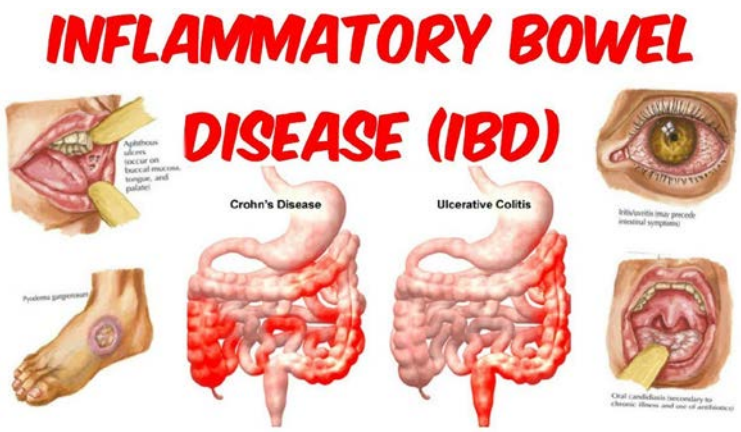
OxyUC :
The impact of hypoxia on inflammation and tumorigenesis in ulcerative colitis

Inflammatory bowel disease (IBD) is a severe and common disorder with a limited range of therapeutic opportunities and a risk to develop intestinal cancer which affects approximately 2% of the population of the EU.
The treatment of IBD has improved since the introduction of biologic therapeutics such as anti-TNF antibodies. However, there remain significant issues relating to cost, side effects and non-responsiveness in patients.



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OxyUC is a collaborative project of clinicians, gastroenterologists and mathematical biologists which main goal is to investigate and develop new therapeutic approaches for IBD. This new methodology is based on the hypothesis that the body's innate capacity to adapt to hypoxia (i.e. low oxygen concentration). For example, mountain climbers need to allow their body to adapt to a relative drop in oxygen concentration.

One such avenue is to target the individual patients capacity to adapt to hypoxia through the introduction of drugs which enhance the activity of the Hypoxia Inducible Factor (HIF) pathway. Such drugs have recently been approved for the treatment of anemia. We hypothesize that by understanding the individual patients capacity for responsiveness to hypoxia, we can identify which patients would benefit from this new therapeutic approach.

OxyUC uses a combination of clinical measurements taking intestinal biopsies, cell culture experiments, transgenic animal studies and mathematical modelling to make prognostic predictions about an individual patient's IBD based on intestinal mucosal oxygen measurements and the strength of the individual Hypoxia Inducible Factor-1 (HIF-1) response.

The successful achievement of this work requires the use of experimental models, patient based data and mathematical modelling to provide a personalized approach to the diagnosis, prognosis and potentially therapeutic approach to IBD on a patient-by-patient basis.

The mathematical model will be informed by an individual patient's mucosal oxygen level and the strength of their hypoxic response, i.e. how the individual patient respond to hypoxia.

This project will generate a new way to evaluate the nature of an individual patient's disease and to optimize its treatment by mathematical modelling. This allows to make predictions about the prognosis as well as to inform the design of optimal therapeutic protocols.

The main beneficiaries of this research will be IBD patients (including both Crohn's Disease and Ulcerative Colitis patients) and the field of gastroenterology related researchers.

The project outcomes will provide understanding of the homogeneity of IBD to clinicians and help them to make informed decisions about therapeutics based on the genetic and biologic background of individual patients. One possibility is that mucosal oxygen measurements taken during endoscopy could become part of disease assessment. The introduction of a new effective therapeutic approach to IBD would have significant economic benefit for the EU in terms of having a healthier and more productive workforce.

PROJECT DURATION > 36 Months

Onset project: May 2016

Project ends: September 2019

Inflammatory bowel disease (IBD) is an umbrella term used to describe disorders that involve chronic inflammation of the digestive tract. Types of IBD include: Ulcerative Colitis and Crohn's Disease. Ulcerative Colitis causes long-lasting inflammation and sores (ulcers) in the innermost lining of the large intestine (colon) and rectum.

Hypoxia-Inducible Factor (**HIF**)-1 is a dimeric protein complex that plays an integral role in the body's response to low oxygen concentrations, or **hypoxia**. **HIF**-1 is among the primary genes involved in the homeostatic process, which can increase vascularization in **hypoxic** areas such as localized ischemia and tumors.

Mathematical model is a description of a system using mathematical concepts and language. The process of developing a mathematical model is termed mathematical modeling. A model may help to explain a system and to study the effects of different components, and to make predictions about behaviour.

Click here to watch the OxyUC movie

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