**Supplementary Materials**

**Supplementary Table S1** Summary of family members WGS was performed on, including personal data and the consideration of being a carrier of the cancer-causing mutation. CRC – colorectal cancer, CRP – colorectal polyps.

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| --- | --- | --- | --- | --- | --- | --- |
| **Classification** | **ID** | **Sex** | **Age at recruitment** | **Diagnosis** | **Age of onset** | **Considered as a carrier****of the mutation?** |
| Cases | III-1 | male | 77 | CRC, CRP | 57, 60 | Yes |
|  | IV-8 | male | 54 | CRC | 23 | Yes |
| Possible carrier | IV-7 | female | 40 | - | - | Yes/No |

**Supplementary Table S2.** Alphabetical list of qPCR primers with respective forward and reverse sequences.

|  |  |  |
| --- | --- | --- |
| **Gene** | **Forward primer sequence** | **Reverse primer sequence** |
| AKT | Quantitect primer assay purchased from Qiagen |
| CTNNB | CACAAGCAGAGTGCTGAAGGTG | GATTCCTGAGAGTCCAAAGACAG |
| HPRT | Quantitect primer assay purchased from Qiagen |
| PXN | CTGATGGCTTCGCTGTCGGATT | GCTTGTTCAGGTCAGACTGCAG |
| STAT3 | CTTTGAGACCGAGGTGTATCACC | GGTCAGCATGTTGTACCACAGG |

**Supplementary Table S3.** Alphabetical list of primary and secondary antibodies with respective product details and dilution conditions.

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| --- |
| **PRIMARY ANTIBODIES** |
| **Protein target** | **Host** | **Catalog Number** | **Company** | **Dilution buffer** | **Dilution factor** |
| β-Actin | Rabbit  | ab119716 | Abcam | 5% milk in TBST | 1:4000 |
| CCND1 | Rabbit | ab134175 | Abcam | 5% milk in TBST | 1:3000 |
| CREB | Mouse | 86B10 | Cell Signaling Technology | 5% milk in TBST | 1:1000 |
| pERK | Rabbit | PA5-37823 | ThermoFisher | 5% milk in TBST  | 1:500 |
| GAPDH | Mouse | CB1001 | Millipore | 5% milk in TBST | 1:3000 |
| p53 | Mouse | 1C12 | Cell Signaling Technology | 5% milk in TBST | 1:1000 |
| pSRC(Y419) | Rabbit | ab185617 | Abcam | 4% BSA in TBST | 1:5000 |
| **SECONDARY ANTIBODIES** |
| **Species reactivity** | **Class** | **Catalog number** | **Company** | **Dilution buffer** | **Dilution factor** |
| Mouse | Horse | 7076s | Cell Signaling Technology | 5% milk in TBST | 1:5000 |
| Rabbit | Goat | 7074s | Cell Signaling Technology | 5% milk in TBST | 1:5000 |

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**Supplementary Figure S1.** Alignment of multiple SRC protein sequences.SRC protein sequences were downloaded from Ensembl (GRCh37/hg19) for human (ENST00000373578.2), cow (ENSBTAT00000011767.3), mouse (ENSMUST00000029175.7), chicken (ENSGALT00000006127.2), cat (ENSFCAT00000006993.2) and zebra fish (ENSDART00000102843.4) and respectively aligned. Sequence alignment indicates an overall strong conservation of SRC across the species. The amino acid residue affected by the *SRCV177M* variant is colored in red.