Abstracts

from 32 patients (9 CD, 14 UC, 8 healthy controls) to identify differentially expressed cell-specific miRNAs.

Top miRNAs were then validated in whole blood in 294 treatment naïve newly diagnosed IB and non-IBD patients (97 UC, 98 CD, 98 non-IBD) using RT-qPCR, recruited across 5 centres in UK and Europe. Phenotype and outcome data were collected and Cox proportional hazards were derived to assess the contribution of each miRNA to disease outcomes; defined as the need for 2 or more immunosuppressants and/or surgery after initial disease remission. RT-qPCR target miRNA relative quantification were calculated using 2$^{-\Delta\Delta Cq}$ method.

Results Each leucocyte subset (30 CD4+ T-cells, 28 CD8+ T-cells and 32 CD14+ monocytes) was analysed between disease and controls, adjusting for age, gender and batch effects. A total of 3 miRNAs differentiated IB from controls in CD4+ T-cells including miR-1307-3p (False discovery rate (FDR) p=0.01), miR-3615 (p=0.02) and miR-4792 (p=0.01); these signals being UC specific. In CD8 T-cells, miR-200b-3p was the only differentially expressed miRNA and no CD14+ signals were seen.

Three miRNAs were validated in whole blood in an independent multi-centre cohort of 294 patients using RT-qPCR. miR-1307-3p predicted IBD (1.55 fold change (fc),IQR:1.00-1.87; p=2.77×10$^{-3}$) in particular UC (1.69 fc, IQR:1.01-2.00; p=1.56×10$^{-3}$). Similarly, miR-3615 and miR-4792 were up-regulated in UC compared to controls (1.21 fc, IQR:0.91-1.48; p=8.26×10$^{-3}$and 1.91 fc, IQR:0.81-2.56; p=9.21×10$^{-3}$ respectively). There was no correlation with conventional inflammatory markers.

Follow up data were available on 195 IBD patients of which 80 patients required treatment escalation over a median time of 371 days (IQR:140-711). miR-1307-3p was able to predict disease course in IBD (HR 1.98, IQR:1.20-3.27; log-rank p=1.80×10$^{-3}$), in particular UC (HR 2.81; IQR:1.11-3.53, p=6.50×10$^{-4}$). In UC, both miR-3615 (HR 3.34, CI:1.43-7.78, p=0.01) and miR-4792 (HR 3.96, CI:1.65-9.52; p=2.11×10$^{-3}$) predicted treatment escalation.

Conclusion We have identified unique CD4+ T-cell miRNAs that are differentially regulated in IBD. These blood-based miRNAs are able to predict treatment escalation at disease inception and have the potential for clinical translation.

015 EVOLUTIONARY CHARACTERISTICS OF NEOANTIGENS IN INFLAMMATORY BOWEL DISEASE AND COLORECTAL CANCER

1Jatinder Stanley*, 2Eszter Lakatos, 1Ann-Marie Baker, 1William Cross, 2Ailsa Hart, 1Trevor Graham. 3Barts Cancer Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK; 4Inflammatory Bowel Disease Unit, St Mark’s Hospital, London, UK

Abstract O15 Figure 1 Comparison of neoantigen burden between CA-CRCs and SPCRCs

Introduction The immune system plays an active role in fighting growing tumours via recognising tumour-specific neoantigens and initiating an immune response. Consequently, the abundance and diversity of tumour neoantigens is shaped by the interaction with immune cells. Colonic mucosa in patients with inflammatory bowel disease (IBD) has a high immune cell presence, and we hypothesised this would cause increased immune predation on neoantigen-bearing epithelial cells. To test this, we compared neoantigen burdens in ulcerative colitis-associated colorectal cancers (CA-CRCs) and sporadically arising colorectal cancers (SPCRCs).

