ST MARK'S HOSPITAL FOUNDATION

A future free from the fear of bowel disease

# *How St Mark's Hospital & St Mark's Hospital Foundation are combatting bowel disease*

## *Successes, contributions and impact of our research*

## Foreword from the Clinical Director of St Mark's Hospital and the Chairman of St Mark's Hospital Foundation

**St Mark's Hospital is at an exciting stage in its development as the national bowel disease hospital for the treatment of complex diseases requiring an especially high level of expertise and specialism.**

More than 60% of the people treated at St Mark's have been referred by other UK hospitals. Our national reach is well established. The expertise that exists at St Mark's is primarily built on innovative research that drives clinical improvements and the development of new services.

In this brochure we are delighted to share details of new research-driven services that we are currently implementing at St Mark's, including:

HIPEC, a novel and highly effective way of delivering chemotherapy at the time of surgery for people with advanced cancer.

BiCyCLe, a programme to boost a person's immune system to fight cancer.

PERFECT's, a programme to dramatically increase the accuracy of a non-invasive bowel cancer screening method for frail, weak and fearful people.

PROGRESS, a programme to personalise bowel cancer screening and surveillance so that those who require more intensive surveillance receive it, and those at very low risk are spared unnecessary colonoscopies.

You will read too about a spectrum of promising new treatments for people with inflammatory bowel disease.

We also present our ground breaking Surgical Robotics Programme to take surgery for colorectal and anorectal cancers, inherited cancer syndromes, Crohn's disease and ulcerative colitis to a new level.

Pushing the frontiers of treatment for bowel disease requires philanthropic funders willing to invest in exciting, transformational research. After reading this brochure we hope that you will intensify your support or will wish to join us in a partnership to create a future free from the fear of bowel disease.

Mr Omar Faiz
Clinical Director
St Mark's Hospital

Sir Tom Troubridge
Chairman
St Mark's Hospital Foundation

*Mr Omar Faiz*

*Sir Tom Troubridge*

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## Section 1

# History of St Mark's and why fighting bowel disease is so important

# St Mark's Hospital No #1 in the world

**In 1835 St Mark's Hospital opened in London as the world's first specialist bowel disease hospital for the relief of poor people afflicted by bowel disease. Nothing like St Mark's had existed before.**

St Mark's has always been an extraordinary hospital, with extraordinary people. One of its first governors was the famous author, Charles Dickens who, having been treated successfully at St Mark's for a painful condition, donated ten guineas in gratitude.

From its inception, St Mark's Hospital has been dedicated to researching and developing new and more effective ways of treating, managing and curing bowel disease.

For over 180 years, there has been an unbroken chain of world leading experts at St Mark's building their knowledge and skills through research that translates into improved clinical practice and patient benefits. One generation of world leading experts has passed on their skills and expertise to a new generation of doctors. This makes St Mark's unique in the world. It is what enables St Mark's to be the national and international referral centre for people with the most complex and difficult to treat bowel diseases that others cannot treat: more than 60% of the patients treated at St Mark's are referred by other hospitals.

*St Mark's most recently appointed consultant, Mr Philip Tozer, laying flowers at the grave of St Mark's first consultant, Frederick Salmon, upon the 150th anniversary of his passing.*

## The need to continue to invest to maintain and build St Mark's as a world centre of excellence

As you read through this brochure, you will discover the monumental strides that have been achieved in the field of bowel disease, and the pivotal role St Mark's Hospital has played. For example, the survival rate from bowel cancer has increased as a result of surgical and medical research from 2% in the 1950's without surgery to over 52% with surgery today.

The medical and surgical treatment of Crohn's disease and Ulcerative Colitis, which are collectively known as Inflammatory Bowel Disease (IBD), has improved in leaps and bounds and IBD can now often be managed and controlled well for long periods. You will also read how there are currently no cures for these conditions and how people can struggle for decades with the devastating effects of these illnesses. In this document we are proud to describe the spectrum of research projects St Mark's is undertaking in order to redress this situation.

## Why supporting St Mark's fight against bowel disease is of paramount importance

We know, and appreciate, that there are many calls on the philanthropic giving of generous donors. There are however good reasons why we believe you may consider supporting St Mark's or intensifying the support you are already giving.

## Bowel disease adversely affects very many people

Bowel cancer is the second highest cause of cancer fatalities in the UK and the western world, claiming more than 630,000 lives annually. If new, more effective treatments are not developed, over six million people will die from bowel cancer over the next ten years.

Crohn's disease and ulcerative colitis devastate the lives of over 300,000 people in the UK alone and over five million worldwide.

Crohn's disease is typically a young person's disease, manifesting between the ages of 15 and 40. People can live with the challenging and devastating effects of Crohn's disease for more than 70 years. The health challenges from Crohn's disease include flare-ups, with the bowel becoming inflamed, painful and ulcerated. It can cause strictures, where the bowel gets blocked and the patient becomes very sick, and it can cause weight loss. 70% of Crohn's disease patients require surgery at least once during their lifetime and may lose large parts of

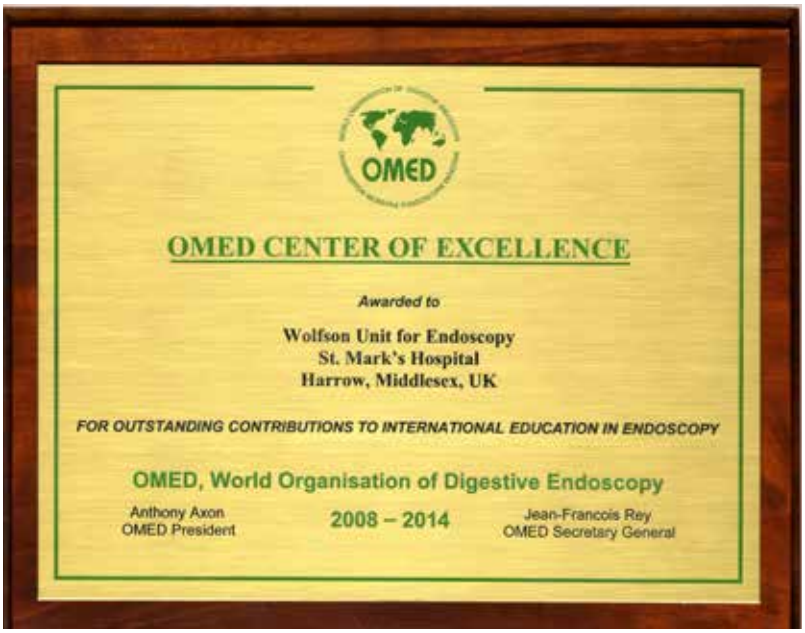
their bowel. This can lead to short bowel syndrome whereby nutrients can no longer be absorbed from food and individuals must be fed artificially via a tube inserted into the heart. This leads to a sharp downward spiral of diminishing health, leaving patients weak, emaciated and susceptible to illness and infection.

