**Supplementary Methods and Tables:**

**Supplemental Methods:**

**MSKCC Data Analysis:**

The MSKCC dataset was downloaded from the cBioPortal for Cancer  
Genomics (Cerami et al., 2012 & Gao et al., 2013) and all analysis was  
done in R v3.6.2.  Differences in survival were visualized with Kaplan-  
Meier curves and analyzed with multivariate Cox proportional hazards  
models accounting for race and genetic mutation.  Fisher tests were  
used to find genes that showed statistical difference in mutational  
frequency by race.

We examined the association of age(<50, >50), sex(M,F), race(black, white), cancer stage(1-4), molecular subtype(MSS, MSI), and colon site(proximal, distal) with survival outcome using a multivariate Cox proportional hazards model. After checking the Shoenfield residuals for proportional hazards, we stratified the model by molecular subtype and computed coefficients on the remaining variables. Separate comparisons between Kaplan-Meier curves were made with a Logrank test.

**Supplemental Table 1:** Range of ancestry admixture % for each population group ( EUR= European, AFR = African, EAS = East Asian, SAS= South Asian, AMR= Admixed American).

|  |  |
| --- | --- |
| **Ancestry** | **Median (range) of ancestry %** |
| EUR | 96 (16-100) |
| AFR | 83 (35-100) |
| EAS | 97 (50-100) |
| SAS | 82 (37-100) |
| AMR | 32 (0-100) |

**Supplementary Table 2: Frequency of POLE/D1 Mutations by Ancestry**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **AFR (n = 5,301)** | **EUR (n = 33,770)** | **Q value** |
| **Hypermutated (%)** | 222 (4.2) | 1,884 (5.6) | Q < 0.0001 |
| MSI-H | 193 (3.9) | 1,742 (5.5) | Q < 0.0001 |
| POLE/D | 29 (0.54) | 142 (0.42) | 0.22 |
| **MSS non-POLE/D1 (%)** | 4,727 (89) | 29,544 (87) | 0.0004 |
| TMB ≥ 10 | 179 (3.3) | 915 (2.7) | 0.007 |
| TMB < 10 | 4,548 (86) | 28,629 (85) | 0.06 |

MSI was available for 4,949 AFR and 31,418 EUR patients.

**Supplementary Table 3: Gene alteration frequencies between AFR and EUR MSS non-POLE/D1, TMB < 10 mut/Mb CRC patients.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Stat** | **AFR N (%)** | **EUR N (%)** | **Q value** | **OR** | **95% CI** |
| **KRAS** | 2,708 (60) | 14,244 (50) | Q < 0.0001 | 1.49 | 1.39-1.58 |
| **BRAF** | 213 (4.7) | 2,442 (8.5) | Q < 0.0001 | 0.53 | 0.46-0.61 |
| **CHEK2** | 14 (0.31) | 461 (1.6) | Q < 0.0001 | 0.19 | 0.11-0.32 |
| **APC** | 3,819 (84) | 22,952 (80) | Q < 0.0001 | 1.30 | 1.19-1.41 |
| **MUTYH** | 36 (0.79) | 584 (2.0) | Q < 0.0001 | 0.38 | 0.27-0.54 |
| **PIK3CA** | 930 (20) | 4,812 (17) | Q < 0.0001 | 1.27 | 1.18-1.38 |
| **FAM123B** | 366 (8.0) | 1,663 (5.8) | Q < 0.0001 | 1.42 | 1.26-1.60 |
| **PRDM1** | 29 (0.64) | 44 (0.15) | Q < 0.0001 | 4.17 | 2.61-6.67 |
| **GATA6** | 12 (0.26) | 237 (0.83) | 0.0001 | 0.32 | 0.18-0.57 |
| **MLL3** | 62 (3.9) | 228 (2.1) | 0.0009 | 1.87 | 1.41-2.49 |
| **PREX2** | 25 (1.6) | 61 (0.57) | 0.0009 | 2.80 | 1.75-4.47 |
| **NF2** | 21 (0.46) | 40 (0.14) | 0.0006 | 3.32 | 1.95-5.63 |
| **EP300** | 66 (1.5) | 239 (0.83) | 0.002 | 1.75 | 1.33-2.30 |
| **MST1R** | 11 (0.37) | 13 (0.07) | 0.003 | 5.13 | 2.30-11.46 |
| **CHD4** | 30 (1.9) | 90 (0.84) | 0.004 | 2.28 | 1.50-3.46 |
| **ABL1** | 14 (0.31) | 26 (0.09) | 0.008 | 3.40 | 1.77-6.51 |
| **FH** | 19 (0.42) | 46 (0.16) | 0.01 | 2.61 | 1.53-4.45 |
| **RNF43** | 95 (2.1) | 824 (2.9) | 0.03 | 0.72 | 0.58-0.89 |
| **MAP2K1** | 72 (1.6) | 309 (1.1) | 0.05 | 1.47 | 1.14-1.91 |
| **RAD21** | 79 (2.7) | 668 (3.7) | 0.04 | 0.71 | 0.56-0.90 |
| **FLT1** | 12 (0.26) | 24 (0.08) | 0.03 | 3.15 | 1.58-6.31 |