Methods Existing multi-region whole-exome and whole-genome sequencing data from CA-CRCs (n=15) and SPCRCs (n=10) was used to computationally predict the abundance and diversity of immunogenic neoantigens using NeoPredPipe.3 Variant call data was filtered to retain high confidence variants. Neoantigen burden was compared between groups using a normalised measure, representing the proportion of non-synonymous mutations predicted to produce ≥1 immunogenic neoantigen. Multi-region data from normal, histologically normal adjacent-to-tumour (NAT) and tumour samples was used to calculate the clonality and subclonality of neoantigens.

Results The neoantigen burden of CA-CRCs was lower than SPCRCs (figure 1). Excluding cancers with microsatellite instability, CA-CRCs had relatively higher numbers of subclonal neoantigens per clonal neoantigens (p=0.029, Wilcoxon test), suggesting a greater degree of intra-tumour heterogeneity in CA-CRCs. In a subset of patients with CA-CRCs, 50–100% of clonal neoantigens found in tumour samples were shared with NAT samples in the same patient, revealing evidence of field cancerisation at the neoantigen level.

Conclusions These novel results support the hypothesis of increased immune surveillance in CA-CRCs compared to SPCRCs. Subclonal neoantigens accrue following immune escape, and so the higher burden of subclonal neoantigens in CA-CRCs points to the early evolution of effective immune escape, and so the higher burden of subclonal neoantigens in CA-CRCs points to the early evolution of effective immune predation on neoantigen-bearing epithelial cells. To test this, we compared neoantigen burdens in ulcerative colitis-associated colorectal cancers (CA-CRCs) and sporadically arising colorectal cancers (SPCRCs).
escape mechanisms in these tumours. These data have implications for prognostication and immunotherapy treatment decisions for patients with CA-CRCs.

REFERENCES

Introduction
Reduced bone mineral density (BMD) and muscle dysfunction are complications of Crohn’s Disease (CD). This study evaluates the effect of exercise on BMD and muscular function in adults with CD.

Methods
This was a randomised, parallel-group and assessor-blind trial (Trial registration: BR3CTR11470370). Adults (>16 years) in clinical remission or with a mildly active CD (Crohn’s Disease Activity Index <220; Faecal Calprotectin <250 mcg/g) were recruited from The Newcastle Upon Tyne Hospitals NHS Foundation Trust, UK. Eligible patients were randomly allocated (1:1) to receive either a 60-minute, thrice-weekly, 6-month progressive impact and resistance training programme with usual care or usual care only, stratified by gender and disease activity using a computer based programme.

Primary outcomes were BMD, (lumbar spine (L2-L4), femoral neck, greater trochanter) and muscle function parameters at 6 months in the intention-to-treat population, with analyses adjusted for baseline values, gender and disease status.

Results
Between February 2018 and March 2019, 76 patients were assessed for eligibility, of whom 47 patients were recruited and randomised (68% female; mean age 49.3 [SD 13.0] years) to the exercise intervention (n=24) or control (n=23). 6-month follow up data were recorded for 43 (91%) patients and create a visual risk communication web-tool.

Methods
We performed a retrospective multi-centre cohort study. Adult UC patients with an index diagnosis of LGD were identified in four UK tertiary centres between 2001 and 2018. Patients were followed until progression to AN or censoring. Data from a single centre (n=248) was used as a discovery cohort, and Cox proportional hazards regression was performed to create a multivariate risk prediction model based on endoscopic features. The model was then validated on the pooled cohort of patients from the 3 external centres (n=201).

Results
In the discovery cohort, the 4 clinical variables that were significantly associated with future AN progression and were included in our final multivariate model were: Presence of endoscopically-visible LGD lesion >1 cm (HR = 2.8; 95% CI 1.3–6.0; p=0.008), incomplete endoscopic resection of index LGD (HR = 2.9; 95% CI 1.3–6.9; p=0.009), moderate/severe histological inflammation in the 5 years before

Abstract O17 Figure 1 UC-CaRE online risk report. Pacing chart demonstrating predicted cumulative risk of advanced neoplasmia at 1, 5, and 10 years since LGD diagnosis.