

SDH-C epimutated gastrointestinal stromal tumours: Clinical and pathological features and SDH-C promoter methylation analysis

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Gastrointestinal Stromal Tumour (GIST)

85% Somatic mutation
KIT, PDGFRA, BRAF

SDH 85% deficient

Germline (75%) or somatic mutation
SDHA, SDHB, SDHC, SDHD

SDH deficient GIST:
Carney's triade (ca 20%) Carney's Stratakis syndrome

Succinate dehydrogenase (SDH)

15% "wild type" GIST
Incidence ca. 1/Mio

SDH 15% preserved

Germline mutation
NF1

Succinate accumulation to act as 'oncometabolite' ->-> HIFa ↑

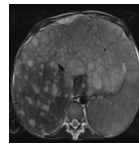
Three patients with KIT, PDGFRA and BRAF 'wild type' GIST

Patient 1

- F, 19y
- Gastric GIST
- 65mm,
- 1 mitosis / 50 HPF
- hemi-gastrectomy
- 27y new gastric GISTs and liver metastases

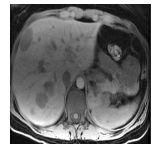
Patient 2

- F, 15y
- Gastric GIST with liver metastases
- Gastrectomy
- 2 mitoses / 5mm2

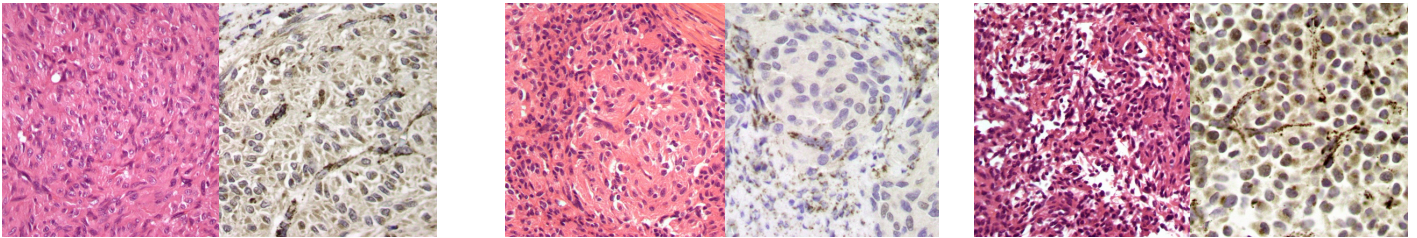


Patient 3

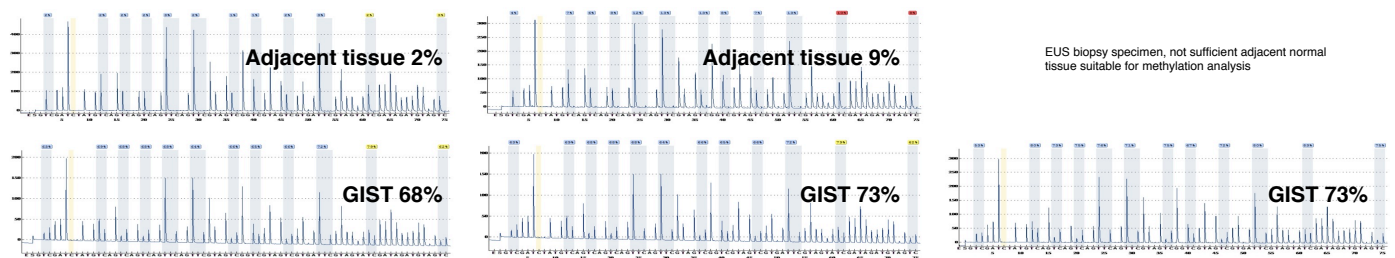
- F, 24y
- Multifocal gastric GIST and liver metastases
- EUS biopsy (MIB <2%)



Tumours show loss of SDHB immunoreactivity



Tumours show SDHC promoter hypermethylation (pyrosequencing analysis)



SDHC expression is down-regulated in SDHC epimutated GIST

Patient 2 CTL
□ Adjacent tissue
■ GIST

in vivo 1H-MR spectra demonstrating a succinate peak in SDHC epimutated GIST