15% of Crohn's disease sufferers are disabled by their condition and incapable of working after 10 to 20 years from the original diagnosis.

## A Cinderella disease that has never attracted the level of philanthropic giving it deserves

Sadly, Crohn's disease is a Cinderella disease. It is the poor relation in the field of philanthropic giving to medical research. It has never attracted the level of popular philanthropic support of other chronic conditions, yet IBD is affecting growing numbers with 3,000 to 6,000 new cases being reported annually in the UK alone.

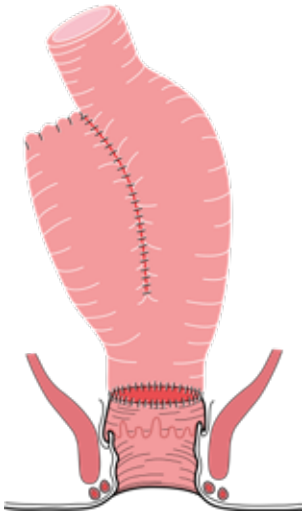
We hope that after reading this brochure you will wish to join the fight to create a future free from the fear of bowel disease, or intensify the support you are already giving. We hope that you will be left in no doubt that supporting St Mark's Hospital is an excellent way to create a better, healthier future for the hundreds of thousands of people who are struggling to cope with bowel disease.




*The Wolfson Unit for Endoscopy is an OMED world centre of excellence, one of only 14 in the world.*

## Section 2

# Contributions, breakthroughs and impact



*In the 1970's, Sir Alan Parks and Professor John Nicholls, surgeons from St Mark's, were the first to develop the operation of choice for ulcerative colitis patients. This procedure, known as the ileo-anal pouch, or J pouch, has now been performed on more than 25,000 patients worldwide. This operation is a highly effective treatment for the pain and disruption Ulcerative Colitis causes to a person's life.*

## Why St Mark's is a world centre of excellence - highlights of St Mark's Hospital's contributions, breakthroughs and impact

What follows is a brief summary of some of the breakthroughs and impact of St Mark's Hospital in the fight against Inflammatory Bowel Disease (IBD). Crohn's disease and Ulcerative Colitis fall into the disease group commonly referred to as IBD. It affects predominantly younger people and is a lifelong disease, associated with symptoms that can together have a significant detrimental impact on an individual's social and personal development.

### Inflammatory Bowel Disease:

- **First description of 'colonic Crohn's disease'**. Crohn's disease is not a single disease. There are five types of Crohn's disease, with ileo-colonic Crohn's disease being the most prevalent. The identification of colonic Crohn's disease was a major breakthrough in establishing the different types of Crohn's disease and, importantly, different treatments for different types of Crohn's disease.

- **First trial of amino salicylates and steroids for IBD.** These drugs are used to keep Crohn's disease patients in remission and to avoid flare-ups. When the inflammation flares up, amino salicylates and steroids can be given to control it and to give relief from the symptoms.

  As a result of St Mark's Hospital carrying out a successful large-scale drugs trial of amino salicylates and steroids, the path was laid for hundreds of thousands of patients to receive effective relief from the symptoms of Crohn's disease flare-ups. These drugs however are not a cure; they can have side-effects, such as thinning and weakening of bones (osteoporosis), and are not effective in controlling flare-ups in all people.

- **First widespread use of the drug Azathioprine for maintaining remission.** Azathioprine is an immunosuppressant. Crohn's disease behaves like an autoimmune disease, like arthritis and multiple sclerosis, in which the body is not able to distinguish between good and bad foreign bodies and attacks its own immune system, causing inflammation which damages healthy tissue. Azathioprine, like all immunosuppressants, dampens the immune system to stop it attacking itself. This undermines a person's ability to fight off infections, and can result in

recurrent infections and a susceptibility to become unwell. St Mark's was the first hospital to provide widespread treatment of Crohn's disease flare-ups with Azathioprine. Today, hundreds of thousands of patients benefit from Azathioprine to prevent flare-ups or keep them at bay. However, it too is not a cure and it is not effective for all people with Crohn's disease.

- **First controlled trial of a biologic drug for Crohn's disease.** Biologic medication, such as Infliximab and Humira, is an immunosuppressant medication like Azathioprine, which blocks the body's immune system from attacking the lining of the gut. Whilst biologic therapy has brought about a major leap forward in the treatment, management and control of Crohn's disease and can lead to relief from symptoms, sadly, like Azathioprine, biologic medication does not work in all patients, stops working in others and can cause extra intestinal manifestations (EIM's) such as skin problems. Whilst biologics represent an additional option in the medical arsenal of Crohn's disease treatment, it does not offer a cure but rather a way to manage disease.

## Surgery for IBD and Ulcerative Colitis – the ileo-anal pouch

Sadly, many patients with IBD are diagnosed much later than when they first developed symptoms. Subsequently, this can compromise the effectiveness of medical therapy to induce remission and make surgery essential to the management and control of their symptoms.

70% of all Crohn's disease patients will require surgery at least once in their lifetime for their disease. The way surgery is used to control Crohn's disease has radically changed over the past ten years. Surgery is employed as part of a multi-faceted treatment regime, which at St Mark's Hospital may include a care pathway that begins with accurate diagnosis, genetic profiling, enhanced endoscopic examination of the colon and MRI (magnetic resonance imaging). Patients will then be prescribed the medication that fits the profile of their disease i.e. the severity indicated by a battery of tests. A patient will be escalated up the drug pathway to more potent drugs if their disease shows signs of becoming aggressive. In the most severe cases, which involve frequent flare-ups, ulceration and damage to the gut, surgery cannot be avoided and can bring much relief from symptoms. Surgery is often the best solution.

