IBD RESEARCH

Professor Ailsa Hart, Director
St Mark's Hospital
Imperial College London

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MISSION STATEMENT OF IBD CENTRE

"St Mark's Hospital is a centre of excellence which offers individualized, exceptional, multi-disciplinary care for people with inflammatory bowel diseases, allowing healing of their disease and empowering them to lead normal lives."

VISION OF RESEARCH CENTRE

"A dynamic research group underpinned by mutual collaborative relationships with a wider scientific community"

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1 INTRODUCTION

St Mark's Hospital strives for clinical excellence, innovative research and top quality education and teaching.

Research in the field of inflammatory bowel diseases has always been one of the major strengths at St Mark's Hospital. In particular, it was here at St Mark's that clinicians in the early twentieth century first used the technology of lighted examination of the rectum to assess the bowel mucosa. The first description of *colonic* Crohn's disease was made here. The early trials demonstrating therapeutic efficacy of 5 aminosalicylates, steroids and thiopurines in the management of inflammatory bowel diseases were performed at St Mark's; and the first controlled trial of a biological drug for Crohn's disease was at St Mark's. The first cancer surveillance programme for colitis was developed here at St Mark's Hospital, and in the treatment of ulcerative colitis, surgeons described the ileo-anal pouch operation or restorative proctocolectomy.

2 ACHIEVEMENTS IN IBD RESEARCH

On the background of this inspirational historical platform, the IBD research team at St Mark's Hospital, led by Professor Ailsa Hart, continues to make novel, innovative and clinically relevant contributions in the field of inflammatory bowel disease. These advances include:

1) at the **basic science** level, description of key mucosal immune pathways and interactions with the host microbiota that drive intestinal inflammation in IBD;
2) **novel therapeutics** for IBD, such as faecal microbiota transplantation and probiotics;
3) **augmenting current therapeutics** for IBD, such as with adjunctive vitamin D supplementation;
4) **developing Core Outcome Sets** (COS) and Core Measurement Sets (CMS) for assessment of perianal Crohn's disease for use in ongoing clinical trials and within the clinic setting;
5) **developing novel techniques for assessment and monitoring of Crohn's perianal fistulas**, such as volume assessment and 3D modelling of fistula tracts;
6) **developing and maintaining the world's largest and longest running IBD cancer surveillance database** to improve IBD cancer surveillance and understand the biology of the inflammation to cancer pathway;
7) studies highlighting the **importance of psychological factors and quality of life/ symptom control in IBD**
8) **endoscopic therapies** in the management of IBD e.g. double balloon endoscopy and dilatation of intestinal strictures
9) contribution to **epidemiological studies** in IBD
10) novel **surgical therapies**
11) **tissue remodelling** in intestinal failure
12) assessment of **outcomes and quality** from large national datasets

The research activities cover cross-cutting themes bringing expertise from different backgrounds, medical, surgical, radiological, nursing, dietitian, psychological and basic science into projects to drive IBD clinical care and research.

Highlights of our contributions are discussed in more detail below. A selection of key references from our work is presented.

1. We published detailed descriptions of the **mucosal immune system in human inflammatory bowel diseases** (IBD), describing key immune pathways which are now targets of current therapies used to treat patients with IBD (e.g. vedolizumab, targeting gut-homing effector T-cells, and ustekinumab targeting the IL-12/IL-23 pathway)

- We published the first detailed description of **mucosal dendritic cells** in human inflammatory bowel disease[1]; a pathway now **widely recognised as a key part of the aberrant mucosal response** in these diseases. In particular, we described the activated phenotype of mucosal dendritic cells and their increased production of pro-inflammatory cytokines, including IL-6 and IL-12. Other properties of human dendritic cells and their interaction with gut microbiota have been described by the group[1-15]
- In both ulcerative colitis and Crohn's disease, we published a detailed description of **intestinal homing (β7 positive) effector T-cells** demonstrating increased production of pro-inflammatory cytokines by this cell type in IBD; the **specific targeting of mucosal homing T-cells is now in clinical use with the NICE-approved therapy, vedolizumab**, an α4β7 anti-integrin therapy[16,17]

2. As a part of the **UK IBD Genetics consortium**, we have contributed to the **evolving genetic landscape** in these complex inflammatory bowel diseases, which now have over 240 independent susceptibility loci.

- We contributed to the identification of **links between side effects with therapies used to treat inflammatory bowel diseases and genetic susceptibility**, such as an HLA-link with pancreatitis and use of azathioprine[57] and HLA association of 5-aminosalycilate induced nephrotoxicity[58].

3. We described the gut microbiota in health and in IBD[29] and the effects of **probiotic therapies on human immune dendritic cells** *in vitro*, which were subsequently validated in humans[18-26]. We participated in clinical trials using probiotic therapies as a treatment for inflammatory bowel disease[19]. These **probiotic therapies are within international guidelines for treating some forms of inflammatory bowel disease** (ECCO guidelines 2018).

Furthermore, we described **decreased microbiota diversity in inflammatory bowel disease**[28]; decreased microbial diversity is still recognised to be a **key aspect of the dysbiosis** which drives inflammation in IBD; we also described the **interaction between the intestinal microbiota and the mucosal immune system**[2]. These studies contributed to the rationale to use **modalities to manipulate the microbiota as a therapeutic modality** with **probiotics**[23]**, prebiotics and faecal microbiota transplantation (FMT)**[49].

- We contributed to a clinical trial of prebiotics in Crohn's disease[27] and we published a first pilot study of faecal microbiota transplantation in IBD[48].
- FMT is now approved by NICE for refractory *clostridium difficile* infection and **we are conducting the largest FMT clinical trial in ulcerative colitis funded by a NIHR EME grant** (commenced January 2018).

4. Vitamin D not only has effects on calcium metabolism, but also has immunomodulatory effects. We have demonstrated **immunoregulatory effects of vitamin D**[41,42] on dendritic cells and a **potential to augment therapy with anti-TNF drugs** used to treat Crohn's disease. Furthermore, we have demonstrated **effects of vitamin D on the microbiota**, which may impact on the immunomodulatory roles in IBD.

5. There is an unmet need to have outcome measures that are universally used in clinical trials and indeed in clinical practice, so that we all "speak the same language" when describing outcomes from trials. In the field of perianal Crohn's disease, which represents a particularly aggressive form of the disease, **we have developed a Core Outcome Set (COS) for perianal Crohn's disease**[70] with collaborators from all over the UK and in all disciplines (surgical, medical, nursing, radiology and importantly with patient representation). The ENiGMA group (Evaluating Goal Directed Therapy for Perianal Crohn's disease) from across the UK aims to build on this to develop improved strategies for managing perianal Crohn's disease. From this Core Outcome Set, there is a need to develop Core Measurement Sets, for example, assessing the quality of life of patients with perianal Crohn's disease. A Crohn's Anal Fistula Quality of Life Questionnaire (CAF-QoL) is in development.

Box 2 Core outcome set for fistulising perianal Crohn's disease

Patient-reported outcomes

- Global assessment of quality of life.
- Combined score of patient priorities.
  - Lifestyle restriction (general)
  - Lifestyle restriction based on toileting needs
  - Depression
  - Inability to attend school/work
  - Restriction of sexual activity and avoidance of intimacy.
- Global assessment of incontinence.

Clinician-reported outcomes

- A validated score to assess perianal disease activity.
- Development of a perianal abscess.
- Development of a new/recurrent fistula.
- Unplanned surgical reintervention.
- Faecal diversion or proctectomy.

Imaging (optional module)

- Fistula response on MRI.
- An activity-based MRI score responsive to change.

6. We have developed improved approaches for assessment and monitoring fistulating perianal Crohn's disease[39]. **MRI volume assessment of perianal fistulas** is being developed and **novel 3D models** have been developed to aid pre-operative surgical planning and assist in surgical teaching[39.40,69].

