Protocol 7
Investigations for Lynch Syndrome in patients with colorectal cancer

Immunohistochemistry of tumour for MLH1, MSH2, MSH6, PMS2

**Normal IHC**
- Return to protocol 6 and re-evaluate family

**Loss of MLH1 +/- PMS2**
- Test tumour for BRAF V600E
  - BRAF V600E present: Return to protocol 6 and re-evaluate family
  - BRAF V600E absent (wt): MLH1, MSH2, MSH6 panel
    - No pathogenic mutation. Return to protocol 6 and re-evaluate family
    - Pathogenic mutation see protocol 9

**Loss of PMS2 alone**
- Test tumour for BRAF V600E
  - BRAF V600E present: Return to protocol 6 and re-evaluate family
  - BRAF V600E absent (wt): PMS2. If normal MLH1, MSH2, MSH6 panel
    - No pathogenic mutation. Return to protocol 6 and re-evaluate family
    - Pathogenic mutation see protocol 9 or 12

**Loss MSH2 and/or MSH6**
- MLH1, MSH2, MSH6 panel
  - No pathogenic mutation. Return to protocol 6 and re-evaluate family
  - Pathogenic mutation see protocol 10 or 11

**Notes:**
1. Re-evaluate residual family history excluding individual(s) in whom tumour testing has shown tumour to be sporadic/non-Lynch. If additional family member eligible for investigation for Lynch, discuss case at MDT.
2. If rare variant detected, proceed with investigations as per “No Pathogenic Mutation”, email report to vus@icr.ac.uk and discuss at MDT

See FAQ document for further details: http://www.icr.ac.uk/protocols

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