

OC-006

SETTING UP A CENTRALISED DECONTAMINATION SERVICE: LESSONS LEARNT

doi:10.1136/gutjnl-2012-302514a.6

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Introduction Decontamination is moving towards a centralised service within secondary care. The aim of such is to maximise expertise and maintain quality standards. The development of centralised decontamination will minimise risk and assist the audit process. Within the authors workplace the decision was taken to house this service within the endoscopy department.

Methods An analysis of current services that used flexible endoscopes was undertaken including workforce, equipment and current usage of decontamination within the area it was undertaken. This included endoscopy, ENT & MFU outpatient and inpatient, ITU, Theatres. This led to a business case to request appropriate resource to enable implementation and deliver of required service for all users.

Results There was a difference in perceptions of a centralised decontamination service from all stakeholders. Each department had a tunnel vision with little regard for others. This led to a conflict due to all users having different priorities with little understanding of other pressures. Out of hours decontamination was an expectation from management with no acknowledgement of the impact this would have on the workforce. It was understood that all capital equipment would be pooled, however this was not accepted by some departments and led to shortages of endoscopes as services were reluctant to "share". The development of a band 4 decontamination supervisor helped the implementation of the service by offering expertise and leadership to all user groups. Management expectations of the service were often unrealistic due to lack of expertise in the area. The band 4 role offered a realistic solution using the knowledge and skills from their own experience in the field. Savings were delivered by the reduction of reproprocessors required for maintenance contracts.

Conclusion Clear understanding of objectives is required prior to the development of any service. It is vital that a stakeholders group is formed and gives all involved the time to voice any concerns at any stage. Workforce requirements must be analysed to ensure the right skill mix is available to deliver the required knowledge and skills for implementation and sustainability. There needs to be greater emphasis on business continuity plans when centralising any service.

Competing interests None declared.

BSG plenary session

OC-007

THE NATIONAL COLONOSCOPY AUDIT: A NATIONWIDE ASSESSMENT OF THE QUALITY AND SAFETY OF COLONOSCOPY IN THE UK

doi:10.1136/gutjnl-2012-302514a.7

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Introduction Colonoscopy is the gold standard procedure for the diagnosis and non-surgical management of colonic disease. Poor quality colonoscopy is associated with complications and reduced effectiveness in disease prevention. A previous large-scale study of colonoscopy practice in the UK demonstrated disappointing results

with poor caecal intubation rates and higher than expected complication rates.¹ Since then there has been significant investment in endoscopic training, a quality assurance framework for endoscopy units has been implemented and the National Bowel Cancer Screening Program has been rolled out nationally. The aim of this study was to assess the quality of contemporary UK colonoscopy.

Methods A nationwide audit of colonoscopy practice was conducted over a 2-week period from 28 February 2011 until 11 March 2011. The study was performed prospectively, with data entry occurring electronically through a purpose built website (<http://www.endoaudit.com>). All units performing >100 colonoscopies annually on NHS patients were included. All colonoscopies performed on adults (>16 years of age) were included. Data on key performance indicators and complications was collected and analysed.

Results Data on 20 085 colonoscopies and 2681 colonoscopists were collected from 301 units. A validation exercise indicated that data were collected on >94% of all procedures performed nationally. The overall, unadjusted caecal intubation rate (CIR) was 92.3%. When adjusted for impassable strictures and poor bowel preparation the CIR was 95.8%. The polyp detection rate (PDR) was 32.1%. The PDR for significant polyps (>1 cm diameter) was 11.7%. 92.3% of resected polyps were retrieved. 90.2% of procedures achieved acceptable levels of patient comfort. A total of eight perforations and 52 significant haemorrhages were reported. Eight patients underwent surgery as a consequence of a complication.

Conclusion This is the first national audit of colonoscopy that has successfully captured the majority of adult colonoscopy performed during a defined time period. The data confirm that there has been a significant improvement in performance of colonoscopy in the UK since the last study reported 7 years ago (CIR 76.9%) and that performance is above the required national standards.

Competing interests None declared.