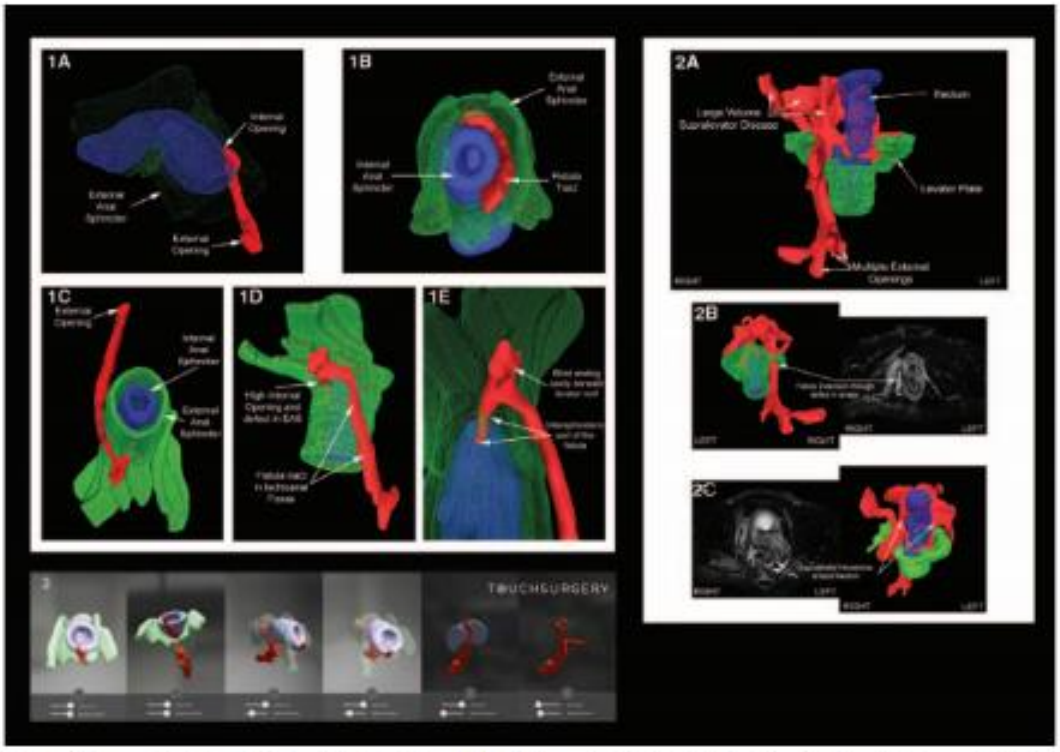

FIGURE 1. 1, 3D reconstructions of intersphincteric (A and B) and transphincteric (C–E) fistulas. (1A) Angled view of the fistula from the right with a translucent EAS visualizing the intersphincteric fistula and internal opening. (1B) View of the sphincter complex with patient in lithotomy position showing the intersphincteric fistula. (1C) View of the sphincter complex with patient in lithotomy position and anal canal angled anteriorly showing the trans-sphincteric fistula. (1D) Angled view of the fistula from the right visualizing the ischioanal portion of the fistula, the defect in the external sphincter (mesh view) and the external opening. (1E) Closeup view from the right visualizing the proximal fistula and defect in the external sphincter. 2, 3D reconstruction of a complex perianal Crohn fistula with large supralevator and infralevator components. (2A) Anteroposterior view of the sphincter complex and levator plate with extensive fistulising disease. (2B) Angled view from the right of posterior sphincter complex showing fistula tract traversing through a defect in the levator plate on the right. (2C) Angled view from the left of the anterior sphincter complex showing a large volume supralevator extension around the rectum. 3, Screenshots of a segmented trans-sphincteric tract. The images denote the ability to manipulate the image on the screen and to also "ghost" the surrounding structure as the operator choses.

7. We have the **world's largest and longest running IBD cancer surveillance programme** running at St Mark's Hospital. We have continued to develop and maintain this invaluable resource to further our understanding of the inflammation to cancer pathway.

- The team have used the database to demonstrate the **changing trends in colorectal cancer (CRC) in IBD patients** over the last 4 decades[79] and also the **features of low grade dysplasia that predict progression to high grade dysplasia or CRC**[64] which is increasingly recognised given the improvements in endoscopic surveillance. This data is used in the updated European Crohn's and Colitis Organisation (ECCO) guidelines[73].
- **Chronic longstanding inflammation in ulcerative colitis has been demonstrated by our group to be associated with poorer outcomes regarding dysplasia**, further highlighting that mucosal healing is a goal of therapy in treating these disease[65].

- **Novel markers of progression to higher grade lesions** are being developed.
- **Tools to communicate risks** to patients are also under development.

8. The **pyschological burden of living with inflammatory bowel disease** cannot be understated. We have published studies highlighting the association of **stress with IBD**[31,32]. Furthermore, we have published on **chronic symptoms (such as pain, fatigue and continence issues) which impact in a major way on quality of life**. The team are involved in an NIHR programme grant (IBD-BOOST) to optimise mangement of chronic sympyoms in patients with IBD.

9. **Endoscopy** contributes to management of patients with inflammatory bowel disease, particulalrly with regards to stricture dilatation. We have used **double balloon endoscopy and dilatation** in the management of small bowel strictures[33] and asseessed factors influencing outcomes after dilatation[67].

10. There is a change in the **epidemiology of Crohn's disease and ulcerative colitis** across the world. This change across time and geography cannot be explained by genetics; environmental factors play a key role. St Mark's participates in a European initiative assessing epidemiological changes in IBD over time[37,38]. In particular, differences in South Asians living locally has been assessed[38].

11. Novel **surgical therapies.** Transanal total mesorectal excision (TaTME) is an evolving surgical technique for colorectal surgery in the field of IBD. We are prospectively monitoring the quality of life of those undergoing ileo-anal pouch procedure following Ta TME. Preliminary results have been presented and the final analysis will be published shortly in collaboration with a leading IBD centre in Milan, Italy as a multicentre study. St Mark's has participated in a study assessing early surgical resection in the management of ileocaecal Crohn's disease[68].

12. Tissue remodelling in intestinal failure

13. Assessment of **outcomes and quality** from large national datasets[44,45].

3 NATIONAL AND INTERNATIONAL COLLABORATIONS

We collaborate nationally and internationally in basic science research, translational research and clinical trials. For example, we are a key site for the UK IBD Bioresource, which aims to recruit 25,000 patients with IBD. This project brings together the Medical Research Council and the NIHR to support ground-breaking studies looking at the genetics and new treatments of IBD that have the potential to make a real difference to patients' lives.

Collaborators include:

- Professor Trevor Graham (QMUL)
- Professor Stella Knight (Imperial College)
- Professor Jeremy Nicholson/ Professor Elaine Holmes, Professor Julian Marchesi (Imperial College)
- Professor Christine Norton (Kings College)
- Professor Simon Carding (Institute of Food Research, Norwich)
- Professor Tariq Iqbal (Birmingham)
- Dr Miles Parks Lead of UK Genetics Consortium (Cambridge)

- Dr Rupa Banergee (Asian Institute of Gastroenterology, Hyderabad, India)
- Professor Siew Ng (Hong Kong)

3.1 NATIONAL AND INTERNATIONAL GUIDELINES /BOOKS

We contribute to national and international guidelines in inflammatory bowel disease: ECCO guidelines[73], World Consensus Guidelines[50]; International guidelines on FMT[74].

We have written/ edited two books on inflammatory bowel diseases;

- Gut Ecology. A.L. Hart, A.J. Stagg, H. Glise, H. Graffner, P. Falk, M. A. Kamm. . London: Martin Dunitz, 2002
- Inflammatory Bowel Disease- An Evidence-based Guide. Editors A. L. Hart & S. C. Ng: TFM Publishing Ltd (2012). Over 8000 copies sold – "best seller" at ECCO and BSG meetings. A book review in Colorectal Disease states "The authors should be congratulated for achieving their aim of writing a succinct evidence-based account that will be referred to frequently for practical advice on the medical management of patients with IBD"

4 CLINICAL TRIAL RESEARCH

We have had a strong track record in multi-centre clinical trial research, which is reported separately (IBD Clinical Research Annual Report 2017).

5 PATIENT AND PUBLIC INVOLVEMENT AND ENGAGEMENT

Professor Ailsa Hart is UK Gastroenterology Lead for Patient and Public Involvement and Engagement (PPIE) in research. We have a particular interest in this field and are very keen to engage with our patients with regards to ensuring we ask the correct and relevant questions, design optimal studies, have feasible recruitment strategies and disseminate the information to our patients so that they can keep up to date with the research.

