Additional diagnostic techniques
SSL & dysplasia
## Molecular pathways

<table>
<thead>
<tr>
<th>Serrated pathways</th>
<th>Adenoma-carcinoma sequence*</th>
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<tbody>
<tr>
<td>BRAF†</td>
<td>APC</td>
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<tr>
<td>KRAS‡</td>
<td>KRAS</td>
</tr>
<tr>
<td>hMLH-1§</td>
<td>p53</td>
</tr>
<tr>
<td>p16</td>
<td>SMAD4</td>
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<tr>
<td>MGMT</td>
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</tbody>
</table>

*Familial CRC proceeds down a very similar pathway to the adenoma-carcinoma sequence: in familial adenomatous polyposis a germline mutation in the APC gene is present while in Lynch syndrome a germline mutation in one of the DNA mismatch repair enzymes is present. In both conditions, the second allele of the corresponding gene is then lost or inactivated through mutation.

†Mutations in *BRAF* are an early event in the SSL pathway.

‡Mutations in *KRAS* are an early event in the TSA pathway.

§hMLH-1 is inactivated in the SSL pathway via the CIMP mechanism.

APC, adenomatous polyposis coli; CIMP, CpG island methylator phenotype; CRC, colorectal cancer; SSL, sessile serrated lesion; TSA, traditional’ serrated adenoma.
Molecular pathways

Pathways to mismatch repair deficiency in colorectal cancer

- Germline mutation (MLH1, MSH2, MSH6, PMS2)
- Biallelic MLH1 methylation CIMP+
- Lynch syndrome (~3%)
- Sporadic (~12%)

Deficient MMR repair

Second hit (mutation, LOH, methylation)

Microsatellite instability (MSI)

- Frameshift mutations in genes with coding microsatellites
- Other mutations

Colorectal cancer

BRAFV600E mutation

Southampton Cellular Pathology
Guidelines
REPORTING LESIONS IN THE NHS BOWEL CANCER SCREENING PROGRAMME

Guidelines from the Bowel Cancer Screening Programme Pathology Group

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Immunohistochemistry, while sometimes helpful, does not reveal features that are alone diagnostic of SSL.

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Interactive cases