*CHD4*, *MLL3*, *MST1R*, *PREX2*, and *RAD21* were only baited for on a subset of samples. *CHD4*, *MLL3*, and *PREX2* frequencies are out of a total of 1,576 AFR and 10,660 EUR samples. *MST1R* and *RAD21* frequencies are out of a total of 2,972 AFR and 17,969 EUR samples. The remaining genes are out of a total of 4,548 AFR and 28,639 EUR samples.

**Supplementary Table 4:**

**Genomic Alterations in Early Age CRC in AFR and EUR**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **AFR CRC** | **EUR CRC** | **All CRC** | **Q value** |
|  | **< 50 years old (%)** | **<50 years old (%)** | **< 50 years old (%)** | **(AFR vs EUR)** |
| **All samples** | | | | |
| N | 1,266 | 6,778 | 8,044 |  |
| Median age | 43 | 44 | 44 | 0.10 |
| **Hypermutated** | 70 (5.5) | 311 (4.6) | 381 (4.7) | 0.15 |
| MSI-H | 50 (3.9) | 257 (3.8) | 307 (3.8) | 0.81 |
| POLE/POLD1 | 20 (1.6) | 54 (0.80) | 74 (0.92) | 0.01 |
| Median TMB (mut/Mb) | 3.5 | 2.6 | 2.6 | 0.02 |
| TMB > 10 mut/Mb | 111 (8.8) | 487 (7.2) | 598 (7.4) | 0.42 |
| **Site of biopsy** |  |  |  |  |
| Colon | 546 (43) | 2,618 (39) | 3,164 (39) | 0.06 |
| Liver | 288 (23) | 1,477 (22) | 1,765 (22) | 1.0 |
| Rectum | 108 (8.5) | 895 (13) | 1,003 (12) | 0.0002 |
| Lung | 55 (4.3) | 415 (6.1) | 470 (5.8) | 0.17 |
| Soft tissue | 42 (3.3) | 147 (2.2) | 189 (2.3) | 0.24 |
| Lymph node | 25 (2.0) | 226 (3.3) | 251 (3.1) | 0.15 |
| Omentum | 23 (1.8) | 133 (2.0) | 156 (1.9) | 1.0 |
| Ovary | 31 (2.4) | 154 (2.3) | 185 (2.3) | 1.0 |
| Small intestine | 25 (2.0) | 70 (1.0) | 95 (1.2) | 0.12 |
| Peritoneum | 23 (1.8) | 96 (1.4) | 119 (1.5) | 0.95 |
| **MSS, POLE/POLD1-negative, TMB<10 samples** | | | | |
| N | 1,063 | 5,669 | 6,732 |  |
| *APC* | 846 (80) | 4,568 (81) | 5,414 (80) | 1.0 |
| *ATM* | 30 (2.8) | 204 (3.6) | 234 (3.5) | 1.0 |
| *BRAF* Class 1 | 18 (1.7) | 239 (4.2) | 257 (3.8) | 0.001 |
| *CTNNB1* | 43 (4.0) | 196 (3.5) | 239 (3.6) | 1.0 |
| *FAM123B* | 53 (5.0) | 183 (3.2) | 236 (3.5) | 0.13 |
| *FGFR1* | 15 (1.4) | 185 (3.3) | 200 (3.0) | 0.02 |
| *KRAS* | 616 (58) | 2,697 (48) | 3,313 (49) | Q < 0.0001 |
| *PIK3CA* | 212 (20) | 860 (15) | 1,072 (16) | 0.007 |
| *PRDM1* | 10 (0.94) | 9 (0.16) | 19 (0.28) | 0.009 |
| *RNF43* | 30 (2.8) | 128 (2.3) | 158 (2.3) | 1.0 |
| *TP53* | 866 (81) | 4,676 (82) | 5,542 (82) | 1.0 |
| MAPK pathway | 710 (67) | 3,344 (59) | 4,054 (60) | 0.0002 |
| WNT pathway | 909 (86) | 4,842 (85) | 5,751 (85) | 1.0 |
| PI3K pathway | 309 (29) | 1,451 (26) | 1,760 (26) | 0.26 |