We have been contributors to Research Priority Setting Partnerships (James Lind Alliance), which has published the top ten unmet needs in the treatment of inflammatory bowel disease35, 36.

6 FUTURE PLANS FOR IBD RESEARCH

We have an exciting programme of ongoing research in IBD, encompassing basic science research, translational work and clinical trials.

We have the following six key areas that we are actively researching.

6.1 PATHOGENESIS OF IBD

We continue to explore the pathogenesis of IBD assessing genetic, immunological and microbiological contributions to disease.

Current aims are:

1. Continuing to contribute to the UK and International IBD genetics consortium
2. Continue to explore mucosal immune responses in particular alterations in homing molecule expression in different phenotypes of IBD
3. Epigenetic factors involved in IBD

4. Continue to assess microbiological and metabolic factors involved in IBD and their modification as a therapy

6.2 EPIDEMIOLOGY OF IBD

Epidemiological studies are ongoing, in particular assessing microbiological/ metabonomic factors in Asians living in the UK. We have an exciting collaboration with the Asian Institute of Gastroenterology in Hyderabad, enabling a comparison of lifestle and environmental factors in Asians living in India compared with those living in the UK.

Current aims are:

1. Study the epidemiology in South Asian communities in UK
2. Study epidemiology and microbiological factors of Asian communities in India
3. Explore new environmental factors that predispose to the disease
4. Link disease phenotypes of molecular markers

6.3 FISTULA RESEARCH (ROBIN PHILLIPS' FISTULA RESEARCH UNIT)

The fistula group have published on aetiological, in particular, microbiological factors involved in fistula persistence. The group has developed a Core Outcome Set (COS) for assessing fistulas as part of the ENiGMA team, and is developing a quality of Life (QoL) score which is currently being validated. We are also assessing an objective means of monitoring fistulas by volume assessment using software superimposed on MRI scans. The group have been involved in publishing the world consensus statement on perianal Crohn's disease and a systematic review on the role of multi-disciplinary medical and surgical management of perianal Crohn's disease.

Current aims are:

1. Assess pathogenesis of fistulas, in particular to assess changes in microbiota and bacterial receptors in fistula tracts
2. Optimise assessment / monitoring with MRI and develop objective assessments of fistula tracts
3. Develop and validate patient reported outcome / quality of life score for patients with fistulas
4. Contribute to national initiative to evaluate goal directed therapies for perianal Crohn's disease (ENIGMA)
5. Explore new therapies and run randomized controlled trials to improve outcomes for patients with perianal Crohn's disease

6.4 POUCH RESEARCH (ST MARK'S POUCH RESEARCH UNIT)

The group have published on the microbiota and immunological changes in the pouch, in particular alteration of tight junction proteins (in particular Claudin-2) predating changes in innate immune cells in the mucosa, implying the role of these proteins early in disease initiation The group have conducted the first pilot trial of faecal microbiota transplantation in pouchitis. Outcomes of patients undergoing pouch surgery have also been published by the team.

Current aims are:

1. Update and optimise the pouch database at St Mark's
2. Interdigitate with the UK pouch registry
3. Link with other pouch registries e.g. Danish cohort, Mt Sinai
4. Utilise Hospital Episode Statistics to understand outcomes of patients undergoing pouch surgery
5. Assess prospectively quality of life in patients undergoing pouch surgery

6. Assess a longitudinal cohort of pouch patients to understand the pathogenesis of intestinal inflammation (microbiological and immunological)
7. Faecal microbiota transplantation as a novel therapy for pouchitis or prophylactic approach in high risk patients.
8. Assess decision aids in the context of pouch surgery and psychological measures
9. Use imaging strategies to improve assessment of pouch dysfunction

6.5 IBD-RELATED CANCER RESEARCH (ST MARK'S SURVEILLANCE RESEARCH UNIT)

The team have used the database from the largest and longest running IBD surveillance cohort to demonstrate the changing trends in CRC in IBD patients over the last 4 decades and also the features of low grade dysplasia which is increasingly recognised given the improvements in endoscopic surveillance that predict progression to high grade dysplasia or CRC. This data has been used in the updated European Crohn's and Colitis Organisation (ECCO) guidelines.

Current aims are:

1. Explore new endoscopic modalities of dysplasia detection
2. Understand pathogenesis of IBD-related cancer
3. Assess evolutionary biomarkers for cancer risk prediction in IBD
4. Develop tools to improve communication of risk with patients
5. We are currently evaluating the effect of SMAD7, an inhibitory molecule in the TGF β pathway, on ulcerative colitis associated colon cancer. The molecule has lately been of interest as a therapeutic target in ulcerative colitis and has a multifaceted role in colorectal cancer. A project is underway to evaluate its role in epigenetic alterations in colitis associated cancer.

6.6 SYMPTOM IMPROVEMENT / QUALITY OF LIFE OPTIMISATION IN IBD

Patients report fatigue, pain, diarrhoea/ continence issues even when their disease is in remission. An exciting 5-year NIHR programme grant "IBD-Boost" has started in 2018.

Current aims are:

1. Complete systematic reviews on pain, fatigue and continence issues in IBD patients
2. Develop on-line interventions to optimise symptom control

APPENDIX 1:
References

1. A. L. Hart, H. Omar Al-Hassi, M. A. Kamm , S Knight, A.J. Stagg. Characteristics of intestinal dendritic cells in inflammatory bowel diseases. Gastroenterology 2005;129:50-65.

2. Ng S; Benjamin J; Hedin C; Koutsoumpas A; McCarthy N; Hart A L; Kamm M; Sanderson J; Knight S; Forbes A; Stagg A; Whelan K; Lindsay J. The Relationship between Human Intestinal Dendritic Cells, Gut Microbiota and Disease Activity in Crohn's Disease. Inflamm Bowel Dis. 2011 Oct;17(10):2027-37

3. A.J. Stagg, A.L. Hart, M. A. Kamm & S. C. Knight. The dendritic cell: its role in intestinal inflammation and relationship with gut bacteria. Gut 2003; 52: 1522-59

4. A.J. Stagg, A.L. Hart, M. A. Kamm & S. C. Knight. Interactions between dendritic cells and bacteria in the regulation of intestinal immunity. Best Practice & Research Clinical Gastroenterology 2004; 18(2) :255-270

5. Landy J, Al-Hassi HO, Ronde E, English NR, Mann ER, Bernardo D, Ciclitira PJ, Clark SK, Knight SC, Hart AL. Innate immune factors in the development and maintenance of pouchitis. Inflamm Bowel Dis. 2014 Nov;20(11):1942-9

6. Mann E, Bernardo D, Al-Hassi H, English N, Clark S K, McCarthy N, Milestone A, Cochrane S, Hart A L, Stagg A J, Knight S C. Human gut-specific homeostatic dendritic cells are generated from blood precursors by the gut microenvironment. Inflamm Bowel Dis 2012 Jul;18(7):1275-86.

7. Bernardo D, Al-Hassi O, Mann E, Tee C, Murugananthan A, Peake S, Hart A L, Knight S. T-cell proliferation and FoxP3 expression in human T-cells are dependent on T-cell density: physics of a confined space? Human Immunology. 2012 Mar;73(3):223-31.

8. Bernardo D, Vallejo-Díez S, Mann E, Al-Hassi H, Martínez-Abad, Montalvillo E, Tee C, Murugananthan A, Núñez H, Peake S, Hart A L, Fernández-Salazar L, Garrote, Arranz E, Knight SC. IL-6 promotes immune responses in human ulcerative colitis and induces a skin homing phenotype in dendritic cells and T-cells they stimulate. Eur J Immunol. 2012 May;42(5):1337-53

9. Peake ST, Bernardo D, Knight SC, Hart A L. Homing marker expression on circulating dendritic cells correlates with different phenotypes of Crohn's disease. J Crohns Colitis. 2012 Oct 23.

