Genetics and tumor genomics in familial colorectal cancer

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Colorectal cancer (CRC) is one of the most common cancers in the Western world and in about 30% hereditary factors play a role. Although several genetic factors that predispose families to CRC are known, in many families affected with CRC the underlying genetics remain elusive. The work described in this thesis aimed to identify novel genetic factors that lead to an increased risk for CRC in these families. Several approaches were applied, including both germ line genetic analysis and the study of genomic aberrations in colorectal carcinomas.

- Linkage analysis did not provide evidence for a novel high risk factor, but provided supportive evidence for a previously identified region on 3q.
- Enrichment of common low risk variants was observed in a cohort of familial CRC patients but not in early-onset solitary patients (without a family history of CRC).
- Profiling of genomic aberrations in colorectal carcinomas showed distinct profiles for different hereditary CRC syndromes:
- MUTYH-associated carcinomas showed high frequencies of copy-neutral LOH.
- Mismatch repair proficient familial carcinomas appeared to resemble the genomic profile of sporadic CRC, but with a remarkably increased frequency of 20q gain and genome-wide cnLOH.

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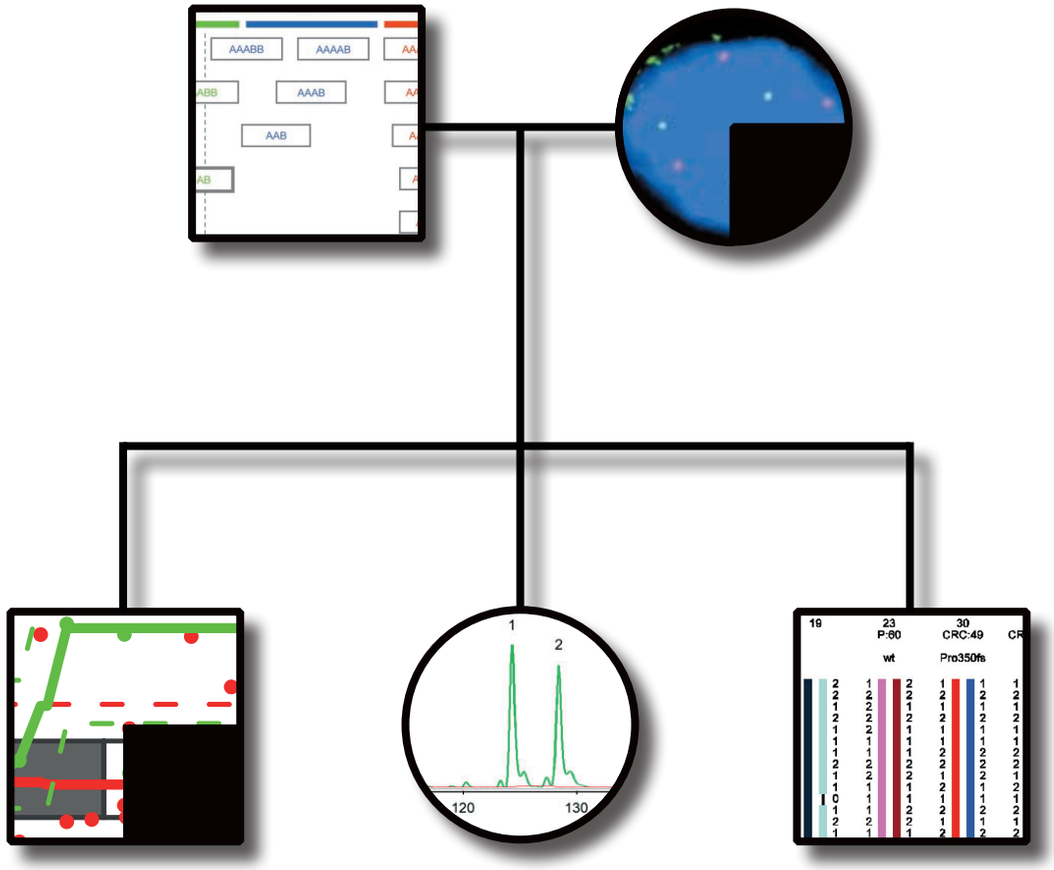

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