Patient age was available for 5,296 AFR and 33,733 EUR samples, and 4,545 AFR and 28,601 EUR samples in the MSS, POLE/POLD1-negative, TMB<10 population.

**Supplementary Table 5:**

**Genomic differences Between Young and Average-age CRC by Ancestry**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Gene** | **AFR < 50 years** | **AFR ≥ 50 years** | **Q (AFR <50 vs ≥50)** | **OR (AFR <50 vs ≥50)** | **EUR < 50 years** | **EUR ≥ 50 years** | **Q (EUR <50 vs ≥50)** | **OR (EUR <50 vs ≥50)** |
| Patients (n) | 1,063 | 3,482 | - | - | 5,669 | 22,932 | - | - |
| ***APC*** | 846 (80) | 2,970 (85) | 0.002 | 0.67 | 4,568 (81) | 18,360 (80) | 0.94 | 1.03 |
| ***ATM*** | 30 (2.8) | 136 (3.9) | 1.0 | 0.71 | 204 (3.6) | 999 (4.4) | 0.12 | 0.82 |
| ***BRAF* Class 1** | 18 (1.7) | 74 (2.1) | 1.0 | 0.79 | 239 (4.2) | 1,469 (6.4) | Q < 0.0001 | 0.64 |
| ***CTNNB1*** | 43 (4.0) | 133 (3.8) | 1.0 | 1.06 | 196 (3.5) | 774 (3.4) | 1.0 | 1.03 |
| ***FAM123B*** | 53 (5.0) | 313 (9.0) | 0.002 | 0.53 | 183 (3.2) | 1,479 (6.4) | Q < 0.0001 | 0.48 |
| ***FGFR1*** | 15 (1.4) | 65 (1.9) | 1.0 | 0.75 | 185 (3.3) | 467 (2.0) | Q < 0.0001 | 1.62 |
| ***KRAS*** | 616 (58) | 2,091 (60) | 1.0 | 0.92 | 2,697 (48) | 11,536 (50) | 0.004 | 0.90 |
| ***MYC*** | 88 (8.3) | 244 (7.0) | 1.0 | 1.20 | 533 (9.4) | 1,684 (7.3) | Q < 0.0001 | 1.31 |
| ***PIK3CA*** | 212 (20) | 717 (21) | 1.0 | 0.96 | 860 (15) | 3,948 (17) | 0.004 | 0.86 |
| ***RNF43*** | 30 (2.8) | 65 (1.9) | 0.79 | 1.52 | 128 (2.3) | 694 (3.0) | 0.03 | 0.74 |
| ***TP53*** | 866 (81) | 2,615 (75) | 0.002 | 1.46 | 4,676 (82) | 17,711 (77) | Q < 0.0001 | 1.39 |
| **MAPK pathway** | 710 (67) | 2,454 (70) | 0.51 | 0.84 | 3,344 (59) | 14,827 (65) | Q < 0.0001 | 0.79 |
| **WNT pathway** | 909 (86) | 3,114 (89) | 0.03 | 0.70 | 4,842 (85) | 19,533 (85) | 1.0 | 1.02 |
| **PI3K pathway** | 309 (29) | 1,121 (32) | 0.77 | 0.86 | 1,451 (26) | 6,558 (29) | 0.0002 | 0.86 |

