

## **SYDNEY CHILDREN'S HOSPITAL**

### **S100 Proteins & Colitis Associated Cancer**

#### **LAY DESCRIPTION**

Long-standing inflammation of the colon in Inflammatory Bowel Disease increases the risk of colon cancer in these patients. Several members of the S100 family of proteins are increased in both IBD and in colonic carcinoma. The roles of these proteins in the development of cancer in the setting of long-standing gut inflammation have not yet been determined. These proteins may contribute to the development of cancer in the setting of long-standing inflammation of the bowel.

These studies will involve the obtaining of additional mucosal biopsies from individuals undergoing clinically-indicated procedures. The proposed study will involve children (aged less than 18 years of age) and adults. None of the clinical studies outlined here will be reviewed and approved by the South East Sydney Area Health Ethics Committee before any studies are commenced. A final letter of approval will be forwarded in due course.

#### **AIMS and HYPOTHESES**

The overall objectives of this project are to characterise relationships between S100 proteins and intestinal epithelial cells and to ascertain whether these proteins may contribute to the increased risk of colonic cancer evident in individuals with longstanding colonic inflammation.

The hypotheses of this project are:

- (1) S100 genes are included in chronic gut inflammation
- (2) Colonic express of S100 proteins during the course of chronic colitis contributes to the development of colitis-associated cancer
- (3) S100 proteins alter the apoptotic potential epithelial cells.

The specific aims if this project are to:

- (1) determine the activation and expression of selected S100 genes and proteins in colonic mucosa
- (2) Contrast levels of S100 proteins in colitis of short duration to colitis of long duration
- (3) Ascertain the effect of S100 proteins upon apoptotic events in epithelial cells.

#### **SIGNIFICANCE**

Chronic inflammation of the colon in the context of ulcerative colitis and Crohn's disease leads to an increased risk of the development of colonic cancer. It is recommended that regular screening programs should commence after 8 years of pan-colonic inflammation and continue yearly to two-yearly thereafter. Furthermore, S100 proteins are known to be elevated in both IBD and in colonic carcinoma. The roles played by these proteins in the development of cancer in the setting of chronic inflammation have not yet been fully determined. Given that these proteins are present in high levels in the colon during inflammation and that they are easily detectable in the stool and that they are elevated in the stool of patients with colonic carcinomas, they may have roles both as markers of cancer development, and contribute to the development of this adverse outcome.