10. Mann E, McCarthy N E, Milestone A, Al-Hassi H, Bernardo D, Pitcher M, Cochrane S A, Stagg A J, Hart A L, Knight S C. Skin and gut homing molecules on human circulating γδ T-cells and their dysregulation in Inflammatory Bowel Diseases. Clin Experimental Immunol 2012 Nov;170(2):122-30

11. Bernardo D, Mann E, Al-Hassi H, English N, Man R, Lee G, Ronde E, Landy J, Peake S, Hart A L, Knight SC. Lost therapeutic potential of monocyte-derived DC through lost tissue homing;

stable restoration of gut specificity with retinoic acid. Clinical Experimental Immunology 16th April 2013

12. Mann ER, Bernardo D, Ng SC, Rigby RJ, Al-Hassi HO, Landy J, Peake ST, Spranger H, English NR, Thomas LV, Stagg AJ, Knight SC, Hart AL. Human gut dendritic cells drive aberrant, gut-specific T-cell responses in ulcerative colitis, characterised by increased IL-4 production and loss of IL-22 and IFNγ. Inflamm Bow Dis 2014 Dec;20(12):2299-307

13. Mann E, Landy J, Bernardo D, Peake S, Hart A L, Al-Hassi H and Knight SC. Intestinal dendritic cells: their role in intestinal inflammation, manipulation by the gut microbiota and differences between mice and men. Immunol Lett 2013 Jan 23;150(1-2):30-40

14. Mann ER, Bernardo D, English NR, Landy J, Al-Hassi HO, Peake ST, Man R, Elliott TR, Spranger H, Lee GH, Parian A, Brant SR, Lazarev M, Hart AL, Li X, Knight SC. Compartment-specific immunity in the human gut: properties and functions of dendritic cells in the colon versus the ileum. Gut. 2015 Feb 9. pii: gutjnl-2014-307916. doi: 10.1136/gutjnl-2014

15. Bernardo D, Durant L, Mann ER, Bassity E, Montalvillo E, Man R, Vora R, Reddi D, Bayiroglu F, Fernández-Salazar L, English NR, Peake ST, Landy J, Lee GH, Malietzis G, Siaw YH, Murugananthan AU, Hendy P, Sánchez-Recio E, Phillips RK, Garrote JA, Scott P, Parkhill J, Paulsen M, Hart AL, Al-Hassi HO, Arranz E, Walker AW, Carding SR, Knight SC. Chemokine (C-C Motif) Receptor 2 Mediates Dendritic Cell Recruitment to the Human Colon but Is Not Responsible for Differences Observed in Dendritic Cell Subsets, Phenotype, and Function Between the Proximal and Distal Colon. Cell Mol Gastroenterol Hepatol. 2015 Sep 3;2(1):22-39

16. AL. Hart, M. A. Kamm , S Knight, A.J. Stagg.Quantitative and functional characteristics of intestinal homing memory T-cells: analysis of Crohn's disease patients and healthy controls. Clinical Experimental Immunology 2004; 135(1):137-45

17. AL. Hart, M. A. Kamm , S Knight, A.J. Stagg. Prospective evaluation of intestinal homing memory T cells in ulcerative colitis. Inflammatory Bowel Diseases 2004; 10(5): 496-503.

18. AL. Hart, K. Lammers, P. Brigidi, B. Vitali, F. Rizzello, P. Gionchetti, M. Campieri, M. A. Kamm, S. Knight and A.J. Stagg,. Modulation of dendritic cell phenotype and function by probiotic bacteria. Gut 2004; 53(11): 1602-9.

19. Ng SC, Plamondon S, Kamm MA, Hart A L, Al-Hassi HO, Guenther T, Stagg AJ, Knight SC. Immunosuppressive effects via human intestinal dendritic cells of probiotic bacteria and steroids in the treatment of acute ulcerative colitis. Inflamm Bowel Dis. 2010 Aug;16(8):1286-98.

20. Hart A L *, K. M. Lammers*, P. Brigidi, P. Gionchetti, B. Vitali, H. O. Al-Hassi, N. English, F. Rizzello, S. Stagg, M. Campieri, S. C. Knight, M. A. Kamm, A. J. Stagg. Probiotic bacterial DNA induces IL-10 production by dendritic cells via TLR9 * joint first authors. International Journal of Probiotics and Prebiotics February 2012; 7(1): 39-48

21. Mann, E.R., You, J., Bernardo, D., Al-Hassi, H.O., Peake, S.T.C., Thomas, L.V., Tee, C.T., Landy, J., Hart, A L, Yaqoob, P. and Knight, S.C. (2012). Dysregulated circulating dendritic cell function in ulcerative colitis is partially restored by probiotic strain Lactobacillus casei Shirota. Mediators Inflamm. 2013;2013:573576.

22. Al-Hassi HO, Mann ER, Sanchez B, English NR, Peake ST, Landy J, Man R, Urdaci M, Hart AL, Fernandez-Salazar L, Lee GH, Garrote JA, Arranz E, Margolles A, Stagg AJ, Knight SC, Bernardo D. Altered human gut dendritic cell properties in ulcerative colitis are reversed by Lactobacillus plantarum extracellular encrypted peptide STp. Mol Nutr Food Res. 2014 May;58(5):1132-43.

23. S. Ng, A. L. Hart, M. A. Kamm , A. J. Stagg and S.C. Knight. Mechanisms of action of probiotic bacteria – recent advances. Inflamm Bowel Dis. 2009 Feb;15(2):300-10.

24. Hart AL, Ng SC, Mann E, Al-Hassi H, Bernado D, Knight SK. Immune homing mechanisms – role in immune homeostasis and inflammation . Inflamm Bowel Dis. 2010 Nov;16(11):1969-77.

25. A.L. Hart, A.J. Stagg, H. Graffner, H. Glise, P. Falk, M. A. Kamm. The gut flora – its role in health and disease and its modification as a therapy. Aliment Pharmacol Ther 2002; 16: 1-11

26. A.L. Hart, A.J. Stagg & M. A. Kamm. Use of probiotics in the treatment of inflammatory bowel disease. Journal of Clinical Gastroenterology 2003; 36(2): 111-119.

27. Benjamin J; Hedin C; Koutsoumpas A; Ng S; McCarthy N; Hart A L; Kamm M; Sanderson J; Knight S; Forbes A; Stagg A; Whelan K; Lindsay J. A randomised, double blind placebo controlled trial of fructo-oligosaccharides in active Crohn's disease. Gut 2010 Jul;60(7):923-9

28. S J. Ott, S. Plamondon, Hart A L, A Begun, A Rehman, M. A. Kamm and S. Schreiber. Dynamics of mucosa-associated flora in ulcerative colitis patients during remission and clinical .J Clin Microbiol. 2008 Oct;46(10):3510-3

29. Marchesi JR, Adams DH, Fava F, Hermes GD, Hirschfield GM, Hold G, Quraishi MN, Kinross J, Smidt H, Tuohy KM, Thomas LV, Zoetendal EG, Hart A. The gut microbiota and host health: a new clinical frontier. Gut. 2016 Feb;65(2):330-9. doi: 10.1136/gutjnl-2015-309990. Review

30. Benjamin JL, Hedin CRH, Koutsoumpas A, Ng SC, McCarthy NE, Prescott NJ, Pessoa-Lopes P, Mathew CG, Sanderson JD, Hart A L, Kamm MA, Knight SC, Forbes A, Stagg AJ, Lindsay JO, Whelan K. Smokers with active Crohn's disease have a clinically relevant dysbiosis of the gastrointestinal microbiota. Inflamm Bowel Dis. July 2011 doi: 10.1002/ibd.21864.

31. Hart A L, S. Plamondon, A Emmanuel and M. A. Kamm. Prospective evaluation of the relationship between stress and relapse in ulcerative colitis relapse: a prospective observational study. J Clin Gastroenterol. 2008 Sep;42(8):963-4.

32. A.L. Hart & M. A. Kamm. Review article: mechanisms of initiation and perpetuation of gut inflammation by stress. Aliment Pharmacol Ther 2002; 16: 2017-2028.

33. Despott EJ, Gupta A, Burling D, Tripoli E, Konieczko K, Hart A L, Fraser C. Effective dilation of small-bowel strictures by double-balloon enteroscopy in patients with symptomatic Crohn's disease (with video). Gastrointest Endosc. 2009 Nov;70(5):1030-6.