*Crohn's disease can impact severely on a teenager's physical development. For a teenager at a stage in life of forming identity, friendships and relationships it can be devastating.*

## Bowel Cancer

- **The development of the adenoma-to-carcinoma sequence** that underpins the medical profession's understanding and treatment of bowel cancer. It is widely accepted in the medical profession that the adenoma-to-carcinoma sequence represents the process by which most, if not all, colorectal cancers arise. Understanding this sequence established the need to remove pre-cancerous polyps (adenomas) before they grow and develop into life threatening cancerous growths (carcinomas). The contribution of leading doctors at St Mark's, such as Sir Basil Morson and Dr H Bussey, to the discovery of this sequence has influenced the treatment of bowel cancer worldwide. This discovery focussed the medical world sharply on developing the 'prevention is better than cure' regime, establishing it as a universal treatment. This work also established the need for regular surveillance, as adenomas can return.

- **The creation of the world's first staging system for cancer that determines future treatment.** Sir Cuthbert Dukes' research at St Mark's established the world's first method of defining the stage that a patient's cancer has reached. Staging establishes how big the tumour is and how widely spread it is in the body, which in turn determines the appropriate treatment regime. For cancer that has spread, the Dukes stage alerts doctors to the need to provide chemotherapy and radiotherapy as well as advanced surgery. While there have been developments in cancer staging since Sir Cuthbert founded TNM (Tumour, Node, Metastasis) staging, his method is still the most widely practiced staging method and much of this follow-on work owes a debt of gratitude to Sir Cuthbert's ground-breaking work.

- **The establishment of the world's first registry of inherited bowel cancer.** Since the days of Cuthbert Dukes and Basil Morson, the documentation of patient records and specific information pertaining to their disease has been fundamental to enabling high quality clinical research and improving our understanding of the different genetic factors that influence the development of colorectal cancer.

- **St Mark's Hospital was instrumental in identifying the gene that causes familial adenomatous polyposis (FAP) and bowel cancer.** This and other important genes in the development of colorectal cancer have been identified through our ability to access this information and tissue from patients with cancer and precancerous conditions.

*Patient receiving biologic medication to control their inflammatory bowel disease.*

- **Establishing surveillance programmes in IBD to detect early cancer.** Our research into the long-term effects of inflammatory bowel disease has contributed to the recognition of the increased risk of developing colorectal cancer once affected with inflammatory conditions of the colon. Many years of seeing patients with this condition has enabled us to define the benefits of regular surveillance to prevent these patients succumbing to a preventable cancer.

## Diagnostics and non-invasive therapies

### Endoscopy:

**St Mark's surgeons were the first to use 'lighted examination' of the colon to accurately assess the level of damage to the cells lining the rectum (called the rectal mucosa).** The level of accuracy of diagnosis provided by this now well-established diagnostic procedure has greatly informed the choice of treatment, thus providing a more tailored, appropriate and effective treatment regime. This procedure is used extensively worldwide.

Named as a World Centre of Excellence, the Wolfson Institute for Endoscopy at St Mark's Hospital has been at the forefront

*St Mark's Hospital surgeons have championed the adoption of minimally invasive, laparoscopic (keyhole) surgery for the treatment of bowel cancer.*

of the development of training and innovation in endoscopic examination of the colon for over three decades.

The development of a magnetic imager and simulator transformed the training techniques and has resulted in a reduction of overall complications and improved outcomes from the examination. Advanced techniques in the excision of large polyps have prevented many patients from the need for conventional surgery.

## Imaging:

The technique of endo anal ultrasound examination of the anal sphincter was developed by Professor Clive Bartram in the 1980s at St Mark's and as a result transformed the understanding of the cause of incontinence in elderly women, identifying the impact of childbirth in causing tears in the anal sphincter muscles which would not reveal themselves until women reached an older age. This in turn led to a whole new approach to the repair of tears experienced during childbirth and has dramatically changed the incidence of incontinence in women.

**In addition to commercially supported research, St Mark's Hospital Foundation supports a number of research programmes at St Mark's Hospital and is fundamental to helping this historic institution continue the research and education that maintains St Mark's as a world leader.**

**We summarise in the following sections some of the research activity that St Mark's is currently undertaking, to demonstrate that St Mark's is a centre of excellence both for research into and the clinical treatment of bowel disease.**

## Section 3

# Colorectal cancer research

*A surgeon at the Da Vinci surgical robot. The surgical robot is used as an advanced tool under the control of the surgeon.*

## Surgical robotics - to achieve the next quantum leap in surgical innovation in the treatment of colorectal cancer

### The issue

The team of surgeons at St Mark's is dedicated to ensuring that patients with colorectal cancer not only survive, but they survive with minimum impact on their overall health so that they can lead full and active lives.

Surgical innovation features strongly in the improvement in the bowel cancer survival rate over the past 40 years. Many of the bowel cancers that surgeons could not operate on in the 1950's are now operable. As a result, the long term survival rate has increased from 2% without surgery in the 1950's to 52% today. However, equally important is the quality of life of the cancer survivor after surgery. Minimally invasive robotic surgery aims to remove the cancer while preserving a patient's health-related quality of life.

### Our response

St Mark's Hospital Foundation is currently supporting a major, far reaching Surgical Robotics Programme to develop the next generation of minimally invasive surgery. This will save lives

and will improve the quality of life of many people across the UK and beyond with bowel cancer and IBD. With the development of robotic surgery, the St Mark's team aims to provide more precise, less invasive surgery, so that patients:

- Experience less tissue loss
- Experience less blood loss during the operation, keeping more healthy tissue alive
- Avoid the need for open surgery with the big scars this causes and the increased likelihood of infections, hernias and leakages from the surgical join, which can all be life threatening
- Avoid incontinence
- Avoid the loss of organ function

## The outcome

St Mark's Hospital will work in collaboration with the European Society of Coloproctology to develop a national training centre to provide the skills and expertise to enable the surgical profession to change practice and establish the best way to learn and build these skills. Through this process we aim to lead the way in surgical robotics for bowel disease in the UK and to collect the evidence to see the NHS upscale surgical robotics for bowel cancer and IBD nationally for thousands of people.

*St Mark's Hospital's surgical team performs the most advanced procedures that are at the forefront of robotic surgery.*

*HIPEC is an innovative treatment that pumps chemotherapy around a patient's body during open surgery, to kill cancer cells.*

## HIPEC – a new, advanced chemotherapy and surgical procedure to save the terminally ill

### The issue

When cancer spreads from its original location in the bowel lumen to other parts of the body, such as the lining of the stomach (peritoneum) and liver, the cancer can become so widespread and advanced that surgery will not save the patient. Conventional chemotherapy and radiotherapy alone are often ineffective in these cases. Currently, patients that experience cancer spread (metastasis) can only be offered end-of-life palliative care. HIPEC aims to give people with advanced cancer a greatly improved chance of survival.

