CRC have higher mortality than non-CD patients also diagnosed with CRC. CRC surveillance could likely be improved and should be focussed on CD patients <40 years at CD onset, patients with colon inflammation, and patients who have PSC.

## Scientific session 5: Cartels in IBD (Part 1)

### OP15

### Multi-omic data integration with network analysis reveals underlying molecular mechanisms driving Crohn's disease heterogeneity

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**Background:** Crohn's disease (CD) is a heterogeneous disease characterised by clinical phenotypes including differences in disease behaviour, disease location and extraintestinal manifestations. However, the molecular mechanisms which orchestrate CD heterogeneity are relatively unexplored. We tried to infer such mechanisms by integrating two -omic datasets (genomics and blood proteomics) generated from CD patients.
**Methods:** 576 unique proteins were measured from blood isolated from CD patients ($n$ = 98) using seven different Olink® panels. All patients were also genotyped using Immunochip. We integrated the above two datasets using an unsupervised data integration algorithm called Multi-Omics Factor Analysis (MOFA). MOFA identifies Latent Factors (LFs) which are hidden representative variables which capture the sources of variation in the provided -omic datasets. LFs capturing less than 2% of the variance were discarded. By using a regression model, we identified explanatory LFs which associate with clinical phenotypes. Proteins and mutations were ranked according to the scores assigned by the corresponding explanatory LF. Potential effects of mutations were inferred by analysing their impacts on coding and non-coding functions. Local network motifs which capture the direct and indirect effects of mutations on protein expression were identified by using the Cytoscape tool ISMAGS. Protein–protein and transcriptional regulatory relationships retrieved from the OmniPath and DoRothEA databases, respectively, were combined to compile the interaction networks used by ISMAGS.
**Results:** From the MOFA analysis, we identified five LFs associated with at least one clinical phenotype. Clustering patients along the explanatory LFs achieved meaningful separation of clinical phenotypes such as perianal penetrating disease. The top-ranking proteins associated with perianal-disease included those involved in inflammatory pathways, autophagy or already known to be involved in CD such as IL-8, Rho-GTPase activators, MIF, Caspase 8, TRIM5 and SNAP29. The networks corresponding to the top ranking proteins associated with the perianal phenotype could be broken down into 102 local network motifs. These local motifs pointed out control mechanisms by which a total of 7 mutations mapped to transcription factors (SMAD3, BACH2) and post-translational regulators (such as IFNGR2, IL10, IL2RA, SLC2A4RG and ZMIZ1) could potentially regulate perianal disease's pathophysiology and could, therefore, be considered novel drug targets.
**Conclusion:** By using integrated signature profiles generated from multiple -omic datasets, we identified molecular mechanisms which could potentially describe CD phenotypes such as the occurrence of perianal disease.

### OP16

### Influence of early life factors on the development of intestinal microbiota of infants born to mothers with and without IBD

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**Background:** Inflammatory bowel diseases (IBD) are associated with a dysregulation of the intestinal microbiota and some of these dysbiotic taxa may be transmitted to the offspring of pregnant patients with IBD. We analysed the influence of early life events on the development of the intestinal microbiota of infants born to mothers with and without IBD.
**Methods:** The MECONIUM (Exploring MEChanisms Of disease traNsmission In Utero through the Microbiome) study is a prospective cohort study including pregnant women with or without IBD and their infants. Stool samples were collected during pregnancy and in babies throughout the first 2 years of life. Stool microbiota composition in the baby stool was assessed using 16S rRNA sequencing.
**Results:** We analysed 1037 faecal samples from 294 infants (born to 80 mothers with and 214 without IBD). The overall composition of the microbiota at 1 month was influenced by the mode of delivery ($r$ = 0.1224, $p$ = 0.001), feeding (breastfeeding, formula feeding or mixed; $r$ = 0.0366, $p$ = 0.013), and antibiotics ($r$ = 0.0446, $p$ = 0.004), and this was mainly driven by α-diversity (Simpson, $r$ = 0.0529, $p$ = 0.012), and the relative abundance of Bacteroides ($r$ = 0.8738, $p$ = 0.001), Bifidobacterium ($r$ = 0.4282, $p$ = 0.001), and Klebsiella ($r$ = 0.6182, $p$ = 0.001). Univariate and

multivariate analysis confirmed the influence of mode of delivery in the relative abundance of Bacteroides (increased in vaginal delivery, Wilcoxon FDR $p$ = 2.50e−07, Maaslin FDR $p$ = 0.0016) at month 1. At month 3, mode of delivery ($r$ = 0.0779, $p$ = 0.001), IBD status of the mothers ($r$ = 0.0253, $p$ = 0.028), and pre-term birth ($r$ = 0.0208, $p$ = 0.045) influenced the overall composition of the microbiota, with the main drivers being Bifidobacterium ($r$ = 0.8844, $p$ = 0.001), Bacteroides ($r$ = 0.8632, $p$ = 0.001), and Klebsiella ($r$ = 0.4374, $p$ = 0.001). Univariate and multivariate analysis confirmed the influence of mode of delivery in the relative abundance of Bacteroides (increased in vaginal delivery, Wilcoxon FDR $p$ = 1.23e−06, Maaslin FDR $p$ = 0.07). None of the evaluated variables could significantly explain the variation of the overall composition of the microbiota at 1 year of life. IBD status of the mother influences the microbiota composition of 2-year-old infants; however, this association was only significant in vector fitting analysis.

