

Supplemental Online Content

Horton C, Hoang L, Zimmermann H, et al. Diagnostic outcomes of concurrent DNA and RNA sequencing in individuals undergoing hereditary cancer testing. *JAMA Oncol*. Published online November 4, 2023. doi:10.1001/jamaoncol.2023.5586

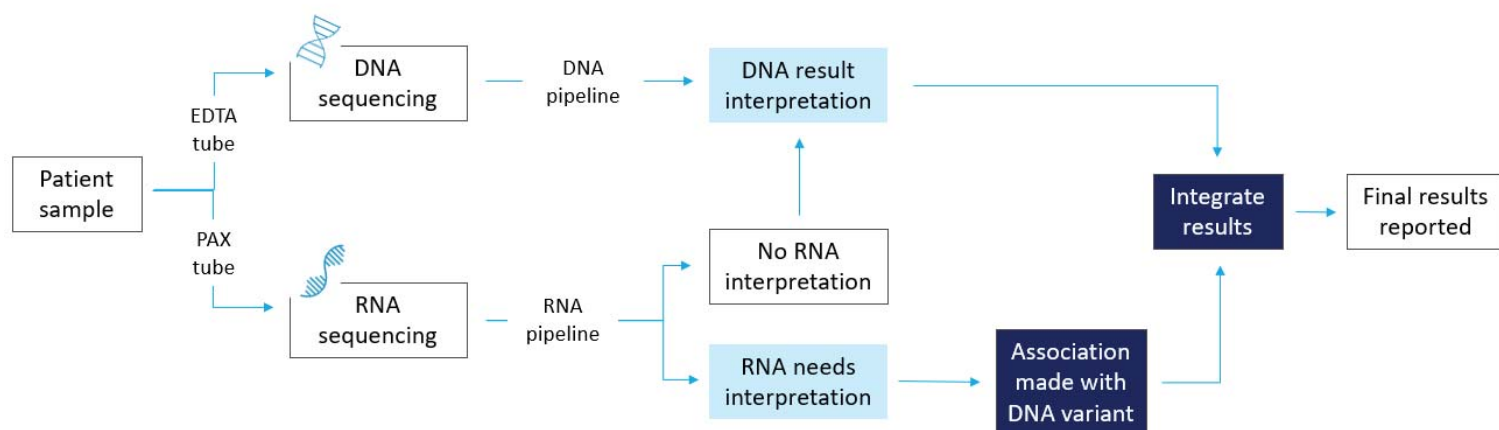
eFigure. Paired DNA and RNA Sequencing and Interpretation Workflow

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This supplemental material has been provided by the authors to give readers additional information about their work.