### Our response

St Mark's Hospital has been pioneering HIPEC treatment, which combines advanced surgery with hot chemotherapy pumped throughout the body of the patient at the time of open surgery. This ensures that chemotherapy is delivered highly effectively, directly to the cancer deposits, so that that rogue cancer cells that break off during surgery are not given the chance to embed and grow. The early results of HIPEC are highly encouraging and lives have already been saved.

### The outcome

St Mark's is collecting data to demonstrate that HIPEC is a highly effective treatment for advanced cancer, with the aim of scaling up HIPEC nationally for the benefit of people with advanced cancer who otherwise would have little or no chance of survival.

## BiCyCLe – A program of research to improve our understanding of the body's own defence mechanisms to fight cancer

### The issue

The purpose of the BiCyCLe project is to find a way to prevent muscle wastage in people with bowel cancer. Two million people – that is 20% of all cancer patients - die annually worldwide due to the consequences of cancer-related muscle wastage, with no clear understanding for why it happens. Muscle is not just body tissue, it is an organ that plays an essential role in the body's immune system to fight infection and keep an individual healthy. BiCyCLe research may enable the combatting of muscle wasting in bowel and other types of cancer, with the potential to save many lives.

### Our response

BICYCLE is carrying our research in four key areas:

1]. The role of the body's white blood cells in cancer-related muscle wastage.

Current thinking about cancer is that it may be treated medically like an infection. The body's white blood cells play an essential role in fighting and killing infection. BiCyCLe research has been looking at a particular type of white blood cell, called a dendritic cell. In anorectal cancer, it can be seen that dendritic cells absorb fat and as a result, become ineffective at helping to fight cancer. Through our highly innovative BiCyCLe research, we aim to identify ways of making dendritic cells tough and impervious to absorbing fat by stopping the process that makes them fatty, and thus preserve their strength to fight infection and stop muscle wasting.

2]. The role of inflammation caused by bowel cancer.

The BiCyCLe project is currently examining the levels and types of inflammation to be found in cancer tumour cells. By doing this we aim to identify biomarkers, which are living organisms, chemicals, or genes that can then be targeted with drugs and chemicals to fight the inflammation, and thus control the cancer.

3]. The role of the bacteria to be found within the gut.

BiCyCLe is analysing the types of bacteria to be found in the gut and the role these bacteria play in cancer. If we can identify what the ideal bacteria is for a healthy gut, we will use this

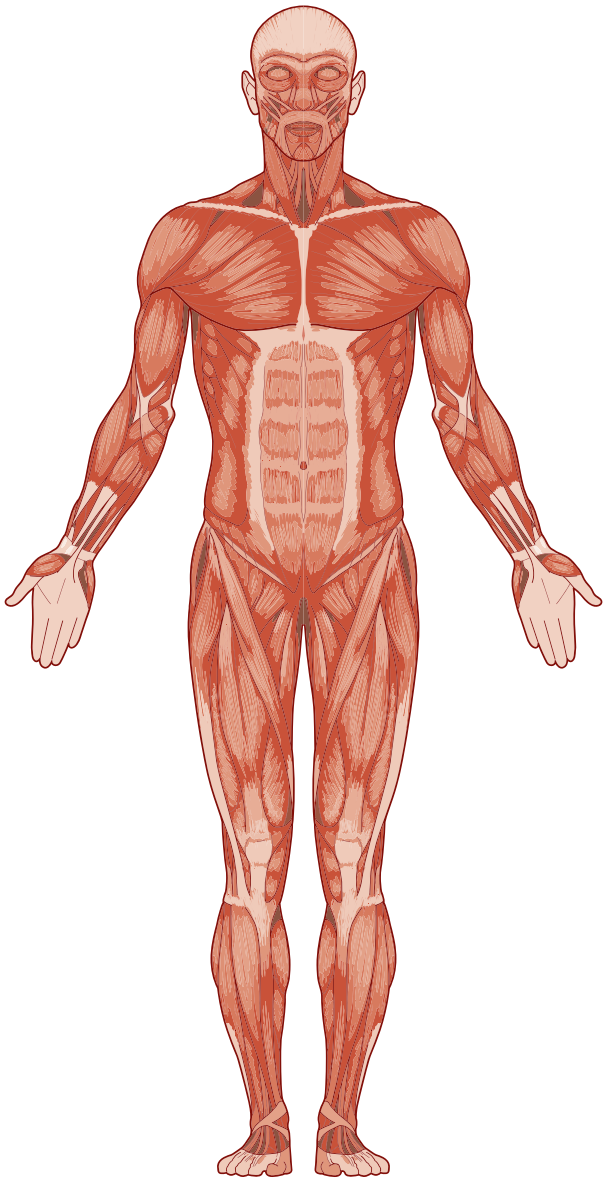
information to control the bacteria with drugs and investigate the possibility of supplementing a person's bacteria by implanting good bacteria.

**4].** Boosting a person's lean muscle bulk to help them fight cancer.

BiCyCLe is using a powerful version of the electrical stimulation machines that can be bought for general exercise of the muscle to help patients who are losing muscle bulk due to their illness, to build up their lean muscles to help them fight cancer.

## The outcomes

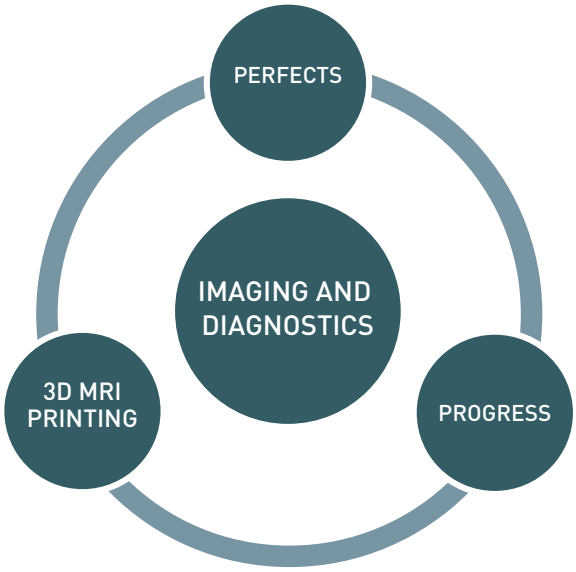
BiCyCle is developing a range of interventions that aim to boost a patient's immune system, both physiologically and physically, to make it strong and efficient at fighting bowel cancer cells and reverse the life-threatening symptom of bowel cancer related weight loss.