REFERENCE

1. Bowles CJ, Leicester R, Romaya C, *et al*. A prospective study of colonoscopy practice in the UK today: are we adequately prepared for national colorectal cancer screening tomorrow? *Gut* 2004;**53**:277–83.

OC-008

DEFINING THE GENETIC LANDSCAPE OF OESOPHAGEAL ADENOCARCINOMA BY NEXT-GENERATION SEQUENCING

doi:10.1136/gutjnl-2012-302514a.8

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Introduction Despite its dismal prognosis and steady increase in prevalence little is known about the genetic alterations that drive oesophageal adenocarcinoma. As part of the International Cancer Genome Consortium: Oesophageal Adenocarcinoma (ICGC-OAC) we performed a pilot study, sequencing the genomes of 32 OAC samples, to assess the feasibility of initiating a large scale project sequencing a total of 500 OAC genomes.

Methods A total of 56 genomes were selected for sequencing including 32 OAC genomes—16 chemotherapy-Naive, 16 chemotherapy-treated—and 24 matched normal genomes. Whole genome sequencing was performed on the Illumina Hiseq 2000 platform. Initial bioinformatic analysis, run by Illumina using the Casava pipeline, detected single nucleotide variants (SNVs), small (<50 bp) Insertion and Deletions events (INDELs) and large scale structural variants (SVs). Additionally, bioinformatic analysis of SVs was performed using a custom Perl script. To determine the specificity of

the bioinformatic approach a subset of SNVs and SVs were selected for verification by Sanger capillary sequencing and PCR respectively.

Results A minimum of 50-fold mappable sequence data were generated for each of the 56 genomes. 161/167 (96%) of predicted SNVs were confirmed as somatic, two were miscalled germline variants while four were undetectable in either sample. For 2/75 (3%) SVs PCR amplicons could not be generated, for 18 of 75 SVs (24%) a PCR amplicon was detectable in the normal showing them to be germline polymorphisms. The True positive rate for SV detection was therefore 73%. Comparison of SNV information across all 24 samples revealed many recurrently mutated genes. These include previously reported mutations in TP53, CDKN2A and APC among others. No genes were significantly associated with chemotherapy-treated or chemotherapy-naïve samples.

Conclusion Analysis of the Illumina bioinformatic pipeline suggests it is highly specific (96% true positive rate) for somatic SNVs. A true positive rate of 73% for SV detection is comparable to recent literature. Further analysis to determine the sensitivity of this pipeline is ongoing including resequencing of putatively non-mutated genes in samples sent for WGS and the application of alternative bioinformatic approaches for the calling of SNVs, INDELs and SVs. Initial analysis of the SNV data from 32 tumour genomes has revealed several recurrently mutated genes known to be altered in OAC validating the ability of our approach to detect candidate “driver” genes.

Competing interests None declared.

DDF inflammatory bowel disease symposium

OC-009 HUMAN ANTI-MICROBIAL Vδ2+ T-CELLS ARE NOVEL INTESTINAL LYMPHOCYTES WITH FUNCTIONAL RELEVANCE IN CROHN'S DISEASE

doi:10.1136/gutjnl-2012-302514a.9

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Introduction Vγ9Vδ2+ “unconventional” (Vδ2) T-cells are a population of circulating anti-microbial lymphocytes found only in higher primates and whose role in human intestinal immunity is unknown. In macaques, microbe-activated Vδ2T-cells expand and accumulate in mucosal tissues, and human Vδ2T-cells can produce key mediators of intestinal inflammation such as IFNγ, TNFα and IL-17A in response to bacterial species present among the gut microbiota. We therefore hypothesised that Vδ2T-cells might contribute to the pathogenesis of Crohn's disease (CD).

Methods Disaggregated intestinal biopsies and peripheral blood were analysed by flow-cytometry in CD patients (n=22), and healthy controls (n=36). Blood and biopsy-derived cell suspensions were stimulated with microbial phosphoantigen (HDMAPP) and IL-2 in vitro to determine Vδ2T-cell phenotype, cytokine production and proliferative potential in the presence or absence of azathioprine.