34. Arebi N, Hart AL, Thomas-Gibson S. A review of endoscopic balloon dilatation techniques for treating Crohn's strictures: time to standardise therapy. Expert Rev Gastroenterol Hepatol. 2016 Jul 27:1-7.

35. Hart AL, Lomer M, Verjee A, Kemp K, Faiz O, Daly A, Solomon J, McLaughlin J. What Are the Top 10 Research Questions in the Treatment of Inflammatory Bowel Disease? A Priority Setting Partnership with the James Lind Alliance. J Crohns Colitis. 2017 Feb;11(2):204-211

36. Lomer MC, Hart AL, Verjee A, Daly A, Solomon J, Mclaughlin J. What are the dietary treatment research priorities for inflammatory bowel disease? A short report based on a priority setting partnership with the James Lind Alliance. J Hum Nutr Diet. 2017 Aug 10. doi: 10.1111/jhn.12494

37. Burisch J, Cukovic-Cavka S, Kaimakliotis I, Shonová O, Andersen V, Dahlerup JF, Elkjaer M, Langholz E, Pedersen N, Salupere R, Kolho KL, Manninen P, Lakatos PL, Shuhaibar M, Odes S, Martinato M, Mihu I, Magro F, Belousova E, Fernandez A, Almer S, Halfvarson J, Hart A L, Munkholm P. Construction and validation of a web-based epidemiological database for inflammatory bowel diseases in Europe An EpiCom study. J Crohns Colitis. 2011 Aug;5(4):342-9.

38. Walker DG, Williams HR, Kane SP, Mawdsley JE, Arnold J, McNeil I, Thomas HJ, Teare JP, Hart A L, Pitcher MC, Walters JR, Marshall SE, Orchard TR. Differences in inflammatory bowel disease phenotype between South Asians and North Europeans lining in North West London. Am J Gastroenterol. 2011 Jul;106(7):1281-9.

39. Tozer P, Ng S C, Siddiqui M R, Plamondon S, Burling D, Gupta A, Swatton A, Tripoli S, Vaizey C J, Kamm M A, Phillips R S K, Hart A L. Long-term MRI-guided combined anti-TNFalpha and thiopurine therapy for Crohn's perianal fistulas. Inflamm Bowel Dis. 2012 Jan 4

40. Siddiqui M R, Tozer P, Hart A L, Phillips R S K. A diagnostic accuracy meta-analysis of endoanal ultrasound and MRI for perianal fistula assessment. Dis Col Rectum Jan 2012.

41. Hart A L Vitamin D and inflammatory bowel disease: chicken or egg? Inflamm Bowel Dis. 2013 Feb;19(2):459-60

42. Raman M, Milestone A, Walters J, Hart A L, Ghosh S. Vitamin D and gastrointestinal diseases:inflammatory bowel disease and colorectal cancer. Therapeutic Advances in Gastroenterology 2010.

43. Gearry RB, Kamm MA, Hart AL, Bassett P, Gabe SM, Nightingale JM. Predictors for Developing Intestinal Failure in Patients with Crohn's Disease. J Gastroenterol Hepatol. 2013 May;28(5):801-7

44. Morar PS, Hodgkinson JD, Thalayasingam S, Koysombat K, Purcell M, Hart AL, Warusavitarne J, Faiz O. Determining Predictors for Intra-abdominal Septic Complications Following Ileocolonic Resection for Crohn's Disease-Considerations in Pre-operative and Peri-operative Optimisation Techniques to Improve Outcome. J Crohns Colitis. 2015 Jun;9(6):483-91

45. Morar PS, Faiz O, Hodgkinson JD, Zafar N, Koysombat K, Purcell M, Hart A, Warusavitarne J. Concomitant colonic disease (Montreal L3) and re-resectional surgery are predictors of clinical recurrence following ileocolonic resection for Crohn's disease. Colorectal Dis. 2015 Nov;17(11):O247-55

46. Ding NS, Malietzis G, Lung PFC, Penez L, Yip WM, Gabe S, Jenkins JT, Hart A. The body composition profile is associated with response to anti-TNF therapy in Crohn's disease and may offer an alternative dosing paradigm. Aliment Pharmacol Ther. 2017 Sep 7. doi: 10.1111/apt.14293.

47. Landy J, Hart A. The effects of probiotics on barrier function and mucosal pouch microbiota during maintenance treatment for severe pouchitis in patients with ulcerative colitis. Aliment Pharmacol Ther. 2013 Dec;38(11-12):1405-6. doi: 10.1111/apt.12517.

48. Landy J, Walker AW, Li JV, Al-Hassi HO, Ronde E, English NR, Mann ER, Bernardo D, McLaughlin SD, Parkhill J, Ciclitira PJ, Clark SK, Knight SC, Hart AL. Variable alterations of the microbiota, without metabolic or immunological change, following faecal microbiota transplantation in patients with chronic pouchitis. Sci Rep. 2015 Aug 12;5:12955

49. Landy J, Al-Hassi HO, McLaughlin SD, Walker AW, Ciclitira PJ, Nicholls RJ, Clark SK, Hart A L. Review Article: Faecal Transplantation therapy for gastrointestinal diseases. Aliment Pharmacol Ther. 2011 Aug;34(4):409-415

50. Gecse KB, Bemelman W, Kamm MA, Stoker J, Khanna R, Ng SC, Panés J, van Assche G, Liu Z, Hart A, Levesque BG, D'Haens G; for the World Gastroenterology Organization, International Organisation for Inflammatory Bowel Diseases IOIBD, European Society of Coloproctology and Robarts Clinical Trials. A global consensus on the classification, diagnosis and multidisciplinary treatment of perianal fistulising Crohn's disease. Gut. 2014 Sep;63(9):1381-92

51. Tozer PJ, Whelan K, Phillips RK, Hart AL. Etiology of perianal Crohn's disease: role of genetic, microbiological, and immunological factors. Inflamm Bowel Dis. 2009 Oct;15(10):1591-8.

52. Yassin N; Askari A; Warusavitarne J; Faiz O; Athanasiou T; Phillips R; Hart A Systematic Review: Combined Surgical and Medical Treatment of Fistulising Perianal Crohn’s Disease Aliment Pharmacol Ther. 2014 Oct;40(7):741-9

53. Singh S, Ding NS, Mathis KL, Dulai PS, Farrell AM, Pemberton JH, Hart AL, Sandborn WJ, Loftus EV Jr.Systematic review with meta-analysis: faecal diversion for management of perianal Crohn's disease. Aliment Pharmacol Ther. 2015 Oct;42(7):783-92

54. Luke Jostins, Stephan Ripke, Rinse K Weersma, Richard H Duerr, Dermot P McGovern, Ken Y Hui, James C Lee, L Philip Schumm, Yashoda Sharma, Carl A Anderson, Jonah Essers, Mitja Mitrovic, Kaida Ning, Isabelle Cleynen, Emilie Theatre, Sarah L Spain, Soumya Raychaudhuri, Philippe Goyette, Zhi Wei, Clara Abraham, Jean-Paul Achkar, Tariq Ahmad, Leila Amininejad, Ashwin N Ananthakrishnan, Vibeke Andersen, Jane M Andrews, Leonard Baidoo, Tobias Balschun, Peter A Bampton, Alain Bitton, Gabrielle Boucher, Stephan Brand, Carsten Büning, Ariella Cohain, Sven Cichon, Mauro D'Amato, Dirk De Jong, Kathy L Devaney, Marla Dubinsky, Cathryn Edwards, David Ellinghaus, Lynnette R Ferguson, Denis Franchimont, Karin Fransen, Richard Gearry, Michel Georges, Christian Gieger, Jürgen Glas, Talin Haritunians, Hart A L, Chris Hawkey, Matija Hedl, Xinli Hu,Tom H Karlsen, Limas Kupcinskas, Subra Kugathasan, Anna Latiano, Debby Laukens, Ian C Lawrance, Charlie W Lees, Edouard Louis, Gillian Mahy, John Mansfield, Angharad R Morgan, Craig Mowat, William Newman, Orazio Palmieri, Cyriel Y Ponsioen, Uros Potocnik, Natalie J Prescott, Miguel Regueiro, Jerome I Rotter, Richard K Russell, Jeremy D Sanderson, Miquel Sans, Jack Satsangi, Stefan Schreiber, Lisa A Simms, Jurgita Sventoraityte, Stephan R Targan, Kent D Taylor, Mark Tremelling, Hein W Verspaget, Martine De Vos, Cisca Wijmenga, David C Wilson, Juliane Winkelmann, Ramnik J Xavier, Sebastian Zeissig, Bin Zhang, Clarence K Zhang, Hongyu Zhao, The International IBD Genetics Consortium, Mark S Silverberg, Vito Annese, Hakon Hakonarson, Steven R Brant, Graham Radford-Smith, Christopher G Mathew, John D Rioux, Eric E Schadt, Mark J Daly, Andre Franke, Miles Parkes, Severine Vermeire, Jeffrey C Barrett, Judy H Cho. Host-microbe interactions have shaped the genetic architecture of inflammatory bowel disease. Nature. 2012 Nov 1;491(7422):119-24