*Muscle is an essential element of the body's immune system and helps to fight cancer. St Mark's aims to improve the quality of a patient's lean muscle so that they are more able to fight cancer.*

## Section 4

# Imaging and diagnostics research




## PERFECTS – improving the skill level of radiologists to increase the lives saved from bowel cancer

### The issue

Bowel cancer screening saves lives. Since the national bowel cancer screening programme was established in the UK over 20 years ago, it has saved thousands of lives by identifying people at the pre- and early stages of cancer, when it is 100% treatable. If bowel cancer is detected later when it has spread, it is much harder to treat. Currently, the most effective form of screening is colonoscopy, where a camera is inserted through the rectum into the bowel lumen allowing the doctor to see if there are any small growths indicative of the patient developing cancer. Colonoscopy is, however, not suitable for all patients, especially the elderly, frail and fearful patients, as it involves an invasive procedure.

### Our response

An alternative to colonoscopy is a negligibly invasive procedure called, 'virtual colonoscopy' or 'CT Colonography' which is where a three-dimensional (3D) picture of the entire bowel is created using a non-invasive radiological scan. The doctor can see the entire 3D image of a patient's bowel on a computer screen and identify what is normal and what is cancerous.

When performed skilfully, CT Colonography is as effective as colonoscopy. St Mark's Hospital's radiology department has a world leading level of skill and accuracy in CT Colonography. There are, however, massive variations throughout the UK in the accuracy of radiologists performing virtual colonoscopy to identify the early signs of bowel cancer. Accuracy rates have been as low as 14%, compared to a near perfect rate at St Mark's Hospital and other proficient hospitals. This means that

thousands of pre- and early stage cancers are being missed.

The PERFECTs research programme aims to train all CT colonographers in the UK to a high standard of proficiency and to provide professional accreditation. The research started by training 50% of practitioners within the study group and will then collect evidence of improved accuracy. We will then train the remaining 50%.

## The outcome

This research has already started to raise standards and skills by training colonographers via workshops. This follows a large program of work across the UK to train the technicians performing the scan to ensure all scans acquired are of an optimum quality to demonstrate these small pre-cancerous growths. Participants recruited to date represent regions throughout the UK, including Huddersfield, Worcestershire, Leicester, Sheffield and Newcastle. The PERFECTs programme is already improving the national skill level of radiologists practicing and reporting on a technique that is increasingly being used for certain groups of patients.

This research has strong potential to address the current, highly variable reporting of bowel cancer diagnoses via virtual colonoscopy throughout the UK. For patients, this should mean that the successful diagnosis and subsequent treatment of their bowel cancer will not be a postcode lottery.

PERFECTS ultimately aims to train and provide professional validation of all colonographers in the UK, saving up to 2,000 lives a year.


*St Mark's Hospital is the national training hub for the non-invasive CT Colonographic screening for bowel cancer*

## PROGRESS - a programme to improve the national bowel cancer screening programme to save more lives

### The issue

A polyp is a pre-cancerous growth in the bowel. People who have a polyp or polyps removed at colonoscopy are entered into a surveillance programme which involves having a colonoscopy at one, three and five years. The 'adenoma-carcinoma sequence' continues to define our understanding of the development of colorectal cancer and the fundamental research that led to this understanding was carried out at St Mark's Hospital. The current surveillance programme is based simply on the size and number of polyps as a marker of future cancer risk. This means that patients at high risk of developing bowel cancer are not necessarily receiving the intensive surveillance they require, and low-risk patients are having unnecessary, invasive procedures. Our team at St Mark's aims to accurately establish the risk level of a person developing bowel cancer through the application of molecular pathology combined with a colonoscopy and an assessment of family cancer history. People who have a very low risk of developing cancer will not have to undergo unnecessary, repeat colonoscopies.

People over the age of 60 are offered bowel cancer screening every two years. In this group, however, are people at extremely low risk who do not need such intensive surveillance and monitoring.

*Dr Siwan Thomas-Gibson, a Consultant Gastroenterologist and Endoscopist at St Mark's Hospital, is a world leading proponent of bowel cancer screening.*

### Our response

This project aims to further knowledge of the growth patterns and evolution of polyps to a cancerous state using advanced molecular techniques to enable accurate, personalised clinical risk stratification for patients diagnosed with polyps and thereby better inform national guidelines. This more targeted approach will save more lives and will mean that NHS resources are used in a much more effective way.

### The outcomes

This research has the potential to influence national and international guidelines of colonoscopic surveillance, based on knowledge of how polyps grow and evolve to a cancerous state.

By understanding how polyps grow and the pathway they take, there is enormous potential to offer patients much more personalised treatment based on their risk level of developing bowel cancer. Limited NHS endoscopic resources could be

targeted more accurately on high-risk patients and unnecessary, invasive procedures that carry risks of complications would be avoided in low-risk patients. The numbers of patients affected would potentially be in the tens of thousands as the work could influence national and international guidelines.

## Novel use of MRI and 3D modelling for perianal fistulae

### The issue

One in three patients with Crohn's disease, a type of Inflammatory Bowel Disease (IBD), will develop a perianal fistula. A perianal fistula is a small tunnel that develops between the end of the bowel and the skin near the anus. They are notoriously difficult to treat and to heal completely and are associated with sometimes crippling symptoms and a significant negative impact on normal social interactions and quality of life.

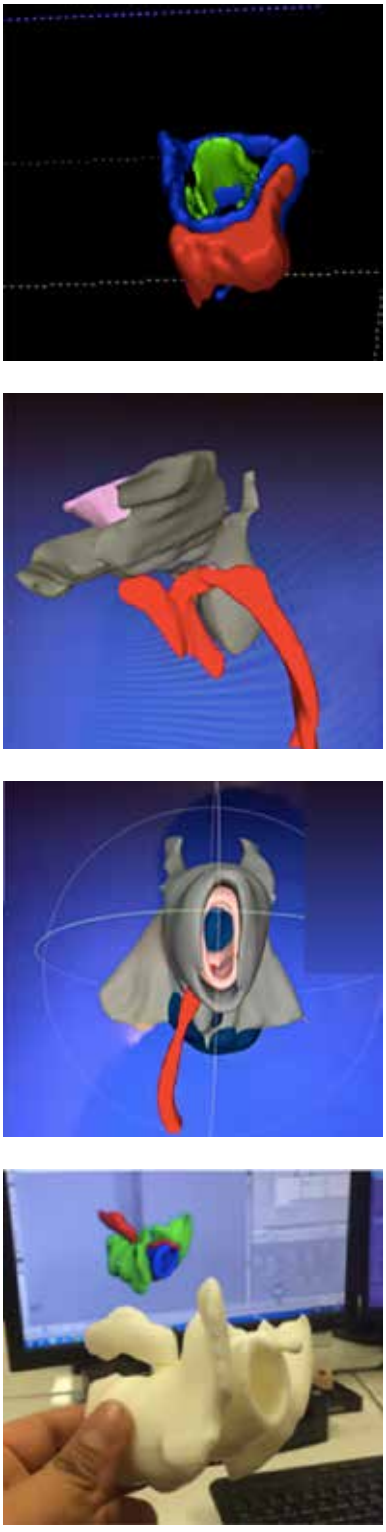
The surgical treatment of complex perianal fistulae poses significant challenges. For the surgeon, fistula anatomy can be difficult to visualise, making surgery more challenging. For the patient, the involvement of the sphincter muscles means that the risk of impairment of continence during surgery is a significant threat.

