

# The molecular pathology of gastric cancer

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Understanding of the molecular pathology of gastric cancer has been revolutionised by the application of next-generation sequencing platforms to the disease. The Cancer Genome Atlas (TCGA) group described four molecular subtypes of gastric cancer: Epstein-Barr virus positive, microsatellite unstable, genomically stable and chromosomal instability. Recognition of these subgroups and their underlying common gene mutations and driver events is leading to the development of targeted therapies, including immunotherapies. Similar genetic classifications are now available for other tumours of the gastrointestinal tract, meaning that novel treatments can be applied across tumour types. A range of mutations in genes related to genome integrity (e.g. BRCA2, TP53, ARID1A), chromatin remodelling (e.g. SMARCA1, CHD3, CHD4) and cell-cell adhesion and motility (e.g. RHOA, CDH1) have been described in gastric cancer. In addition, cell signalling pathways commonly mutated in other solid organ tumours are also often found perturbed in gastric cancer. Michael Anthony Epstein, b. 1921, Professor of Pathology, University of Bristol, Bristol, UK. Yvonne Barr, 1931–2016, virologist who emigrated to Australia. Epstein and Barr discovered this virus in 1964. Charles Emile Troisier, 1844–1919, Professor of Pathology, Paris, France. Unsurprisingly gastric cancer exhibits a range of mutations in receptor tyrosine kinases and PI3K/MAPK signalling (see Chapter 11). The rapid development of sequencing technologies, including single-cell platforms and the development of real-time sequencing, offers the promise of precision therapy for gastric cancer in the future, but currently treatment is still based on surgery with or without conventional chemo/radiotherapy.

Mucosa Type I Submucosa Muscularis Type IIa Type IIb Type IIc Type III Cancer Figure 67.25  
Japanese classification of early gastric cancer: type I, protruding; type II, superficial, a, elevated, b, flat, c, depressed; type III, ulcerated.

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