farms—might be a major reservoir of *C. difficile*. Similarly, antibiotic exposures might predispose farm animals for colonization with multidrug resistant Gram-negative organisms. The aim of this study was to determine the prevalence of *C. difficile* and multidrug resistant gram-negative rods in the soil of Southeastern Wisconsin farms.

Methods. From July to September of 2016, soil samples were collected from farms with livestock animals. Soil samples were collected using gloves and sample containers. Soil samples were collected from farms specifically in or near Washington, Waukesha, and Milwaukee counties which are within the proximity of Milwaukee Metro area. Soil samples were cultured for *C. difficile* and Gram-negative rods on selective plates and by broth enrichment.

Results. A total of 20 farms participated in this study with a total of 40 soil samples. Out of the 40 soil samples, 20 were from an area where animals roam or where manure was used and the remaining 20 were from an area where animals are prohibited or where there was no manure. Out of the 20 soil samples where animals roam, 10 (50%), tested positive for *C. difficile*. Out of 20 soil samples where animals are prohibited, 13 samples (65%) tested positive for *C. difficile*. 2 of the 23 *C. difficile* isolates recovered were toxigenic. Eight (40%) of the 20 soil samples where animals roam tested positive for fluoroquinolone-resistant bacteria (FQR). While 5 (25%) of the 20 soil samples where animals are prohibited, tested positive for FQR bacteria. An *Acinetobacter calcoaceticus* was found to exhibit carbapenem-resistance.

Conclusion. We found soil colonization with *C. difficile* and FQR in 65% and 25%, respectively, where animals are prohibited. Where animals roam we found *C. difficile* and FQR 50% and 40%, respectively. Our study suggests that farms may be a significant community source for *C. difficile* and fluoroquinolone resistant organisms. Additional testing should be done to examine factors that might be increasing antibiotic resistance in farms (e.g., antibiotic exposure).

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

1250. Induced Human Intestinal Organoids (iHIOs) as Model Systems for Chemotherapy-associated *Clostridium difficile* (CD) Infections

Senu Apewokin, MD[1]; Suman Pradhan, Phd[1]; Michael Frerick, BSc[2] and Alison Weiss, PhD[1]; [1]University of Cincinnati, Cincinnati, Ohio, [2]university of Cincinnati, Cincinnati, Ohio

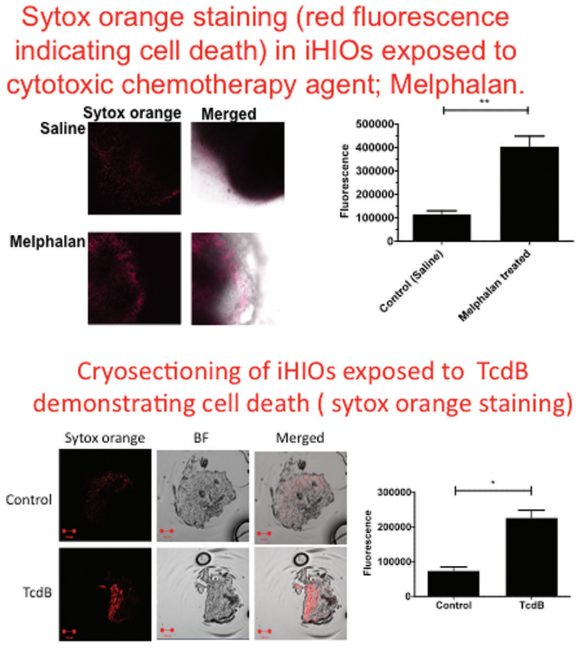
Session: 148. C. difficile: From the Bench to Bedside
Friday, October 6, 2017: 12:30 PM

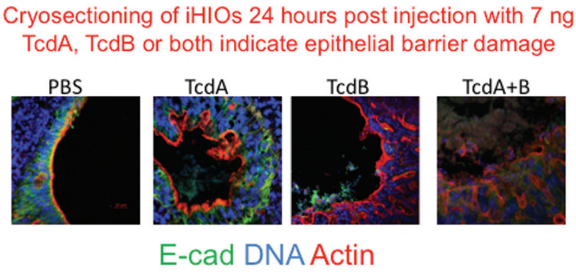
Background. Patients undergoing cytotoxic chemotherapy are ten times more likely to develop *Clostridium difficile* infections (CDI) than the general patient population. Efforts to outline pathophysiologic mechanisms underlying this disproportionate incidence have been limited by the lack of disease-representative experimental models. We hypothesized that iHIOs could serve as toxicity models to evaluate chemotherapy-associated CDI

Methods. Intact iHIOs were exposed to cytotoxic chemotherapy (melphalan) in gut media at therapeutic doses (9 µg/mL; which is the equivalent of 140 mg/m^2 human dose).