55. Goyette P, Boucher G, Mallon D, Ellinghaus E, Jostins L, Huang H, Ripke S, Gusareva ES, Annese V, Hauser SL, Oksenberg JR, Thomsen I, Leslie S; International Inflammatory Bowel Disease Genetics Consortium; Australia and New Zealand IBDGC; Belgium IBD Genetics Consortium; Italian Group for IBD Genetic Consortium; NIDDK Inflammatory Bowel Disease Genetics Consortium; United Kingdom IBDGC (inc. Hart A); Wellcome Trust Case Control Consortium; Quebec IBD Genetics Consortium, Daly MJ, Van Steen K, Duerr RH, Barrett JC, McGovern DP, Schumm LP, Traherne JA, Carrington MN, Kosmoliaptsis V, Karlsen TH, Franke A, Rioux JD. High-density mapping of the MHC identifies a shared role for HLA-DRB1*01:03 in inflammatory bowel diseases and heterozygous advantage in ulcerative colitis. Nat Genet. 2015 Feb;47(2):172-9

56. Liu JZ, van Sommeren S, Huang H, Ng SC, Alberts R, Takahashi A, Ripke S, Lee JC, Jostins L, Shah T, Abedian S, Cheon JH, Cho J, Daryani NE, Franke L, Fuyuno Y, Hart A, Juyal RC, Juyal G, Kim WH, Morris AP, Poustchi H, Newman WG, Midha V, Orchard TR, Vahedi H, Sood A, Sung JJ, Malekzadeh R, Westra HJ, Yamazaki K, Yang SK; International Multiple Sclerosis Genetics Consortium; International IBD Genetics Consortium, Barrett JC1, Franke A, Alizadeh BZ, Parkes M, B K T, Daly MJ, Kubo M, Anderson CA, Weersma RK.Association analyses identify

38 susceptibility loci for inflammatory bowel disease and highlight shared genetic risk across populations. Nat Genet. 2015 Jul 20. doi: 10.1038/ng.3359. Epub ahead of print

57. Heap GA, Weedon MN, Bewshea CM, Singh A, Chen M, Satchwell JB, Vivian JP, So K, Dubois PC, Andrews JM, Annese V, Bampton P, Barnardo M, Bell S, Cole A, Connor SJ, Creed T, Cummings FR, D'Amato M, Daneshmend TK, Fedorak RN, Florin TH, Gaya DR, Greig E, Halfvarson J, Hart A, Irving PM, Jones G, Karban A, Lawrance IC, Lee JC, Lees C, Lev-Tzion R, Lindsay JO, Mansfield J, Mawdsley J, Mazhar Z, Parkes M, Parnell K, Orchard TR, Radford-Smith G, Russell RK, Reffitt D, Satsangi J, Silverberg MS, Sturniolo GC, Tremelling M, Tsianos EV, van Heel DA, Walsh A, Watermeyer G, Weersma RK, Zeissig S, Rossjohn J, Holden AL; International Serious Adverse Events Consortium; IBD Pharmacogenetics Study Group, Ahmad T. HLA-DQA1-HLA-DRB1 variants confer susceptibility to pancreatitis induced by thiopurine immunosuppressants. Nat Genet. 2014 Oct;46(10):1131-4

58. Heap GA, So K, Weedon M, Edney N, Bewshea C, Singh A, Annese V, Beckly J, Buurman D, Chaudhary R, Cole AT, Cooper SC, Creed T, Cummings F, de Boer NK, D'Inca R, D'Souza R, Daneshmend TK, Delaney M, Dhar A, Direkze N, Dunckley P, Gaya DR, Gearry R, Gore S, Halfvarson J, Hart A, Hawkey CJ, Hoentjen F, Iqbal T, Irving P, Lal S, Lawrence I, Lees CW, Lockett M, Mann S, Mansfield J, Mowat C, Mulgrew CJ, Muller F, Murray C, Oram R, Orchard T, Parkes M, Phillips R, Pollok R, Radford-Smith G, Sebastian S, Sen S, Shirazi T, Silverberg M, Solomon L, Sturniolo GC, Thomas M, Tremelling M, Tsianos EV, Watts D, Weaver S, Weersma RK, Wesley E, Holden A, Ahmad T. Clinical Features and HLA Association of 5-Aminosalicylate (5-ASA)-induced Nephrotoxicity in Inflammatory Bowel Disease. J Crohns Colitis. 2016 Feb;10(2):149-58

59. Rivas MA, Graham D, Sulem P, Stevens C, Desch AN, Goyette P, Gudbjartsson D, Jonsdottir I, Thorsteinsdottir U, Degenhardt F, Mucha S, Kurki MI, Li D, D'Amato M, Annese V, Vermeire S, Weersma RK, Halfvarson J, Paavola-Sakki P, Lappalainen M, Lek M, Cummings B, Tukiainen T, Haritunians T, Halme L, Koskinen LL, Ananthakrishnan AN, Luo Y, Heap GA, Visschedijk MC; UK IBD Genetics Consortium.; NIDDK IBD Genetics Consortium., MacArthur DG, Neale BM, Ahmad T, Anderson CA, Brant SR, Duerr RH, Silverberg MS, Cho JH, Palotie A, Saavalainen P, Kontula K, Färkkilä M, McGovern DP, Franke A, Stefansson K, Rioux JD, Xavier RJ, Daly MJ, Barrett J, de Lane K, Edwards C, Hart A, Hawkey C, Jostins L, Kennedy N, Lamb C, Lee J, Lees C, Mansfield J, Mathew C, Mowatt C, Newman B, Nimmo E, Parkes M, Pollard M, Prescott N, Randall J, Rice D, Satsangi J, Simmons A, Tremelling M, Uhlig H, Wilson D, Abraham C, Achkar JP, Bitton A, Boucher G, Croitoru K, Fleshner P, Glas J, Kugathasan S, Limbergen JV, Milgrom R, Proctor D, Regueiro M, Schumm PL, Sharma Y, Stempak JM, Targan SR, Wang MH. A protein-truncating R179X variant in RNF186 confers protection against ulcerative colitis. Nat Commun. 2016 Aug 9;7:12342. doi: 10.1038/ncomms12342.

60. Cleynen I, Boucher G, Jostins L, Schumm LP, Zeissig S, Ahmad T, Andersen V, Andrews JM, Annese V, Brand S, Brant SR, Cho JH, Daly MJ, Dubinsky M, Duerr RH, Ferguson LR, Franke A, Gearry RB, Goyette P, Hakonarson H, Halfvarson J, Hov JR, Huang H, Kennedy NA, Kupcinskas L, Lawrance IC, Lee JC, Satsangi J, Schreiber S, Théâtre E, van der Meulen-de Jong AE, Weersma RK, Wilson DC; International Inflammatory Bowel Disease Genetics Consortium., Parkes M, Vermeire S, Rioux JD, Mansfield J, Silverberg MS, Radford-Smith G, McGovern DP,

Barrett JC, Lees CW.(Hart AL Collaborator)Inherited determinants of Crohn's disease and ulcerative colitis phenotypes: a genetic association study. Lancet. 2016 Jan 9;387(10014):156-67

61. Luo Y, de Lange KM, Jostins L, Moutsianas L, Randall J, Kennedy NA, Lamb CA, McCarthy S, Ahmad T, Edwards C, Serra EG, Hart A, Hawkey C, Mansfield JC, Mowat C, Newman WG, Nichols S, Pollard M, Satsangi J, Simmons A, Tremelling M, Uhlig H, Wilson DC, Lee JC, Prescott NJ, Lees CW, Mathew CG, Parkes M, Barrett JC, Anderson CA. Exploring the genetic architecture of inflammatory bowel disease by whole-genome sequencing identifies association at ADCY7. Nat Genet. 2017 Feb;49(2):186-192. doi: 10.1038/ng.3761.