### Our response

This project uses an existing technology (MRI) in a novel way by assessing the volume of fistula tracts over a specific time period. MRI technology will not only help to understand how many fistula tracts are present and their complexity, but also whether patients are responding to medical therapy. Medical practitioners can then make informed decisions about whether to stop and/or switch patients' treatment. This project will create 3D models of complex fistula anatomy as an aid to surgical planning in order to avoid cutting healthy tissue and muscle, which would leave patients incontinent. 3D models will also be used as educational tools for surgeons whose work involves complex fistula surgery.

### The outcomes

As a proof of concept, we have shown that it is feasible to generate objective fistula volume measurements from MRI studies using computerised software. MRI volumes have been calculated for patients before and after medical therapy over a one-year time period. We have learned that MRI volume measurements can provide an accurate assessment tool, alongside radiology reports and clinical follow-up.



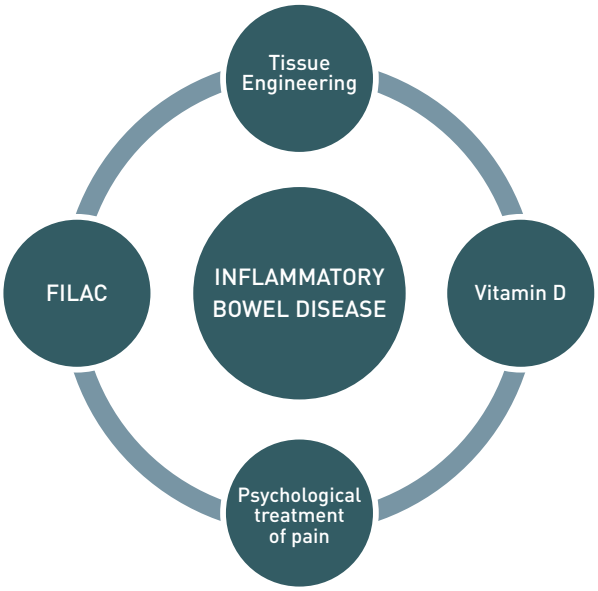
*Novel use of MRI and 3D printing will help surgeons to understand complex fistula anatomy, helping them to navigate the area and avoid patients becoming incontinent.*

The James Lind Alliance, a national Priority Setting Partnerships group of patients and clinicians, identified perianal Crohn's disease, and specifically the factors that influence treatment strategies and outcomes, as one of the top 10 unanswered questions in the field of IBD. The Association of Coloproctologists of Great Britain and Ireland also identified that improving the management of patients with perianal Crohn's disease was one of the top priorities for future research.

This project has the potential to develop an objective radiological measure of response to treatment, supporting the goals to offer personalised medicine in the future and improve the surgery and education in the treatment of complex fistulae.

## Section 5

# Inflammatory bowel disease research




## Tissue engineering - growing the world's first replacement bowel for people with short bowel syndrome from their own cells

### The issue

Individuals who lose large amounts of their bowel through trauma or conditions such as Crohn's disease and ulcerative colitis develop short bowel syndrome. This means that they can no longer absorb nutrition from food and must receive nutrients artificially via a vein into their heart. This process of feeding is known as total parenteral nutrition (TPN). There are approximately 1,000 adults on TPN in the UK. Significant health complications can result from TPN, such as infection of the line that is used for feeding, and the five-year survival rate is poor. The current solution to coming off TPN is a bowel transplant. However, this relies on a suitable donor becoming available. Recipients of organs also face a lifetime on immunosuppressant medication to prevent organ rejection. Immunosuppressants are associated with adverse side-affects, such as a compromised ability to fight infections.

### Our response

Tissue engineering, also known as regenerative medicine, is a solution to the problem of a lack of suitable organ donors, the high level of organ rejection and the need for organ recipients to be on immunosuppressants for life. This novel technique involves growing an organ, using a patient's own cells, thus removing entirely the need for an organ donor and avoiding the possibility of organ rejection.

The tissue engineering programme at St Mark's Hospital has been creating clinically relevant, functional lengths of bowel

called a 'scaffold'. This decellularized bowel lumen, an essential step to achieving the first ever tissue engineered replacement bowel, has been successfully re-implanted into a live pig.

Doctors and scientists at St Mark's Hospital have been working to identify the best type of stem cells to re-implant into the bowel scaffold to regrow the functionality of the bowel, such as motility, digestion and excretion. St Mark's and its partners have identified that the best source of stem cells are adipose (fat) stem cells, because there are ample supplies in the human body. Stem cells have the ability, under the correct environment and conditions, to develop as different functional cells of the body.

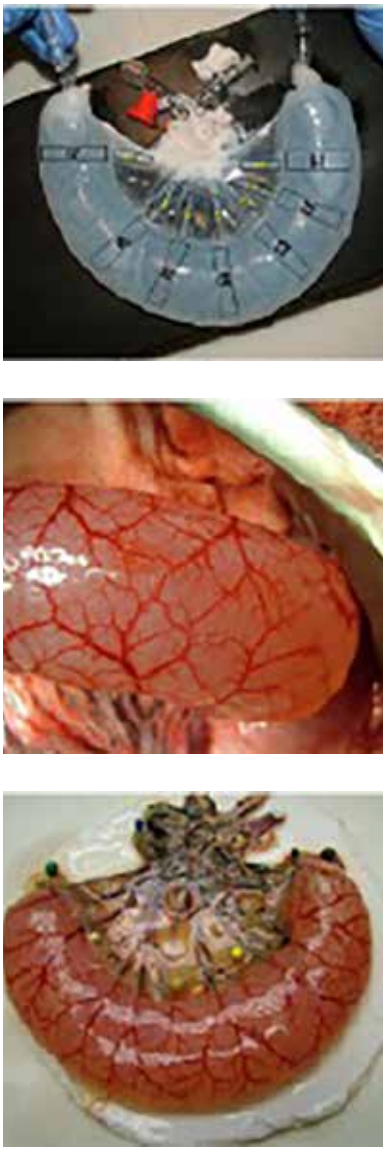
The next step is to bring the bowel scaffold and the stem cells together and direct the growth of the stem cells into the various functional cells that are to be found in the bowel.

