

Project Summaries for 2004

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Grant awarded £77,741 (2 years)

Isolation and characterisation of E.coli in Inflammatory Bowel Disease

The cause of Crohn's Disease and Ulcerative Colitis (inflammatory bowel disease: IBD) remains unclear. Several factors have been implicated such as diet – food sensitivity, an abnormal response to bacteria in the gastrointestinal tract, and environmental factors such as smoking. There is also a link to there being a genetic predisposition to IBD, although from this list no single factor can be associated as causative of the disease. It is more likely to be a combination of these factors that induces onset of disease.

Over many years, bacteria in the gut have been thought to be one of the main culprits in the initiation of IBD. Much research has been done on the composition of the various populations of bacteria in the stool, but this has not shown consistent results. To get over this problem we have focussed our research on one particular factor and that is the involvement of the immunological response to the bacterial flora that colonises the gut of every individual. The bacteria lining our entire gastrointestinal tract can be regarded as being in contact with 'good' as well as 'bad' bacteria. In health, the good bacteria are able to outnumber the bad and by virtue of this fact can keep disease at bay. This has been shown by giving supplements to patients with pouchitis, where the probiotics are seen as effective as drugs in maintaining remission. The distribution of bacteria in the gut is predominantly associated with the transient population in the faeces that is swept along by peristaltic activity through the entire GI tract. Many studies have been undertaken to detect abnormalities in faecal flora of patients with IBD.

Our hypothesis is that it is not this transient population that is responsible for the exaggerated immunological response seen in active disease but a sensitivity to a smaller population of bacteria that are actually attached to the gut wall along its length.

Our preliminary data has shown that in patients with IBD, this ratio of 'good' to 'bad' bacteria adherent to the lining of the intestine is reserved. We suggest that this anomaly contributes to the inflammatory response seen in these patients and therefore manifests as the underlying pathology. We have shown that not only is there an increased number of potentially damaging bacteria adherent to the lining of the gut in patients with IBD, but that some of these bacteria are able to penetrate the gut wall and invade the underlying tissue.

Those bacteria that have penetrated the gut wall from a cluster within some of the cells (macrophages) that lie under the surface of the lining of the gut within the tissue. Using molecular techniques and antibodies we have shown that the bacteria belong to a species of bacteria known as Escherichia. Acknowledging the limitations of the techniques we had used, we sought to further characterise these bacteria using microbiological techniques. This has enabled us to confirm the identity of bacteria as being E.coli and further investigations as to their association with the macrophages are the mainstream of our proposed grant application.

If these bacteria that have invaded the lining of the gut are in any way different to those attached to the surface, the epithelium, we need to find out in what way they differ. Why have they become invasive, and are they damaging by virtue of the fact that they have survived within cells when they should have been destroyed?

If we can identify 'virulence factors' by molecular biology techniques, then we might not only be able to identify which genes have been activated but which have been suppressed.

Such knowledge will help identify methods by which the virulence may be nullified.