62. de Lange KM, Moutsianas L, Lee JC, Lamb CA, Luo Y, Kennedy NA, Jostins L, Rice DL, Gutierrez-Achury J, Ji SG, Heap G, Nimmo ER, Edwards C, Henderson P, Mowat C, Sanderson J, Satsangi J, Simmons A, Wilson DC, Tremelling M, Hart A, Mathew CG, Newman WG, Parkes M, Lees CW, Uhlig H, Hawkey C, Prescott NJ, Ahmad T, Mansfield JC, Anderson CA, Barrett JC. Genome-wide association study implicates immune activation of multiple integrin genes in inflammatory bowel disease Nat Genet. 2017 Feb;49(2):256-261. doi: 10.1038/ng.3760.

63. Tozer P, Rayment N, Al-HassiH, Ansari T, Daulatzai N, Murguranathan A, Sibbons P, Guenther T, Knight SC, Phillips RKS, Whelan K, Hart A L. What role do bacteria play in leading to fistula persistence in idiopathic and Crohn's anal fistulas? Colorectal Dis 2015 Mar;17(3):235-41

64. Choi CH, Ignjatovic-Wilson A, Askari A, Lee GH, Warusavitarne J, Moorghen M, Thomas-Gibson S, Saunders BP, Rutter MD, Graham TA, Hart AL. Low-grade dysplasia in ulcerative colitis: risk factors for developing high-grade dysplasia or colorectal cancer. Am J Gastroenterol. 2015 Oct;110(10):1461-7

65. Choi CR, Al Bakir I, Ding NJ, Lee GH, Askari A, Warusavitarne J, Moorghen M, Humphries A, Ignjatovic-Wilson A, Thomas-Gibson S, Saunders BP, Rutter MD, Graham TA, Hart AL. Cumulative burden of inflammation predicts colorectal neoplasia risk in ulcerative colitis: a large single-centre study. Gut. 2017 Nov 17. pii: gutjnl-2017-314190. doi: 10.1136/gutjnl-2017-314190

66. Choi CR, Bakir IA, Hart AL, Graham TA. Clonal evolution of colorectal cancer in IBD. Nat Rev Gastroenterol Hepatol. 2017 Apr;14(4):218-229

67. Ding NS, Yip WM, Choi CH, Saunders B, Thomas-Gibson S, Arebi N, Humphries A, Hart A Endoscopic Dilatation of Crohn's Anastomotic Strictures is Effective in the Long Term, and Escalation of Medical Therapy Improves Outcomes in the Biologic Era. J Crohns Colitis. 2016 Oct;10(10):1172-8

68. Ponsioen CY, de Groof EJ, Eshuis EJ, Gardenbroek TJ, Bossuyt PMM, Hart A, Warusavitarne J, Buskens CJ, van Bodegraven AA, Brink MA, Consten ECJ, van Wagensveld BA, Rijk MCM, Crolla RMPH, Noomen CG, Houdijk APJ, Mallant RC, Boom M, Marsman WA, Stockmann HB, Mol B, de Groof AJ, Stokkers PC, D'Haens GR, Bemelman WA; LIR!C study group. Laparoscopic ileocaecal resection versus infliximab for terminal ileitis in Crohn's disease: a

randomised controlled, open-label, multicentre trial. Lancet Gastroenterol Hepatol. 2017 Nov;2(11):785-792. doi: 10.1016/S2468-1253(17)30248-0

69. Sahnan K, Adegbola SO, Tozer PJ, Gupta A, Baldwin-Cleland R, Yassin N, Warusavitarne J, Faiz OD, Hart AL, Phillips RKS, Lung PFC.Improving the Understanding of Perianal Crohn Fistula Through 3D Modeling. Ann Surg. 2017 Dec 11.

70. Sahnan K, Tozer P, Adegbola S, Lee M, Heywood N, McNaie A, Hind D, Tassin N, Lobo A, Brown S, Sebastian S, Phillips R, Lung P, Faiz O, Crook K, Blackwell S, Verjee A, Hart A, Fearnhead N. Developing a core outcome set for fistulising perianal Crohn's disease GUT 3rd Feb 2018 on line.

71. Mak WY, Lung PFC, Hart A. In Patients With Perianal Crohn's Fistulas, What Are the Outcomes When 'Radiological Healing' Is Achieved? Does Radiological Healing of Perianal Crohn's Fistulas Herald the Time Point for Stopping a Biologic? J Crohns Colitis. 2017 Jul 10. doi: 10.1093/ecco-jcc/jjx094

72. Gecse KB, Sebastian S, Hertogh Gd, Yassin NA, Kotze PG, Reinisch W, Spinelli A, Koutroubakis IE, Katsanos KH, Hart A, van den Brink GR, Rogler G, Bemelman WA.Results of the Fifth Scientific Workshop of the ECCO [II]: Clinical Aspects of Perianal Fistulising Crohn's Disease-the Unmet Needs. J Crohns Colitis. 2016 Jul;10(7):758-65

73. Magro F, Gionchetti P, Eliakim R, Ardizzone S, Armuzzi A, Barreiro-de Acosta M, Burisch J, Gecse KB, Hart AL, Hindryckx P, Langner C, Limdi JK, Pellino G, Zagórowicz E, Raine T, Harbord M, Rieder F; Third European Evidence-Based Consensus on Diagnosis and Management of Ulcerative Colitis. Part 1: Definitions, diagnosis, extra-intestinal manifestations, pregnancy, cancer surveillance, surgery, and ileo-anal pouch disorders. European Crohn's and Colitis Organisation (ECCO). J Crohns Colitis. 2017 Feb 2. doi: 10.1093/ecco-jcc/jjx008. [Epub ahead of print] No abstract available.

74. Cammarota G, Ianiro G, Tilg H, Rajilić-Stojanović M, Kump P, Satokari R, Sokol H, Arkkila P, Pintus C, Hart A, Segal J, Aloi M, Masucci L, Molinaro A, Scaldaferri F, Gasbarrini G, Lopez-Sanroman A, Link A, de Groot P, de Vos WM, Högenauer C, Malfertheiner P, Mattila E, Milosavljević T, Nieuwdorp M, Sanguinetti M, Simren M, Gasbarrini A; European FMT Working Group.. European consensus conference on faecal microbiota transplantation in clinical practice. Gut. 2017 Jan 13. pii: gutjnl-2016-313017. doi: 10.1136/gutjnl-2016-313017. [Epub ahead of print]

75. Segal JP, Ding NS, Worley G, Mclaughlin S, Preston S, Faiz OD, Clark SK, Hart AL. Systematic review with meta-analysis: the management of chronic refractory pouchitis with an evidence-based treatment algorithm. Aliment Pharmacol Ther. 2017 Mar;45(5):581-592. doi: 10.1111/apt.13905. Review.

76. Quraishi MN, Segal J, Mullish B, McCune VL, Hawkey P, Colville A, Williams H, Hart A, Iqbal TH. National survey of practice of faecal microbiota transplantation for Clostridium difficile

infection in the UK. J Hosp Infect. 2016 Nov 3. pii: S0195-6701(16)30502-3. doi: 10.1016/j.jhin.2016.10.023. [Epub ahead of print]

77. Costello, Soo, Bryant, Jaiath, Hart AL and Andrews JM. Systematic review with meta-analysis: faecal microbiota transplantation for the induction of remission for active ulcerative colitisAliment Pharmacol Ther. 2017 Aug;46(3):213-224

78. Ponsioen CY, de Groof EJ, Eshuis EJ, Gardenbroek TJ, Bossuyt PMM, Hart A, Warusavitarne J, Buskens CJ, van Bodegraven AA, Brink MA, Consten ECJ, van Wagensveld BA, Rijk MCM, Crolla RMPH, Noomen CG, Houdijk APJ, Mallant RC, Boom M, Marsman WA, Stockmann HB, Mol B, de Groof AJ, Stokkers PC, D'Haens GR, Bemelman WA; LIR!C study group. Laparoscopic ileocaecal resection versus infliximab for terminal ileitis in Crohn's disease: a randomised controlled, open-label, multicentre trial. Lancet Gastroenterol Hepatol. 2017 Nov;2(11):785-792.