**Supplementary Table 6: Demographic/Clinical Data of CRC Adenocarcinomas in African Americans and Whites in the MSKCC Data Set.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **MSKCC Dataset** | | |
|  | **African Americans (**n=76) | **Whites**  (n=970) | **P value** |
| **Sex**  **(M: F)** | 39: 37 | 523:447 | 0.72 |
| **Mean Age**  **(years)** | 53 | 56 | 0.04\* |
| **Mean Survival (months)** | 29 | 39 | 0.002\* |
| **MSS (%)** | 71 (93) | 885 (91) | 0.67 |
| **MSI-H (%)** | 5 (7) | 85 (9) | 0.67 |
| **Age under 50 years old (n;%)** | 26 (34) | 313 (32) | 0.70 |
| **Stage 1 (n;%)** | 0 (0) | 43 (4) | 0.07 |
| **Stage II (n;%)** | 8 (11) | 109 (11) | 1 |
| **Stage III (n;%)** | 20 (26) | 228 (24) | 0.57 |
| **Stage IV (n;%)** | 48 (63) | 590 (61) | 0.72 |
| **Proximal Colon (n;%)** | 43 (58) | 650 (67) | 0.08 |
| **Distal Colon (n;%)** | 32 (42) | 309 (33) | 0.08 |

\*Statistically different

**Supplementary Table 7: MSKCC Dataset: Frequency of gene mutations in Blacks and Whites with MSS CRC.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Gene** | **Blacks** n=71 | **Whites** n=885 | **p value** | **Odds Ratio** |
| *APC* (%) | 57 (80) | 672 (76) | 0.47 | 0.78 |
| *KRAS* (%) | 37 (52) | 366 (41) | 0.08 | 0.65 |
| *BRAF* (%) | 4 (5.6) | 112 (13) | 0.09 | 2.4 |

\*p value= Fishers exact test

**Supplementary Table 8: Versions of genomic sequencing and genes included** Foundation One Version 1:

Entire coding sequence for the detection of base substitutions, insertions/deletions, and copy number alterations