The project benefits from the collaboration between cellular scientists and expert clinicians at St Mark's Hospital.

## The outcome

This research has the potential to not only improve the quality of life of patients, but also their survival rate. Patients on TPN have to be connected to their nutrition feed for as many as 23 hours a day. The ability to successfully tissue engineer a bowel that is functional and of a clinically relevant length would enable patients to lead full and active lives without the need for medication and the risk that their body will reject a transplanted organ. This research has tremendous potential to transform the treatment of a large number of patients.

St Mark's aims to be the first centre in the world to grow a fully functional, tissue engineered bowel.



*The world's first tissue engineered bowel scaffold, grown at St Mark's Hospital in conjunction with its research partner Northwick Park Institute of Medical Research.*

*Dr Ayesha Akbar examines a patient*

## FILAC - laser therapy for anal problems, a method for alleviating the pain of fistulae while avoiding the risk of incontinence

### The issue

Anal fistulae represent one of the most common benign conditions of the lower gastrointestinal tract. They account for the vast majority of surgical procedures performed in the region of the anus/rectum. According to the most recent evidence, there are more than 10,500 yearly interventions for fistulas in the UK. Furthermore, they account for a significant degree of morbidity in patients with Crohn's disease, affecting around one in three of these patients. According to the charity Crohn's & Colitis UK, there are at least 115,000 people with Crohn's disease in the UK, and many millions worldwide.

There is a need to effectively evaluate novel techniques that may offer better therapeutic options, such as improved healing and minimal risk to the continence function, for patients with this disabling anal condition.

### Our response

This project assesses the safety and feasibility of fistula tract laser closure (FiLaC) in certain patients with anal fistula. The current surgical treatment of complex fistulae which involves the sphincter muscles poses a high risk of incontinence. Laser therapy has the significant benefit of avoiding the continence issue.

### The outcome

We have introduced a new procedure – laser therapy for anal problems - into the current practice at St Mark's Hospital for the treatment of anal fistulas. Funding from generous donors has enabled us to incorporate this technique into clinical practice.

The patients on whom we have undertaken laser therapy have had a sphincter sparing procedure. As such, there has been minimal disturbance of the anal sphincter muscles for these patients and, as a result, there has been no theoretical risk to their continence status.

Currently, the conventional treatment for anal fistula is surgery but our research is focused on gathering evidence to show that laser therapy is a feasible alternative that achieves long-term healing and reduces the risk of recurrence. Thousands of patients with this disabling anal condition could thereby benefit from an improved quality of life.

## Vitamin D as an additional therapy to conventional medical therapy for inflammatory bowel disease

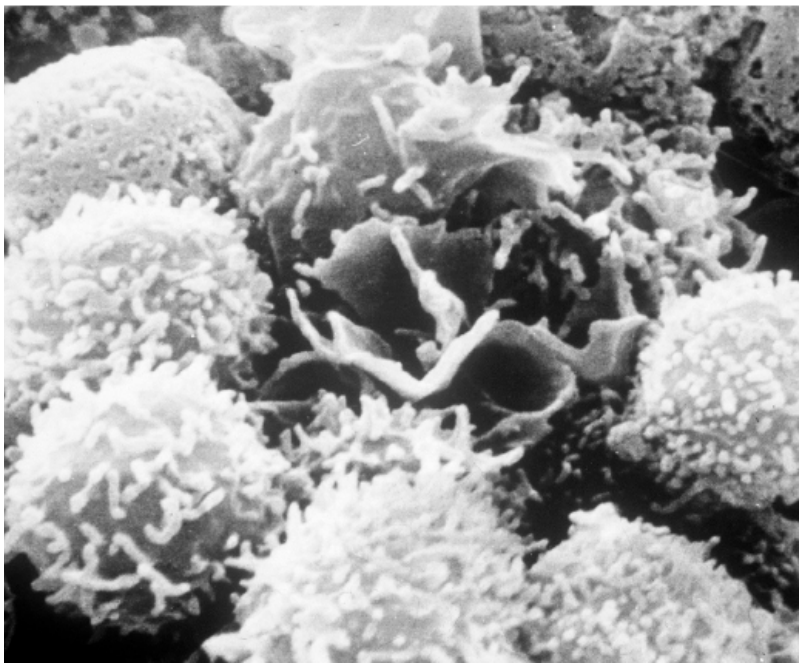
### The issue

The medical arsenal for the treatment of inflammatory bowel disease (IBD) is growing. However, these drugs are not suitable for all patients and do not achieve complete healing in others, as loss of response to drugs is common. In addition, there are several adverse side effects associated with such drugs, such as a compromised ability to fight infections and a higher risk of developing lymphoma, which is cancer of the body's lymphatic system. There is a need to identify natural treatments, which have the benefit of no side effects that can be used alongside conventional medical therapies to reduce the chronic inflammation caused by IBD.

IBD shares similarities with other autoimmune conditions. These are conditions where the immune system attacks itself by behaving hyperactively, causing inflammation. Vitamin D has been shown to be an effective treatment for rickets and is showing great promise as an additional treatment for tuberculosis and multiple sclerosis.

### Our response

For almost a decade, researchers at St Mark's have been studying the immunomodulatory effects of vitamin D for the treatment of IBD. Our research hypothesises that vitamin D supplementation reduces the number of bacteria that cause inflammation and increases numbers of bacteria with anti-inflammatory properties.



*Dendritic cell*

St Mark's Hospital is researching the administration of super-high doses of Vitamin D, to investigate whether it improves the efficacy of the conventional range of pharmacological medicines that are given for IBD. Furthermore, the effectiveness of vitamin D to reduce inflammation may mean that the dosages of the currently used drugs can be lowered.