79. Choi CH, Rutter MD, Askari A, Lee GH, Warusavitarne J, Moorghen M, Thomas-Gibson S, Saunders BP, Graham TA, Hart AL. Forty-Year Analysis of Colonoscopic Surveillance Program for Neoplasia in Ulcerative Colitis: An Updated Overview. Am J Gastroenterol. 2015 Jul;110(7):1022-34.

APPENDIX 2:
The Team

Thank you to all team members, medical, surgical and radiological for their dedication to IBD research. Congratulations to all research fellows for their exceptional hard work. Well done to all the research nursing team for their contribution to clinical trials. And the biggest thank you to all the patients who have participated in any way in the IBD research agenda at St Mark's.

The team meets **weekly** to discuss all clinical research trials, has a **monthly meeting** to which all team members are invited, and the individual research themes hold their own meetings.

The Team

Professor Ailsa Hart (Director IBD Research, Sub-Dean St Mark's Academic Institute)

Dr Ayesha Akbar (Consultant Gastroenterologist)

Dr Naila Arebi (Consultant Gastroenterologist)

Professor Sue Clark (Consultant Colorectal Surgeon, Dean St Mark's Academic Institute)

Mr Omar Faiz (Consultant Colorectal Surgeon)

Mr Janindra Warusavitarne (Consultant Colorectal Surgeon)

Mr Philip Tozer (Consultant Colorectal Surgeon)

Dr Philip Lung (Consultant Radiologist)

Research Nurse Team

Pooja Datt (Team Lead)

Lawrence Penez (Research Coordinator)

Fadumo Nur (Research Coordinator)

Victoria van Loon (Research Nurse)

APPENDIX 3:
Research Students Supervised

Type of Degree	Start Date	Higher degree status	Name of Student	Title of Project	Name of Supervisors
PhD (Imperial College)	9/2017	Current	Sonia Bouri	Metabonomic factors in extreme IBD cohorts, intestinal failure	Professor Ailsa Hart Dr Horace Williams
PhD (Imperial College)	9/2017	Current	Lucia de Campo Braz	Dietary factors in patients with ileo-anal pouches	Professor Ailsa Hart Professor Gary Frost
PhD (Imperial College)	9/2017	Current	Misha Kabir	Improving patient communication of risk in IBD surveillance	Dr Ana Wilson Professor Ailsa Hart
ACF	1/2018	Current	Henry Taylor	Paediatric IBD – clinical, microbiological and metabonomic factors involved	Dr Fell Dr Epstein Dr Hyer Professor Hart
PhD (QMUL)	10/2015	Current	Ibrahim Al Bakir	The role of the immune micro-environment in the evolution of colitis-associated cancer Medical Research Council Clinical Research Training Fellowship (2016) £132,959; Duration: 2 years	Professor Trevor Graham Professor Ailsa Hart
PhD (Imperial College)	10/2015	Current	Dr Jonathan Segal	Quality of life in patients with pouches	Professor Ailsa Hart Professor S Clark Mr O Faiz Professor Marchesi
PhD (Imperial College)	1/9/15	Current	Kaps Sahnan	Optimising assessment and therapy of perianal Crohn's disease	Mr Tozer Professor Ailsa Hart Mr O Faiz Dr P Lung
PhD (Imperial College)	1/9/15	Current	Sam Adegbola	Experimental studies in idiopathic and Crohn's related fistulas	Mr Phil Tozer Prof Ailsa Hart Dr P Lung
PhD (Imperial College)	9/2013	Current	Dr Philip Hendy	Vitamin D optimise anti-TNF therapy in CD by modulating DC	Professor Ailsa Hart Professor S Knight
PhD (Imperial)	2015	Current	Dr Ravi Misra	Epidemiology IBD/ metabonomics in inception cohort Asians	Dr N Arebi

Type of Degree	Start Date	Higher degree status	Name of Student	Title of Project	Name of Supervisors
PhD (King's College)	7/2015	Current	Ann Muls	Predicting patients at risk of developing gastrointestinal symptoms after treatment with pelvic irradiation	Professor Christine Norton, Professor Ailsa Hart
PhD (Melbourne University)	6/2013	Current	Dr John Nik Ding	Predicting response to anti-TNF therapy in IBD – radiological and microbiological predictors	Professor Ailsa Hart
MD (Imperial College)	2013	Current	Dr Zacharias Tsiamoulos	Novel endoscopic therapies for colonic polyps & IBD surveillance	Professor B Saunders Professor Ailsa Hart
PhD (Imperial College)	1/4/13	Current	Dr Rakesh Vora	Paediatric CD – impact of polymeric diet on dendritic cells	Professor S Knight Professor Ailsa Hart
PhD (Barts and the London)	1/10/13	PhD achieved 2017	Dr Ryan Choi	Clinical and Genetic Risk Stratification for Colonoscopic Surveillance Programme in IBD	Professor Ailsa Hart Professor T Graham
MD (Imperial College)	2012	Writing up	Dr Yih-Harn Siaw	Longitudinal study of immunological and microbiological factors in pouchitis	Professor Ailsa Hart
PhD (Imperial College)	1/8/12	Writing up	Mr Pritesh Morar	Improving quality of surgical care for patients with distal ileal Crohn's disease	Mr Warusavitarne Mr O Faiz Professor Hart
PhD (Imperial College)	2012	PhD achieved 2015	Ms Nuha Yassin	Perianal Crohn's fistulas – aetiological factors,	Prof R Phillips Professor Ailsa Hart
PhD (Imperial College)	1/9/13	PhD achieved 2015	Dr J Landy	A study of immunology, microbiology and tight junction characteristics of pouchitis	Professor Ailsa Hart Prof S Knight Prof S Clark
MD (Imperial College)	9/2013	MD achieved	Dr S Peake	Role of dendritic cells in small and large bowel Crohn's disease	Professor Ailsa Hart Prof S Knight
MD (Imperial College)	2010	MD achieved	Mr G Rahbour	Enterocutaneous fistulas	Ms C Vaizey

Type of Degree	Start Date	Higher degree status	Name of Student	Title of Project	Name of Supervisors
MD (Imperial College)	2009	MD achieved	Mr Najib Naultazi	Wound healing in Crohn's disease – pathogenesis	Prof R Phillips Professor Ailsa Hart
MD (Imperial College)	2008	MD achieved	Dr Edward Despott	Techniques to assess small bowel – capsule and DBE including in Crohn's disease	Prof B Saunders Professor Ailsa Hart
MD (Imperial College)	2008	MD achieved	Mr Philip Tozer	Clinical and experimental studies in anal fistulas	Prof R Phillips Professor Ailsa hart
MD (Imperial College)	2008	MD achieved	Dr Andrew Milestone	Role of vitamin D in IBD – in vitro effects on DC	Prof S Knight Professor Ailsa Hart
MD (Imperial College)	2004	MD achieved	Dr S McLaughlin	Pouches in IBD	Professor Clark and Nicholls

APPENDIX 4:
IBD Research Team Report

(see separate annual report for 2017 activity)

APPENDIX 5:
Recent NIHR Grants

IBD Research Grants 2018

1. **5-year NIHR programme grant**. Living well with inflammatory bowel disease: optimising management of symptoms of fatigue, abdominal pain and faecal urgency/ incontinence via tailored online self-management: *the IBD BOOST programme*

2. **5-year NIHR/MRC Efficacy and Mechanism Evaluation (EME) Programme.** *STOP-COLITIS*: a double-blind, randomised controlled trail to investigate the efficacy of faecal microbiota transplantation (FMT) in achieving and maintaining remission for patients with ulcerative colitis