Results Blood Vδ2T-cells proliferated, expressed “gut-homing” integrin β7, and produced IFNγ and TNFα upon activation with HDMAPP and IL-2 in vitro. Vδ2T-cells were also identified by confocal microscopy in both healthy and inflamed colonic lamina propria. In contrast to their blood counterparts, mucosal Vδ2T-cells expressed high levels of CD103 integrin, which is implicated in interactions with the intestinal epithelium. Although the frequency of mucosal Vδ2T-cells was low, these cells proliferated rapidly and up-regulated CD70 co-stimulatory molecule upon exposure to HDMAPP and IL-2 in vitro, consistent with responsiveness to the

gut microbiota. In CD patients receiving azathioprine therapy, Vδ2T-cells were selectively lost from the blood and were markedly depleted from the lamina propria. Accordingly, physiological concentrations of azathioprine were sufficient to block HDMAPP activation of Vδ2T-cells in vitro.

Conclusion Human Vδ2T-cells primarily reside in the blood but display gut-homing potential upon microbial activation and can be detected in the intestinal mucosa. Intestinal Vδ2T-cells may contribute to local pro-inflammatory responses against the gut microbiota but are depleted by azathioprine therapy in CD.

Competing interests None declared.

OC-010 DETAILED ANALYSIS OF ATG16L1 DEMONSTRATES GENE-WIDE EXTENT OF ASSOCIATION WITH CROHN'S DISEASE SUSCEPTIBILITY

doi:10.1136/gutjnl-2012-302514a.10

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Introduction ATG16L1 has been implicated in the susceptibility to Crohn's disease (CD), notably the T300A (rs2241880, exon 9). In ATG16L1-deficient and hypomorphic mice, autophagy, Paneth-cell homeostasis and IL-1b secretion were dependent on ATG16L1 (Saitoh *et al* Nature 2008, Cadwell *et al* Cell 2010). In contrast, studies focusing on T300A have shown conflicting results (Kuballa *et al* PLoS ONE 2008, Fujita *et al* JBC 2009). The association at other susceptibility loci (eg, NOD2 and IL23R) consists of common and rare variants (Rivas *et al* Nat Genet 2011). Exon-sequencing studies have not demonstrated rare variants within the 18 exons of ATG16L1. Our aim was to analyse the ATG16L1 association signal, specifically focusing on common variants.

Methods 38 single nucleotide polymorphisms (SNPs) spanning the ATG16L1 gene were imputed for 1735 subjects (800 CD/935 controls) (Franke *et al* Nat Genet 2010). Single SNP and haplotype frequency (>1%, solid spine of Linkage disequilibrium (LD), D'>0.8) association and permutation (n=10 000) analyses were performed (Haploview). Logistic regression (using SNPs p<0.05 on permutation analysis) was performed (SPSS). Monte Carlo simulation (n=10 000, R) was used to assess the difference in the number of haplotype blocks, based on D'>0.8, between CD and controls.

Results Single SNP permutation analysis yielded association of 16 markers (p<0.001), from intron 1 (rs6752107) to the 3'UTR (rs1045100). Analysis of D' and r² characteristics, showed 12 SNPs were in complete LD with rs2241880 (D' and r² 0.98–1). rs6758317 (r²=0.25, intron 2), rs3792106 (r²=0.76, intron 11), rs4663396 (r²=0.25, intron 12) and rs1045100 (r²=0.84) demonstrated strong association, independent of rs2241880. Regression analysis retained rs3792106, rs6754677 (intron 14) and rs1045100 (3'UTR) (p<0.05). A Monte Carlo simulation showed no significant difference in the number of haplotype blocks between CD and controls (p=1). A strong association with CD was shown for the haplotype block containing the rs2241880 and for the block containing rs1045100, both p<10⁻⁵.

Conclusion We demonstrated that the rs2241880 alone is not sufficient to explain the strong ATG16L1 association. Additional variants, independent of rs2241880, could implicate any of the coiled-coil domain, the WD domain and/or the 3' UTR, in CD susceptibility.

Competing interests None declared.