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| *ABL1* | *BCORL1* | *CDKN2B* | *ERBB3* | *FGFR3* | *IL7R* | *MDM4* | *NOTCH1* | *PTEN* | *SRC* |
| *AKT1* | *BLM* | *CDKN2C* | *ERBB4* | *FGFR4* | *INHBA* | *MED12* | *NOTCH2* | *PTPN11* | *STAG2* |
| *AKT2* | *BRAF* | *CEBPA* | *ERG* | *FLT1* | *IRF4* | *MEF2B* | *NPM1* | *RAD50* | *STAT4* |
| *AKT3* | *BRCA1* | *CHEK1* | *ESR1* | *FLT3* | *IRS2* | *MEN1* | *NRAS* | *RAD51* | *STK11* |
| *ALK* | *BRCA2* | *CHEK2* | *EZH2* | *FLT4* | *JAK1* | *MET* | *NTRK1* | *RAF1* | *SUFU* |
| *APC* | *BRIP1* | *CIC* | *FAM123B (WTX)* | *FOXL2* | *JAK2* | *MITF* | *NTRK2* | *RARA* | *TET2* |
| *AR* | *BTK* | *CREBBP* | *FAM46C* | *GATA1* | *JAK3* | *MLH1* | *NTRK3* | *RB1* | *TGFBR2* |
| *ARAF* | *CARD11* | *CRKL* | *FANCA* | *GATA2* | *JUN* | *MLL* | *NUP93* | *RET* | *TNFAIP3* |
| *ARFRP1* | *CBFB* | *CRLF2* | *FANCC* | *GATA3* | *KAT6A (MYST3)* | *MLL2* | *PAK3* | *RICTOR* | *TNFRSF14* |
| *ARID1A* | *CBL* | *CSF1R* | *FANCD2* | *GID4 (C17orf39)* | *KDM5A* | *MPL* | *PALB2* | *RNF43* | *TOP1* |
| *ARID2* | *CCND1* | *CTCF* | *FANCE* | *GNA11* | *KDM5C* | *MRE11A* | *PAX5* | *RPTOR* | *TP53* |
| *ASXL1* | *CCND2* | *CTNNA1* | *FANCF* | *GNA13* | *KDM6A* | *MSH2* | *PBRM1* | *RUNX1* | *TSC1* |
| *ATM* | *CCND3* | *CTNNB1* | *FANCG* | *GNAQ* | *KDR* | *MSH6* | *PDGFRA* | *SETD2* | *TSC2* |
| *ATR* | *CCNE1* | *DAXX* | *FANCL* | *GNAS* | *KEAP1* | *MTOR* | *PDGFRB* | *SF3B1* | *TSHR* |
| *ATRX* | *CD79A* | *DDR2* | *FBXW7* | *GPR124* | *KIT* | *MUTYH* | *PDK1* | *SMAD2* | *VHL* |
| *AURKA* | *CD79B* | *DNMT3A* | *FGF10* | *GRIN2A* | *KLHL6* | *MYC* | *PIK3CA* | *SMAD4* | *WISP3* |
| *AURKB* | *CDC73* | *DOT1L* | *FGF14* | *GSK3B* | *KRAS* | *MYCL1* | *PIK3CG* | *SMARCA4* | *WT1* |
| *AXL* | *CDH1* | *EGFR* | *FGF19* | *HGF* | *LRP1B* | *MYCN* | *PIK3R1* | *SMARCB1* | *XPO1* |
| *BAP1* | *CDK12* | *EMSY (C11orf30)* | *FGF23* | *HRAS* | *MAP2K1* | *MYD88* | *PIK3R2* | *SMO* | *ZNF217* |
| *BARD1* | *CDK4* | *EP300* | *FGF3* | *IDH1* | *MAP2K2* | *NF1* | *PPP2R1A* | *SOCS1* | *ZNF703* |
| *BCL2* | *CDK6* | *EPHA3* | *FGF4* | *IDH2* | *MAP2K4* | *NF2* | *PRDM1* | *SOX10* |  |
| *BCL2L2* | *CDK8* | *EPHA5* | *FGF6* | *IGF1R* | *MAP3K1* | *NFE2L2* | *PRKAR1A* | *SOX2* |  |
| *BCL6* | *CDKN1B* | *EPHB1* | *FGFR1* | *IKBKE* | *MCL1* | *NFKBIA* | *PRKDC* | *SPEN* |  |
| *BCOR* | *CDKN2A* | *ERBB2* | *FGFR2* | *IKZF1* | *MDM2* | *NKX2-1* | *PTCH1* | *SPOP* |  |

Select introns for the detection of rearrangements

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| *ALK* | *BCL2* | *BCR* | *BRAF* | *EGFR* | *ETV1* | *ETV4* | *ETV5* | *ETV6* | *EWSR1* |
| *MLL* | *MYC* | *NTRK1* | *PDGFRA* | *RAF1* | *RARA* | *RET* | *ROS1* | *TMPRSS2* |  |

**Supplementary Table 9:** **Versions of genomic sequencing and genes included**

**(**Foundation One Version 2)

Entire coding sequence for the detection of base substitutions, insertions/deletions, and copy number alterations