**Conclusion:** Maternal IBD status is shaping early life microbiota in their offspring, likely due to altered microbiota in mothers with IBD. Additionally, the mode of delivery, feeding, and exposure to antibiotics are important determinants of the infant´s microbiota. These influences are lost with time, probably due to increasing exposure to several sources of microbiota and to confounding factors (e.g. diet).

## OP17

### Protein intakes and risk of inflammatory bowel disease in the European Prospective Investigation into Cancer and Nutrition cohort (EPIC-IBD).

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**Background:** Diet may contribute to inflammatory bowel disease (IBD) pathogenesis. In a previous French cohort, we found an association between high protein intake and increased risk of IBD. We aimed to investigate this relationship in the EPIC-IBD (European Prospective Investigation into Cancer and Nutrition – Inflammatory Bowel Diseases) cohort.

**Methods:** 413 593 participants from 8 European countries were included. Dietary data were collected at baseline from validated food frequency questionnaires. Mean daily intake of nutrients was assessed using the EPIC nutrient database. To reduce bias in the estimation of relative risks, calibrated dietary data were obtained from the country and sex-specific calibration models for all participants. Associations between proteins (total, animal, and vegetable) or food sources of animal proteins, and IBD risk were estimated by Cox proportional hazard models.

**Results:** After a mean follow-up of 16 years, 595 incident cases of IBD were identified, including 177 Crohn's disease (CD) and 418 ulcerative colitis (UC) cases. No association was observed between total protein intake and IBD risk (adjusted HR for the fourth vs. the first quartile = 1.25; CI 95% = 0.89–1.77, $P$-trend = 0.33). There was a significant association between the calibrated continuous variable of animal protein intake and IBD risk (adjusted HR per 10 g/day: 1.10; 95% CI = 1.004–1.21) although no association was found for extreme quartiles (HR: 0.99; 95% CI = 0.73–1.34; $P$-trend = 0.91). There was no association between vegetable protein intake and IBD risk. There was an association between meat consumption and IBD risk (adjusted HR for the fourth *vs*.. the first quartile = 1.37; CI95% = 1.02–1.82, $P$-trend = 0.003) and between red meat consumption and IBD risk (adjusted HR for the fourth *vs*. the first quartile = 1.41; CI95% = 1.03–1.92, $P$-trend = 0.006). In separate analyses for CD and UC, there was an association between total meat and UC risk, and between red meat and UC risk. No association was found between food sources of animal proteins and CD risk.

**Conclusion:** Animal protein intake is associated with IBD risk in the EPIC-IBD cohort. Observed associations between meat consumption and IBD or UC risk, and between red meat consumption and IBD or UC risk deserve further investigation.

## OP18

### Surgical prevention of anastomotic recurrence by excluding mesentery in Crohn's disease: The SuPREMe-CD study

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**Background:** Recently, a new antimesenteric, functional end-to-end, hand-sewn ileocolic anastomosis (Kono-S) has shown a significant reduction in endoscopic recurrence score and surgical recurrence rate in Crohn's disease (CD).This trial aimed to provide randomised controlled data comparing Kono-S anastomosis and stapled ileocolic side-to-side anastomosis.

**Methods:** Randomised controlled trial at a tertiary referral institution, enrolling and randomising to undergo either the 'Kono group' or the 'Conventional group', all CD subjects needing surgery. Primary endpoint: endoscopic recurrence (ER) (Rutgeerts score ≥i2) after 6 months. Secondary endpoints: clinical recurrence (CR) after 12 and 24 months, ER after 18 months and surgical recurrence (SR) after 24 months. Also, short-term outcomes and postoperative complications were recorded. A sample size of 70 patients (35 in each group) was considered necessary to demonstrate a reduction >30% in endoscopic recurrence at 6 months follow-up in the Kono group when assuming a 60% endoscopic recurrence expected rate in the control group.

**Results:** 79 CD patients were enrolled and randomised in the Kono group (36) or Conventional group (43) (Table 1). After 6 months, 22.2% in the Kono group and 62.8% in the Conventional group presented an ER ($p$ < 0.001; OR 5.91). A severe postoperative ER