Cellular death was assessed by accumulation of the membrane permeant dye, Sytox-orange added at 5-days post treatment. iHIOs were also exposed to CD toxin A and B (TcdA and TcdB respectively) and epithelial barrier damage assessed by actin mislocalization and loss of E-cadherin. For controls iHIOs were exposed / microinjected with saline/PBS. Morphological and histological changes were then captured using light and confocal microscopy

Results. Morphologic and histologic assessments demonstrated cell death and epithelial barrier damage





TcdA and B damage the epithelial barrier: Induced human intestinal organoids (iHIOs) were injected with TcdA, TcdB, or both (7 ng) and stained at 24 hours for DNA *(blue)*, E-cadherin *(green)*, and *actin (red)*. Toxin injection causes actin mislocalization and a loss of E-cadherin.

Conclusion. iHIOs demonstrate cell death on exposure to CD toxins and melphalan chemotherapy. These properties could be harnessed in establishing toxicity models for evaluation of chemotherapy-associated CDI

Disclosures. **S. Apewokin**, T2 biosystems: Investigator, Research support Astellas: Scientific Advisor, Consulting fee

1251. Change in Bacterial Diversity of Fecal Microbiota Drives Mortality in a Hamster Model of Antibiotic-induced *Clostridium difficile* Colitis

Charles Burdet, MD, MPH[1]; Thu Thuy Nguyen, PhD[2]; Nathalie Saint-Lu, PhD[3]; Sakina Sayah-Jeanne, PhD[3]; Perrine Hugon, PharmD, PhD[3]; Frédérique Sablier-Gallis, PharmD, PhD[3]; Stéphanie Ferreira, PhD[4]; Antoine Andremont, MD, PhD[1]; France Mentré, MD, PhD[1] and Jean De Gunzburg, PhD[3]; [1]INSERM & Paris Diderot University, IAME, UMR 1137; AP-HP, Bichat Hospital, Paris, France, [2]INSERM & Paris Diderot University, IAME, UMR 1137, Paris, France, [3]Da Volterra, Paris, France, [4]Genoscreen, Lille, France

Session: 148. C. difficile: From the Bench to Bedside
Friday, October 6, 2017: 12:30 PM

Background. *C. difficile* (*C diff*) infection results from antibiotic-induced changes in colonic microbiota. DAV131A, an oral adsorbent-based product, can sequester antibiotic (AB) residues in the gut and reduce mortality in a hamster model of moxifloxacin (MXF) or clindamycin (CM) induced *C diff*colitis. We studied the link between changes of the bacterial diversity within the fecal microbiota and mortality in this model.

Methods. Male Syrian hamsters were administered 30 mg/kg MXF or 5 mg/kg CM subcutaneously once a day for 5 days (D1 to D5) and orally infected at D3 with 10^4 *C diff*spores. They were orally administered various doses of DAV131A (0, and 200 to 900 mg/kg twice a day), from D1 to D8. Survival was monitored up to D16 and feces were collected (D1 and D3) to characterize the microbiota by 16S rRNA gene profiling. Changes of various α- (Shannon, Observed OTUs and Chao1) and β- (Bray-Curtis dissimilarity and [un]weighted UniFrac) diversity indices between D1 and D3 were obtained for each animal. We analyzed links between (i) DAV131A dose and changes of bacterial diversity and (ii) changes of bacterial diversity and mortality using non parametric tests and logistic regression.

Results. Data from 70 and 60 animals were available in the MXF and CM studies, among which 10 and 28 died, respectively. Increasing doses of DAV131A reduced mortality from 100% to 0% and reduced changes in bacterial diversity of the fecal microbiota. Very strong predictors of mortality were changes in Shannon and unweighted UniFrac indices, which were markedly less affected in hamsters who survived (see table below median (min; max) according to vital status and area under the ROC curve, AUROC).

	Died	Survived	p	AUROC [95% CI]
MXF				
n	10	60		
Shannon	-1.7 (-3.0; -1.0)	-1.0 (-1.9; 0.1)	$<10^{-4}$	0.91 [0.80; 0.99]
Unweighted UniFrac	0.61 (0.56; 0.76)	0.51 (0.37; 0.65)	$<10^{-6}$	0.95 [0.89; 0.99]
CM				
n	28	32		
Shannon	-2.2 (-4.3; -0.4)	-1.1 (-2.6; 0.0)	$<10^{-7}$	0.88 [0.78; 0.96]
Unweighted UniFrac	0.71 (0.59; 0.84)	0.60 (0.49; 0.68)	$<10^{-10}$	0.94 [0.87; 0.98]

Conclusion. The extent of AB-induced changes in gut bacterial diversity correlated with increased mortality in a hamster model of *C diff* colitis. Higher doses of DAV131A protected fecal microbiota disruption and hence mortality.

Disclosures. **C. Burdet**, Da Volterra: Consultant and Research Contractor, Consulting fee; **N. Saint-Lu**, Da Volterra: Employee, Salary; **S. Sayah-Jeanne**, Da Volterra: Employee, Salary; **P. Hugon**, Da Volterra: Employee, Salary; **F. Sablier-Gallis**, Da Volterra: Employee, Salary; **S. Ferreira**, Genoscreen: Employee, Salary; **A. Andremont**, Da Volterra: Consultant, Consulting fee; **F. Mentré**, Da Volterra: Consultant and Research Contractor, Consulting fee; **J. De Gunzburg**, Da Volterra: Consultant and Shareholder, Consulting fee