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| *ABL1* | *ABL2* | *ACVR1B* | *AKT1* | *AKT2* | *AKT3* | *ALK* | *AMER1 (FAM123B)* | *APC* | *AR* |
| *ARAF* | *ARFRP1* | *ARID1A* | *ARID1B* | *ARID2* | *ASXL1* | *ATM* | *ATR* | *ATRX* | *AURKA* |
| *AURKB* | *AXIN1* | *AXL* | *BAP1* | *BARD1* | *BCL2* | *BCL2L1* | *BCL2L2* | *BCL6* | *BCOR* |
| *BCORL1* | *BLM* | *BRAF* | *BRCA1* | *BRCA2* | *BRD4* | *BRIP1* | *BTG1* | *BTK* | *C11orf30 (EMSY)* |
| *CARD11* | *CBFB* | *CBL* | *CCND1* | *CCND2* | *CCND3* | *CCNE1* | *CD274* | *CD79A* | *CD79B* |
| *CDC73* | *CDH1* | *CDK12* | *CDK4* | *CDK6* | *CDK8* | *CDKN1A* | *CDKN1B* | *CDKN2A* | *CDKN2B* |
| *CDKN2C* | *CEBPA* | *CHD2* | *CHD4* | *CHEK1* | *CHEK2* | *CIC* | *CREBBP* | *CRKL* | *CRLF2* |
| *CSF1R* | *CTCF* | *CTNNA1* | *CTNNB1* | *CUL3* | *CYLD* | *DAXX* | *DDR2* | *DICER1* | *DNMT3A* |
| *DOT1L* | *EGFR* | *EP300* | *EPHA3* | *EPHA5* | *EPHA7* | *EPHB1* | *ERBB2* | *ERBB3* | *ERBB4* |
| *ERG* | *ERRFI1* | *ESR1* | *EPHA3* | *FAM46C* | *FANCA* | *FANCC* | *FANCD2* | *FANCE* | *FANCF* |
| *FANCG* | *FANCL* | *FAS* | *FAT1* | *FBXW7* | *FGF10* | *FGF14* | *FGF19* | *FGF23* | *FGF3* |
| *FGF4* | *FGF6* | *FGFR1* | *FGFR2* | *FGFR3* | *FGFR4* | *FH* | *FLCN* | *FLT1* | *FLT3* |
| *FLT4* | *FOXL2* | *FOXP1* | *FRS2* | *FUBP1* | *GABRA6* | *GATA1* | *GATA2* | *GATA3* | *GATA4* |
| *GATA6* | *GID4 (C17orf39)* | *GLI1* | *GNA11* | *GNA13* | *GNAQ* | *GNAS* | *GPR124* | *GRIN2A* | *GRM3* |
| *GSK3B* | *H3F3A* | *HGF* | *HNF1A* | *HRAS* | *HSD3B1* | *HSP90AA1* | *IDH1* | *IDH2* | *IGF1R* |
| *IGF2* | *IKBKE* | *IKZF1* | *IL7R* | *INHBA* | *INPP4B* | *IRF2* | *IRF4* | *IRS2* | *JAK1* |
| *JAK2* | *JAK3* | *JUN* | *KAT6A (MYST3)* | *KDM5A* | *KDM5C* | *KDM6A* | *KDR* | *KEAP1* | *KEL* |
| *KIT* | *KLHL6* | *KMT2A (MLL)* | *KMT2C (MLL3)* | *KMT2D (MLL2)* | *KRAS* | *LMO1* | *LRP1B* | *LYN* | *LZTR1* |
| *MAGI2* | *MAP2K1* | *MAP2K2* | *MAP2K4* | *MAP3K1* | *MCL1* | *MDM2* | *MDM4* | *MED12* | *MEF2B* |
| *MEN1* | *MET* | *MITF* | *MLH1* | *MPL* | *MRE11A* | *MSH2* | *MSH6* | *MTOR* | *MUTYH* |
| *MYC* | *MYCL (MYCL1)* | *MYCN* | *MYD88* | *NF1* | *NF2* | *NFE2L2* | *NFKBIA* | *NKX2-1* | *NOTCH1* |
| *NOTCH2* | *NOTCH3* | *NPM1* | *NRAS* | *NSD1* | *NTRK1* | *NTRK2* | *NTRK3* | *NUP93* | *PAK3* |
| *PALB2* | *PARK2* | *PAX5* | *PBRM1* | *PDCD1LG2* | *PDGFRA* | *PDGFRB* | *PDK1* | *PIK3C2B* | *PIK3CA* |
| *PIK3CB* | *PIK3CG* | *PIK3R1* | *PIK3R2* | *PLCG2* | *PMS2* | *POLD1* | *POLE* | *PPP2R1A* | *PRDM1* |
| *PREX2* | *PRKAR1A* | *PRKCI* | *PRKDC* | *PRSS8* | *PTCH1* | *PTEN* | *PTPN11* | *QKI* | *RAC1* |
| *RAD50* | *RAD51* | *RAF1* | *RANBP2* | *RARA* | *RB1* | *RBM10* | *RET* | *RICTOR* | *RNF43* |
| *ROS1* | *RPTOR* | *RUNX1* | *RUNX1T1* | *SDHA* | *SDHB* | *SDHC* | *SDHD* | *SETD2* | *SF3B1* |
| *SLIT2* | *SMAD2* | *SMAD3* | *SMAD4* | *SMARCA4* | *SMARCB1* | *SMO* | *SNCAIP* | *SOCS1* | *SOX10* |
| *SOX2* | *SOX9* | *SPEN* | *SPOP* | *SPTA1* | *SRC* | *STAG2* | *STAT3* | *STAT4* | *STK11* |
| *SUFU* | *SYK* | *TAF1* | *TBX3* | *TERC* | *TERT (promoter only)* | *TET2* | *TGFBR2* | *TNFAIP3* | *TNFRSF14* |
| *TOP1* | *TOP2A* | *TP53* | *TSC1* | *TSC2* | *TSHR* | *U2AF1* | *VEGFA* | *VHL* | *WISP3* |
| *WT1* | *XPO1* | *ZBTB2* | *ZNF217* | *ZNF703* |  |  |  |  |  |

