

Lay Summary – Andrew Silver

Crohn's Disease (CD) is an inflammatory condition of the intestine. CD patients are prone to obstruction of the intestine caused by narrowing of the lumen as a result of a build up of scar tissue fibres (fibrosis) in the outer muscle layer that surround the intestine. This stricturing process often requires surgery. Unfortunately, there are no blood tests available to detect fibrosis or strictures and no therapies available obtainable to prevent, delay or reverse this type of disease progression. Patients often require many x-ray based and endoscopic tests that can be uncomfortable and carry a small risk of harm in order to detect whether their symptoms are caused by strictures.

A new class of gene regulatory elements called microRNAs has been discovered recently and we have found that there are changes in the expression of microRNAs in strictured regions of the gut compared to non-strictured areas. Also, we have shown that microRNAs can be detected in blood samples providing opportunities for minimally invasive patient surveillance. We now propose to undertake a full microRNA profiling study using both tissue and blood to evaluate the potential for developing new tests to measure disease progression. These tests will lead to new insights into molecular genetic changes that accompany chronic inflammation and fibrosis by detecting microRNAs using proven techniques, which are available in our laboratory. We plan to test whether changes in microRNA profiles reflect fibrotic changes in the gut and to find if microRNAs profiles in blood correlate with those in tissues taken from the gut by surgery. Our work has the potential to lead to identification of gene targets for miRNA that cause fibrosis and which are amenable to therapy. In addition, it may be possible in the future to develop blood tests that establish the degree of fibrosis and inflammation in the stricture, which would inform clinical decision-making as part of patient management.