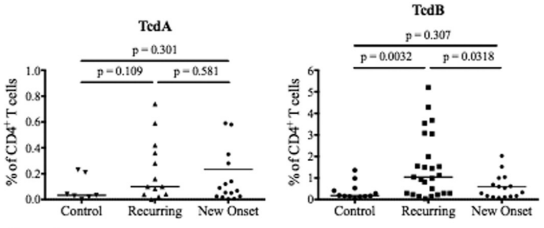

Figure 2

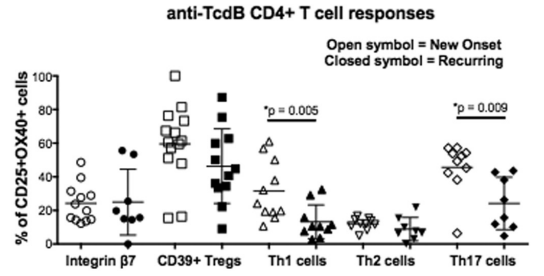

Figure 3

Disclosures. **All authors:** No reported disclosures.

1253. Discordance of SHEA/IDSA *Clostridium difficile* Disease Severity Scale in Solid Organ Transplant Patients

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Session: 148. C. difficile: From the Bench to Bedside

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Background. Solid organ transplant (SOT) patients are at high risk for *Clostridium difficile* infections (CDI) due to chronic immunosuppression and a propensity to receive antimicrobials. Management of CDI in SOT patients poses unique challenges as this population has disease-altered clinical and laboratory parameters. The objective of this study was to assess concordance between various CDI severity scales and the Society for Healthcare Epidemiology of America/Infectious Diseases Society of America (SHEA/IDSA) guidelines.

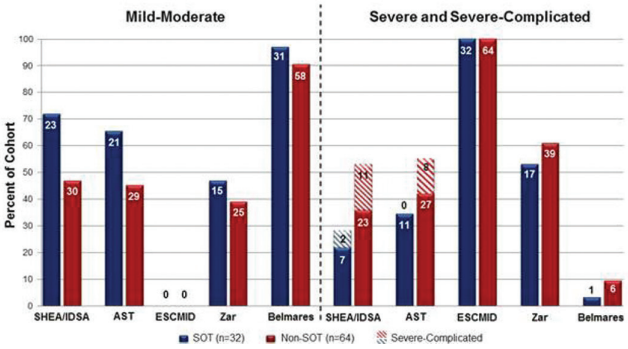
Methods. This retrospective study included all SOT recipients with a first CDI episode following transplant and time-matched (2:1) to non-SOT patients experiencing first CDI episodes between 2008 and 2016. The primary endpoint was concordance rates of CDI episodes considered mild-moderate or severe/severe-complicated in published CDI scales compared with the SHEA/IDSA guidelines. We also sought to compare the distribution of CDI severity across all scales between SOT and non-SOT patients.

Results. Overall, 32 SOT patients and 64 non-SOT patients were included. The SOT group had significantly higher leukopenia rates at CDI diagnosis; however, the magnitude of serum creatinine change did not differ between groups. According to the SHEA/IDSA scale, CDI episodes in SOT recipients were categorized as mild-moderate and severe/severe-complicated in 23 (72%) and 9 (28%) patients, respectively. Overall concordance rates among SHEA/IDSA guidelines and other scales ranged from 28% to 72%. Concordance rates were highest for mild-moderate CDI with Belmares and for severe/severe-complicated CDI with ESCMID (Table 1). No scale evenly categorized SOT and non-SOT patients across all severities (Figure 1).

Conclusion. Severity scales with heavy emphasis on white blood cell counts may not adequately categorize SOT patients. Immunocompromised status may need to be considered on its own when categorizing CDI severity and prescribing therapy.

Table 1

	Number (%) of Severity Classification-Concordant CDI Episodes, in Comparison to SHEA/IDSA Guidelines		
	Overall n = 32	Mild/Moderate n = 23	Severe or Severe-Complicated n = 9
AST	23 (71.9)	18 (78.3)	5 (55.6)
ESCMID	9 (28.1)	0	9 (100)
Zar	20 (62.5)	13 (56.5)	7 (77.8)
Belmares	22 (68.8)	22 (95.7)	0



Disclosures. **C. D. Alonso**, Merck: Grant Investigator and Scientific Advisor, Research grant sanofi pasteur: Investigator and Scientific Advisor, Research support GSK: Investigator, Research support; **E. B. Hirsch**, Merck: Grant Investigator, Grant recipient The Medicines Company: Speaker's Bureau, Speaker honorarium

1254. Prospective, Open-label Trial to Evaluate Efficacy of Lyophilized Fecal Microbiota Transplantation for Treatment of Recurrent *C. difficile* Infection

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