Select introns for the detection of rearrangements

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| *ALK* | *BCL2* | *BCR* | *BRAF* | *BRCA1* | *BRCA2* | *BRD4* | *EGFR* | *ETV1* | *ETV4* |
| *ETV5* | *ETV6* | *FGFR1* | *FGFR2* | *FGFR3* | *KIT* | *MSH2* | *MYB* | *MYC* | *NOTCH2* |
| *NTRK1* | *NTRK2* | *PDGFRA* | *RAF1* | *RARA* | *RET* | *ROS1* | *TMPRSS2* |  |  |

**Supplementary Table 10: Versions of genomic sequencing and genes included.** Foundation One CDx (Version 3)

Entire coding sequence for the detection of base substitutions, insertions/deletions, and copy number alterations

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| *ABL1* | *ACVR1B* | *AKT1* | *AKT2* | *AKT3* | *ALK* | *ALOX12B* | *AMER1 (FAM123B)* | *APC* |
| *AR* | *ARAF* | *ARFRP1* | *ARID1A* | *ASXL1* | *ATM* | *ATR* | *ATRX* | *AURKA* |
| *AURKB* | *AXIN1* | *AXL* | *BAP1* | *BARD1* | *BCL2* | *BCL2L1* | *BCL2L2* | *BCL6* |
| *BCOR* | *BCORL1* | *BRAF* | *BRCA1* | *BRCA2* | *BRD4* | *BRIP1* | *BTG1* | *BTG2* |
| *BTK* | *C11orf30 (EMSY)* | *C17orf39 (GID4)* | *CALR* | *CARD11* | *CASP8* | *CBFB* | *CBL* | *CCND1* |
| *CCND2* | *CCND3* | *CCNE1* | *CD22* | *CD274 (PD-L1)* | *CD70* | *CD79A* | *CD79B* | *CDC73* |
| *CDH1* | *CDK12* | *CDK4* | *CDK6* | *CDK8* | *CDKN1A* | *CDKN1B* | *CDKN2A* | *CDKN2B* |
| *CDKN2C* | *CEBPA* | *CHEK1* | *CHEK2* | *CIC* | *CREBBP* | *CRKL* | *CSF1R* | *CSF3R* |
| *CTCF* | *CTNNA1* | *CTNNB1* | *CUL3* | *CUL4A* | *CXCR4* | *CYP17A1* | *DAXX* | *DDR1* |
| *DDR2* | *DIS3* | *DNMT3A* | *DOT1L* | *EED* | *EGFR* | *EP300* | *EPHA3* | *EPHB1* |
| *EPHB4* | *ERBB2* | *ERBB3* | *ERBB4* | *ERCC4* | *ERG* | *ERRFI1* | *ESR1* | *EZH2* |
| *FAM46C* | *FANCA* | *FANCC* | *FANCG* | *FANCL* | *FAS* | *FBXW7* | *FGF10* | *FGF12* |
| *FGF14* | *FGF19* | *FGF23* | *FGF3* | *FGF4* | *FGF6* | *FGFR1* | *FGFR2* | *FGFR3* |
| *FGFR4* | *FH* | *FLCN* | *FLT1* | *FLT3* | *FOXL2* | *FUBP1* | *GABRA6* | *GATA3* |
| *GATA4* | *GATA6* | *GNA11* | *GNA13* | *GNAQ* | *GNAS* | *GRM3* | *GSK3B* | *H3F3A* |
| *HDAC1* | *HGF* | *HNF1A* | *HRAS* | *HSD3B1* | *ID3* | *IDH1* | *IDH2* | *IGF1R* |