eFigure. Paired DNA and RNA Sequencing and Interpretation Workflow



eTable 1. Test Panels and Genes Included in the Study Group

Panel name	Genes tested	Number of Tests‡
BrainTumorNext +RNAinsight	<i>AIP, ALK, APC*, CDKN1B, CDKN2A, DICER1, MEN1, MLH1*, MSH2*, MSH6*, NBN, NF1*, NF2, PHOX2B, PMS2*, POT1, PRKAR1A, PTCH1, PTEN*, SMARCA4, SMARCB1, SMARCE1, SUFU, TP53*, TSC1, TSC2, VHL</i>	14
BreastNext +RNAinsight	<i>ATM*, BARD1, BRCA1*, BRCA2*, BRIP1*, CDH1*, CHEK2*, MRE11A, MUTYH*, NBN, NF1*, PALB2*, PTEN*, RAD50, RAD51C*, RAD51D*, TP53*</i>	1378
CancerNext +RNAinsight	<i>APC*, ATM*, BARD1, BRCA1*, BRCA2*, BRIP1*, BMPR1A, CDH1*, CDK4, CDKN2A, CHEK2*, DICER1, EPCAM, GREM1, HOXB13, MLH1*, MRE11A, MSH2*, MSH6*, MUTYH*, NBN, NF1*, PALB2*, PMS2*, POLD1, POLE, PTEN*, RAD50, RAD51C*, RAD51D*, SMAD4, SMARCA4, STK11, TP53*</i>	14847
CancerNext Expanded +RNAinsight	<i>AIP, ALK, APC*, ATM*, BAP1, BARD1, BLM, BMPR1A, BRCA1*, BRCA2*, BRIP1*, CDH1*, CDK4, CDKN1B, CDKN2A, CHEK2*, DICER1, EPCAM, FANCC, FH, FLCN, GALNT12, GREM1, HOXB13, MAX, MEN1, MET, MTF, MLH1*, MRE11A, MSH2*, MSH6*, MUTYH*, NBN, NF1*, NF2, PALB2*, PHOX2B, PMS2*, POLD1, POLE, POT1, PRKAR1A, PTCH1, PTEN*, RAD50, RAD51C*, RAD51D*, RB1, RET, SDHA, SDHAF2, SDHB, SDHC, SDHD, SMAD4, SMARCA4, SMARCB1, SMARCE1, STK11, SUFU, TMEM127, TP53*, TSC1, TSC2, VHL, XRCC2</i>	7717
ColoNext +RNAinsight	<i>APC*, BMPR1A, CDH1*, CHEK2*, EPCAM, GREM1, MLH1*, MSH2*, MSH6*, MUTYH*, PMS2*, POLD1, POLE, PTEN*, SMAD4, STK11, TP53*</i>	353
GYNPlus +RNAinsight	<i>BRCA1*, BRCA2*, BRIP1*, EPCAM, MLH1*, MSH2*, MSH6*, PALB2*, PMS2*, PTEN*, RAD51C*, RAD51D*, TP53*</i>	84
CustomNext +RNAinsight†	any number of the following genes: <i>AIP, ALK, APC*, ATM*, AXIN2, BAP1, BARD1, BLM, BMPR1A, BRCA1*, BRCA2*, BRIP1*, CASR, CDC73, CDH1*, CDK4, CDKN1B, CDKN2A, CFTR, CHEK2*, CPA1, CTNNA1, CTSC, DICER1, EGFR, EPCAM, FANCC, FH, FLCN, GALNT12, GREM1, HOXB13, KIT, MAX, MEN1, MET, MTF, MLH1*, MRE11A, MSH2*, MSH3, MSH6*, MUTYH*, NBN, NF1*, NF2, NTHL1, PALB2*, PDGFRA, PHOX2B, PMS2*, POLD1, POLE, POT1, PRKAR1A, PRSS1, PTCH1, PTEN*, RAD50, RAD51C*, RAD51D*, RB1, RET, SDHA, SDHAF2, SDHB, SDHC, SDHD, SMAD4, SMARCA4, SMARCB1, SMARCE1, SPINK1, STK11, SUFU, TMEM127, TP53*, TSC1, TSC2, VHL, XRCC2</i>	16085
MelanomaNext +RNAinsight	<i>BAP1, BRCA2*, CDK4, CDKN2A, MTF, PTEN*, RB1, TP53*</i>	25
OvaNext +RNAinsight	<i>ATM*, BARD1, BRCA1*, BRCA2*, BRIP1*, CDH1*, CHEK2*, DICER1, EPCAM, MLH1*, MRE11A, MSH2*, MSH6*, MUTYH*, NBN, NF1*, PALB2*, PMS2*, PTEN*, RAD50, RAD51C*, RAD51D*, SMARCA4, STK11, TP53*</i>	2548
PancNext +RNAinsight	<i>APC*, ATM*, BRCA1*, BRCA2*, CDKN2A, EPCAM, MLH1*, MSH2*, MSH6*, PALB2*, PMS2*, STK11, TP53*</i>	254
PGLNext +RNAinsight	<i>FH, MAX, MEN1, NF1*, RET, SDHA, SDHAF2, SDHB, SDHC, SDHD, TMEM127, VHL</i>	38
ProstateNext +RNAinsight	<i>ATM*, BRCA1*, BRCA2*, CHEK2*, EPCAM, HOXB13, MLH1*, MSH2*, MSH6*, NBN, PALB2*, PMS2*, RAD51D*, TP53*</i>	164
RenalNext +RNAinsight	<i>BAP1, EPCAM, FH, FLCN, MET, MTF, MLH1*, MSH2*, MSH6*, PMS2*, PTEN*, SDHA, SDHB, SDHC, SDHD, TP53, TSC1, TSC2, VHL</i>	92
Cases with all 18 RNA Covered Genes Ordered		35145

‡ 74 individuals had >1 test ordered

* RNA covered gene

† Orders consist of 1-81 genes (mean=52; median=55)

eTable 2. Reference Sequences for RNA Covered Genes

GENE	Transcript RefSeq
<i>APC</i>	NM_000038.6
<i>ATM</i>	NM_000051.3
<i>BRCA1</i>	NM_007294.3
<i>BRCA2</i>	NM_000059.3
<i>BRIP1</i>	NM_032043.2
<i>CDH1</i>	NM_004360.5
<i>CHEK2</i>	NM_007194.4
<i>MLH1</i>	NM_000249.3
<i>MSH2</i>	NM_000251.2
<i>MSH6</i>	NM_000179.2
<i>MUTYH</i>	NM_001128425.1
<i>NF1</i>	NM_000267.3
<i>PALB2</i>	NM_024675.3
<i>PMS2</i>	NM_000535.7
<i>PTEN</i>	NM_000314.7
<i>RAD51C</i>	NM_058216.9
<i>RAD51D</i>	NM_002878.3
<i>TP53</i>	NM_000546.4