

Colon CFR Phase II and III Molecular Characterization Scheme

First Round Testing: Testing listed here will be conducted on All Phase-II and -III Probands (unless other wise specified). The results of these tests will direct the testing below as shown.

A. Tumor testing:

1. IHC for MMR genes (*MLH1*, *MSH2*, *MSH6*, *PMS2*) will be conducted on ALL Phase III tumors (Phase II tumors were tested previously).
2. *BRAF* point mutation testing will be conducted on **all** Phase I, II, and III Proband tumors (*BRAF* testing has not been conducted to date).

B. Germline mutation analysis:

1. For Phase II and III Probands (Phase I Probands were tested previously): If no tumor is available, but blood is, *MLH1*, *MSH2* and *MSH6* germline DNA will be tested by custom capture. If tumor tissue is available, germline MMR testing will be triaged by IHC result as per below.
2. *MYH* testing will be conducted on all Phase II and III Probands (Phase I Probands were tested previously) for the two common mutations only (accounts for ~85% of mutations so of biallelic carriers, 72% homozygous/cmpd het for these 2 mutations and 26% show at least 1 of these and only ~2% of biallelics will be missed completely).

