

Familial colorectal cancer: Search for novel predisposition genes

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Family history of colorectal cancer (CRC) and multiple primary CRCs in a single person may indicate inherited CRC predisposition. About 15% of CRC patients have a first degree relative diagnosed with CRC, but only about one quarter of these are explained by variants in the known high-penetrance genes. We used a set of *in silico* tools in combination with a STRING protein-protein interaction and pathway analysis to identify the most likely predisposition variants in 19 CRC families and in family members with multiple CRCs from seven additional families. We had previously whole-exome or whole-genome sequenced the germline DNA from these families. In addition to four families with a mismatch repair (MMR) gene mutation, we identified one family with a moderate penetrance variant in CHEK2, Ile157Thr. According to STRING, several additional variants affected proteins within the Cell cycle and DNA repair pathways as well as the TGF β signaling pathway together with the Focal adhesion and Extracellular matrix organization, highlighting the importance of these pathway in CRC predisposition.