Occasional viewpoint

Is the colonic reparative cell lineage yet to be discovered?

The gastrointestinal mucosa displays a number of different cell lineages in response to injury. The presence of such phenomena has been known for a number of years but their significance is only now being realised.^{1–3} A number of these are thought to be reparative mechanisms, such as the ulcer associated cell lineage (UACL) at the edge of small bowel ulcers (see fig 1).⁴ Other examples include spasmolytic polypeptide expressing metaplasia⁵ and pseudopyloric metaplasia in the stomach. Other metaplastic cell lineages, such as intestinal metaplasia in the stomach and the glandular metaplasia of Barrett's oesophagus, have a neoplastic potential but are also a response to an initial mucosal injury. In an animal model of duodenal content reflux oesophagitis there is evidence of a UACL-like glandular structure that occurs at the oesophagojejunostomy anastomosis site.⁶ These cell lineages share a number of morphological and phenotypic similarities.⁷ Certainly they appear to express epidermal growth factor (EGF), members of the trefoil factor family (TFF) peptides,⁸ and the protease inhibitor pancreatic secretory trypsin inhibitor (PSTI),⁹ in an aberrant fashion to the surrounding indigenous mucosa. TFF peptides and EGF appear to be important motogens to the gastrointestinal epithelia and are involved in the process of mucosal restitution following injury. PSTI is probably important in maintaining gastrointestinal mucous layer integrity.

The presence of the UACL in the colon in response to active Crohn's disease and possibly to ulcerative colitis (UC) is poorly documented.^{4–10} No other reparative cell lineage has been described in the colon. The UACL has been demonstrated in the ileoanal pouch of UC patients and in the exteriorised mucosa of ileostomies with colonic phenotypic change. Colonic metaplastic polyps share some phenotypic similarities with other metaplastic phenomena but the underlying aetiology in response to injury has not been proved and they are quite rare in inflammatory bowel disease. Tongues of restitutional epithelia are seen extending across UC or Crohn's colitis ulcers in the reparative phase following an acute episode of the disease but this bears no morphological similarity to the aforementioned reparative responses in the rest of the gut. If a UACL-like

structure occurs in the colon it might be expected in the proximal colon that is derived from the embryonic mid-gut.

Our hypothesis is that the colon does not rely on the UACL as its sole reparative cell lineage. The rarity of a reparative metaplasia or the UACL in the colon has never been fully appreciated. The ability to histologically review the whole colonic mucosa following panproctocolectomy for active inflammatory bowel disease would be a great undertaking. However, the vast numbers of colonic biopsies and resection tissues that have been removed and viewed under a microscope would suggest that if the UACL is important in colonic restitution it would be seen more frequently. This would suggest that the large bowel possesses fundamentally different mechanisms for mucosal repair compared with the rest of the gastrointestinal mucosa and, therefore, it is possible that other reparative cell lineages or restitutional mechanisms have yet to be characterised. Knowledge of the reparative mechanisms involved in inflammatory conditions of the large bowel is essential in understanding the pathogenesis of the disease and the development of new therapeutic modalities.

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Abbreviations used in this paper: UACL, ulcer associated cell lineage; PSTI, pancreatic secretory trypsin inhibitor; EGF, epidermal growth factor; TFF, trefoil factor family; UC ulcerative colitis.

Figure 1 (A) Ulcer associated cell lineage at the mucosal surface demonstrating re-epithelialisation of a fissure in the terminal ileum of a patient with active small bowel Crohn's disease (haematoxylin and eosin; $\times 50$). (B) Ulcer associated cell lineage acini (large arrow) and duct (small arrow) adjacent to the mucosal fissure in a serial section of (A) (periodic acid Schiff/alcan blue stain; $\times 50$).

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