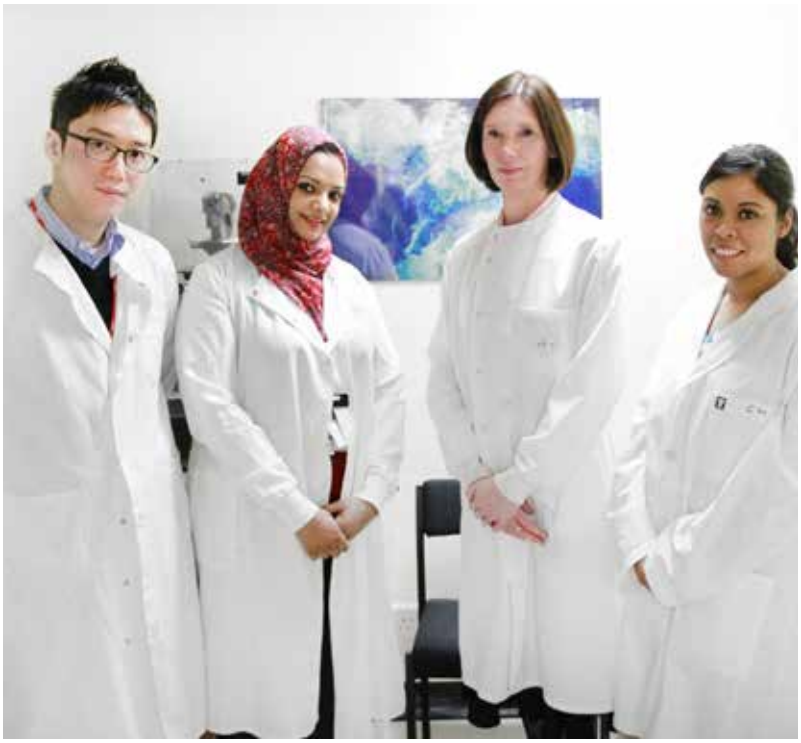
The results from our research support the hypothesis that vitamin D supplementation may reduce disease activity in patients with active IBD.

## The outcome

Information arising from this project will add to our knowledge of environmental factors; vitamin D that is provided naturally in ample amounts by the sun in sunny climates may modify the types of bacteria in the bowel of patients with IBD.

More widely, recent recognition of the role of the gut bacteria in other diseases means that the potential modification of the gut bacteria with vitamin D supplementation may have wider therapeutic implications in conditions like diabetes, heart disease and other autoimmune conditions.

We continue to collect data and investigate whether vitamin D is an effective addition to conventional medical therapy and whether it can be used to reduce the dosages of currently used drugs, such as biologics.



*Professor Ailsa Hart with her research team*

## Psychological treatment of chronic abdominal pain (PTCAP) programme

### The issue

The gut is one of the most innervated organs - that is, furnished by nerves - in the body, yet not all the information from the gut goes to the brain, as this would cause sensory overload. There is a 'gate' which prevents this overload but for many gastrointestinal patients, this gate opens and the patients feel more abdominal pain. These are frequently patients that have had bowel surgery or bowel infection and inflammation and, interestingly, also patients who were 'gutted' or could not 'digest' a severe emotional trauma and are chronically anxious.

Chronic abdominal pain is one of the most common clinical problems that St Mark's Hospital patients suffer with. It is a severe and enduring symptom of nearly all gastrointestinal diseases and disorders which are treated by our physicians and surgeons.

There has been a constant stream of growing evidence that mind-body therapies are effective at significantly helping patients to cope better with their pain, to improve the quality of their life and to reduce the need for pain killers. However, no comprehensive comparative research has been carried out to test the efficacy of psychological treatments or to explore how they can be integrated with traditional medical therapies.

### Our response

Our pioneering Psychological Treatment of Chronic Abdominal Pain (PTCAP) programme will identify and create the most cost-effective, efficient treatment programme which will help sufferers of chronic abdominal pain to cope and manage their pain significantly better, minimising or even eliminating the need for permanent use of pain killers (mainly opiates), which can have adverse side effects, such as addiction. It will specifically look at the mind-body therapies, Act (Acceptance and Commitment Therapy) and hypnosis as methods of controlling chronic abdominal pain.

### The outcome

The Psychological Gastroenterology Unit (PGU) at St Mark's Hospital is conducting this research in collaboration with Professor Lance McCracken, a world-renowned pain

management clinician and researcher at Kings College, and Dr Lin Yu, a research psychologist at St George's Hospital. As a result, this multi-centre collaboration benefits from access to a large group of patients to recruit to this pilot study.

We aim to disseminate our PTCAP programme through our partner centres with a view to building up national coverage in the longer term. We anticipate that this service will be offered to over 2,000 patients struggling to cope with abdominal pain annually.

## Conclusion

St Mark's is highly committed to researching and developing new, improved treatments and to disseminating clinical best practice worldwide through St Mark's Academic Institute, which educates and trains thousands of practitioners annually. Please support St Mark's Hospital and St Mark's Hospital Foundation to continue to lead the world towards a healthier future for people with bowel disease.

In this era of ever increasing specialism in medicine, where complex and difficult to treat conditions are referred from general hospitals to specialist centres of excellence, there is a need to invest in St Mark's, the UK's national referral centre for complex bowel diseases. This investment will enable St Mark's to continue its work in developing improved treatments and striving to cure conditions that are devastating the lives of many people throughout the world and continue to be inadequately treated through lack of a full understanding of the disease. It will also enable St Mark's to continue educating and training the world in clinical best practice for the benefit of people in need across the world.

To talk to us about sponsoring a specific research programme or becoming a Patron or Friend of St Mark's, please contact our Fundraising team on 0208 235 4042 or info@stmarkshospitalfoundation.org.uk

## A final word about the most important measure of the impact of St Mark's Hospital's research

At St Mark's, there is one highly important impact measurement that we aim to achieve for each of our 50,000 patients and all those patients who, although not treated directly at St Mark's, benefit from our sharing of best practice with their doctors. That measurement is the difference our research-driven services make to the quality of life of people with bowel disease. The photos opposite provide the last word about the difference our research makes to patients' lives.

*The above 'before and after treatment' photos of Nancy Fahmy, a fabulous individual who is treated at St Mark's for her bowel disease, illustrates what we aim to achieve for each and every one of the individuals who seek help from St Mark's. Others might call these individuals patients.*


A future free from the
fear of bowel disease

***St Mark's Hospital Foundation***

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St Mark's Hospital Foundation is dedicated to bringing about a future free from the fear of bowel disease through research, education and dissemination of clinical excellence

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