

OncoNext™ 15 Genes

Investigated genes and principal associated tumor types

| Gene | Associated tumor types |
|--------|--|
| AKT1 | Breast, Lung, Colorectal* |
| BRAF | Melanoma*, Colorectal * Lung, Ovarian, Gastric, Glioma, Thyroid, Pancreas, Prostate |
| EGFR | Lung *; Head & Neck, Prostate |
| ERBB2 | Breast, Lung |
| FOXL2 | Ovarian |
| GNA11 | Melanoma |
| GNAQ | Melanoma |
| KIT | Gastric, Melanoma*, Tymic Carcinoma |
| KRAS | Colorectal *, Gastric, Lung *, Ovarian, Thyroid, Endometrial, Pancreas, Prostate |
| MET | Lung *, Colorectal, Gastric |
| NRAS | Colorectal *, Lung, Melanoma, Thyroid |
| PDGFRA | Gastric, Melanoma, |
| PIK3CA | Lung, Breast, Prostate, Colorectal, Ovarian, Head & Neck, Pancreas, Thyroid |
| RET | Lung *, Thyroid |
| TP53 | Lung, Melanoma, Ovarian, Colorectal, Breast; Endometrial, Head & Neck, Kidney, Pancreas, Prostate, Thyroid |

* NCCN Clinical Practice Guidelines in Oncology.

Hotspot mutations detected by OncoNext™ 15 Genes

| REFSEQ | GENE | Exon | Mutation | Nucleotide Changes | Sequencing depth |
|--------------|------------------------------------|--------|------------------------------------|--|------------------|
| NM_005163 | AKT1 | 3 | E17K | c.49 G>A | 340.000 |
| | | | D594E | c.1782T>A | 308.000 |
| | | | D594E | c.1782T>G | 308.000 |
| | | | D594G | c.1781A>G | 308.000 |
| | | | D594H | c.1780G>C | 308.000 |
| | | | D594N | c.1779_1780delTGinsGA | 308.000 |
| | | | D594N | c.1780G>A | 308.000 |
| | | | D594V | c.1781A>T | 308.000 |
| | | | G596R | c.1786G>C | 308.000 |
| | | | K601E | c.1801A>G | 308.000 |
| | | | L597Q | c.1790T>A | 308.000 |
| | | | L597R | c.1790T>G | 308.000 |
| | | | L597S | c.1789_1790delCTinsTC | 308.000 |
| | | | L597V | c.1789C>G | 308.000 |
| | | | V600D | c.1799_1800delTGinsAT | 308.000 |
| | | | V600E | c.1799T>A | 308.000 |
| NM_004333 | BRAF | 15 | V600E | c.1799_1800delTGinsAA | 308.000 |
| | | | V600G | c.1799T>G | 308.000 |
| | | | V600K | c.1798_1799delGTinsAA | 308.000 |
| | | | V600M | c.1798G>A | 308.000 |
| | | | V600R | c.1798_1799delGTinsAG | 308.000 |
| | | | G719A | c.2156G>C | 84.200 |
| | | | G719C | c.2155G>T | 84.200 |
| | | | G719S | c.2155G>A | 84.200 |
| | | | Exon 19 Deletions | | 50.000 |
| | | | Exon 19 Insertions | | 50.000 |
| | | | A763_Y764insFQEA | c.2290_2291ins | 50.000 |
| | | | Exon 20 Insertions | | 50.000 |
| | | | S768I | c.2303G>T | 50.000 |
| | | | T790M | c.2369C>T | 29.400 |
| | | | E746_A750>IP | c.2235_2248delGGAATTAAGAGAAG insAATTC | 50.000 |
| | | | E746_A750del | c.2235_2249delGGAATTAAGAGAAG C | 50.000 |
| E746_A750del | c.2236_2250delGAATTAAGAGAAGC A | 50.000 | | | |
| E746_P753>VS | c.2237_2257delI21insTCT | 50.000 | | | |
| E746_S752>A | c.2237_2254delI18 | 50.000 | | | |
| E746_S752>D | c.2238_2255delI18 | 50.000 | | | |
| E746_S752>I | c.2235_2255delinsAAT | 50.000 | | | |
| E746_S752>V | c.2237_2255delinsT | 50.000 | | | |
| E746_T751>A | c.2237_2251delI15 | 50.000 | | | |
| E746_T751>I | c.2235_2252delinsAAT | 50.000 | | | |
| E746_T751>IP | c.2235_2251delinsAATTC | 50.000 | | | |
| E746_T751>V | c.2237_2252delinsT | 50.000 | | | |
| E746_T751>VA | c.2237_2253delinsTTGCT | 50.000 | | | |
| E746_T751del | c.2236_2253delI18 | 50.000 | | | |
| K745_E749del | c.2233_2247delI15 | 50.000 | | | |
| L747_A750>P | c.2238_2248delATTAAGAGAAGinsG C | 50.000 | | | |
| L747_A750>P | c.2239_2248delTTAAGAGAAGinsC | 50.000 | | | |
| L747_E749del | c.2239_2247delTTAAGAGAA | 50.000 | | | |
| L747_P753>Q | c.2239_2258delinsCA | 50.000 | | | |
| L747_S752>Q | c.2239_2256delinsCAA | 50.000 | | | |
| L747_S752del | c.2239_2256delI18 | 50.000 | | | |
| L747_T751>Q | c.2238_2252delinsGCA | 50.000 | | | |
| L747_T751>S | c.2240_2251del | 50.000 | | | |
| L747_T751del | c.2238_2252del | 50.000 | | | |
| NM_004448 | ERBB2 | 19 | D769H | c.2305G>C | 150.000 |
| | | | D769Y | c.2305G>T | 150.000 |
| | | | G776S | c.2326 G>A | 150.000 |
| | | | c.2263_2264delTTinsCC | c.2263_2264delTTinsCC | 150.000 |
| | | | c.2322_2334dupATACGT GATGGC | c.2322_2334dupATACGTGATGGC | 150.000 |