| *IKBKE* | *IKZF1* | *INPP4B* | *IRF2* | *IRF4* | *IRS2* | *JAK1* | *JAK2* | *JAK3* |
| *JUN* | *KDM5A* | *KDM5C* | *KDM6A* | *KDR* | *KEAP1* | *KEL* | *KIT* | *KLHL6* |
| *KMT2A (MLL)* | *KMT2D (MLL2)* | *KRAS* | *LTK* | *LYN* | *MAF* | *MAP2K1 (MEK1)* | *MAP2K2 (MEK2)* | *MAP2K4* |
| *MAP3K1* | *MAP3K13* | *MAPK1* | *MCL1* | *MDM2* | *MDM4* | *MED12* | *MEF2B* | *MEN1* |
| *MERTK* | *MET* | *MITF* | *MKNK1* | *MLH1* | *MPL* | *MRE11A* | *MSH2* | *MSH3* |
| *MSH6* | *MST1R* | *MTAP* | *MTOR* | *MUTYH* | *MYC* | *MYCL (MYCL1)* | *MYCN* | *MYD88* |
| *NBN* | *NF1* | *NF2* | *NFE2L2* | *NFKBIA* | *NKX2-1* | *NOTCH1* | *NOTCH2* | *NOTCH3* |
| *NPM1* | *NRAS* | *NSD3 (WHSC1L1)* | *NT5C2* | *NTRK1* | *NTRK2* | *NTRK3* | *P2RY8* | *PALB2* |
| *PARK2* | *PARP1* | *PARP2* | *PARP3* | *PAX5* | *PBRM1* | *PDCD1 (PD-1)* | *PDCD1LG2 (PD-L2)* | *PDGFRA* |
| *PDGFRB* | *PDK1* | *PIK3C2B* | *PIK3C2G* | *PIK3CA* | *PIK3CB* | *PIK3R1* | *PIM1* | *PMS2* |
| *POLD1* | *POLE* | *PPARG* | *PPP2R1A* | *PPP2R2A* | *PRDM1* | *PRKAR1A* | *PRKCI* | *PTCH1* |
| *PTEN* | *PTPN11* | *PTPRO* | *QKI* | *RAC1* | *RAD21* | *RAD51* | *RAD51B* | *RAD51C* |
| *RAD51D* | *RAD52* | *RAD54L* | *RAF1* | *RARA* | *RB1* | *RBM10* | *REL* | *RET* |
| *RICTOR* | *RNF43* | *ROS1* | *RPTOR* | *SDHA* | *SDHB* | *SDHC* | *SDHD* | *SETD2* |
| *SF3B1* | *SGK1* | *SMAD2* | *SMAD4* | *SMARCA4* | *SMARCB1* | *SMO* | *SNCAIP* | *SOCS1* |
| *SOX2* | *SOX9* | *SPEN* | *SPOP* | *SRC* | *STAG2* | *STAT3* | *STK11* | *SUFU* |
| *SYK* | *TBX3* | *TEK* | *TET2* | *TGFBR2* | *TIPARP* | *TNFAIP3* | *TNFRSF14* | *TP53* |
| *TSC1* | *TSC2* | *TYRO3* | *U2AF1* | *VEGFA* | *VHL* | *WHSC1* | *WT1* | *XPO1* |
| *XRCC2* | *ZNF217* | *ZNF703* |  |  |  |  |  |  |

Select introns for the detection of rearrangements

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| *ALK* | *BCL2* | *BCR* | *BRAF* | *BRCA1* | *BRCA2* | *CD74* | *EGFR* | *ETV4* |
| *ETV5* | *ETV6* | *EWSR1* | *EZR* | *FGFR1* | *FGFR2* | *FGFR3* | *KIT* | *KMT2A (MLL)* |
| *MSH2* | *MYB* | *MYC* | *NOTCH2* | *NTRK1* | *NTRK2* | *NUTM1* | *PDGFRA* | *RAF1* |
| *RARA* | *RET* | *ROS1* | *RSPO2* | *SDC4* | *SLC34A2* | *TERC (NCRNA)* | *TERT (promotor)* | *TMPRSS2* |