

Crypt Cell Dysplasia with Maturation in Barrett's Esophagus Shows Clonal Identity between the Crypt and Surface Cells

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Dysplasia in epithelia is an important histological diagnosis. The specific genetic changes which are responsible for the induction of this phenotypic change are unknown. Recent reports indicate that the dysplastic phenotype may not be immutable: in basal crypt dysplasia-like atypia (BCDA), unequivocal dysplastic changes are seen in the crypts in Barrett's esophagus and other pre-invasive lesions in the gastrointestinal tract, but the upper crypts and surface epithelium associated with these dysplastic crypts show the definitive morphology of a differentiated epithelium. The genotypic relationship between the BCDA and the differentiated surface epithelium is presently unclear.

We obtained 17 examples of BCDA: the lower crypts and upper crypts and surface epithelium were differentially laser-microdissected from formalin-fixed, paraffin embedded sections and mutations were sought in tumour suppressor genes frequently associated with progression in Barrett's esophagus. We found two patients who both showed a c. C238T mutation in the p16 (CDKN2A, p16Ink4A) gene and where the precise microanatomical relationships could be discerned: this mutation was present in both the BCDA at the crypt base and in the upper crypt and surface epithelium. In BCDA, the dysplastic basal crypt epithelium and the upper crypt and surface epithelium show clonal mutations in p16, showing that the surface epithelium is derived from the dysplastic crypt epithelium: the dysplastic phenotype is therefore not fixed and can be reversed. The mechanism of this change is unclear: dysplastic cells may, probably at an early stage in their progression, respond to differentiation signals. We are some way from a definition of the genotypic correlates of the dysplastic phenotype, and from an understanding of its plasticity.