| | | | | | | |
|-----------|-------|----|------------------------------------|--|--------------------------|---------|
| | | 19 | c.2328_2336dupTGTGG GCTC | | c.2328_2336dupTGTGGGGCTC | 150.000 |
| | | 19 | L755_T759del | | c.2264_2278del | 150.000 |
| | | 19 | L755S | | c.2264T>C | 150.000 |
| | | 20 | Exon 20 Insertions | | | 150.000 |
| | | 20 | G778_P780dup | | c.2339_2340ins | 150.000 |
| | | 20 | V777L | | c.2329G>T | 150.000 |
| NM_023067 | FOXL2 | 1 | C134W | | c.402 C>G | 500.000 |
| NM_002067 | GNA11 | 5 | Q209L | | c.626A>T | 90.000 |
| | | 5 | Q209P | | c.626A>C | 90.000 |
| NM_002072 | GNAQ | 5 | Q209L | | c.626A>T | 60.000 |
| | | 5 | Q209P | | c.626A>C | 60.000 |
| | | 5 | Q209R | | c.626A>G | 60.000 |
| | | 11 | 556 ins L | | | 25.000 |
| | | 11 | 575 ins PE | | | 25.000 |
| | | 11 | Del 554-558 | | | 25.000 |
| | | 11 | Del 554-559 | | | 25.000 |
| | | 11 | Del 566-572 | | | 25.000 |
| | | 11 | Del 566-574 | | | 25.000 |
| | | 11 | Del 579 | | | 25.000 |
| | | 11 | Del V559 | | | 25.000 |
| | | 11 | E583_E589dupPYDHWKE | | | 25.000 |
| | | 11 | Exon 11 Mutation | | | 25.000 |
| | | 11 | G565V | | | 25.000 |
| | | 11 | K550N | | | 25.000 |
| | | 11 | K558N | | | 25.000 |
| | | 11 | L576P | | c.1727T>C | 25.000 |
| NM_000222 | KIT | 11 | N566D | | | 25.000 |
| | | 11 | P577_D579del | | c.1730_1738del | 25.000 |
| | | 11 | V559A | | c.1676T>C | 25.000 |
| | | 11 | V559D | | c.1676T>A | 25.000 |
| | | 11 | V559G | | | 25.000 |
| | | 11 | V560A | | | 25.000 |
| | | 11 | V560D | | c.1727T>C (V560D) | 25.000 |
| | | 11 | V560del | | c.1679_1681del | 25.000 |
| | | 11 | V560G | | | 25.000 |
| | | 11 | V569G | | | 25.000 |
| | | 11 | W557R | | c.1669T>A | 25.000 |
| | | 11 | W557R | | c.1669T>C | 25.000 |
| | | 11 | Y553N | | c.1657T>A | 25.000 |
| | | 14 | Exon 14 Mutation | | | 25.000 |
| | | 14 | H697Y | | c.2089C>T | 25.000 |
| | | 2 | G12A | | c.35G>C | 25.000 |
| | | 2 | G12C | | c.34G>T | 25.000 |
| | | 2 | G12D | | c.35G>A | 25.000 |
| | | 2 | G12R | | c.34G>C | 25.000 |
| | | 2 | G12S | | c.34G>A | 25.000 |
| | | 2 | G12V | | c.35G>T | 25.000 |
| | | 2 | G13A | | c.38G>C | 25.000 |
| | | 2 | G13C | | c.37G>T | 25.000 |
| | | 2 | G13D | | c.38G>A | 25.000 |
| | | 2 | G13R | | c.37G>C | 25.000 |
| | | 2 | G13S | | c.37G>A | 25.000 |
| | | 2 | G13V | | c.38G>T | 25.000 |
| NM_004985 | KRAS | 2 | Q22K | | c.64C>A | 25.000 |
| | | 3 | Q61H | | c.183A>C | 25.000 |
| | | 3 | Q61H | | c.183A>T | 25.000 |
| | | 3 | Q61H | | c.183A>C | 25.000 |
| | | 3 | Q61K | | c.181C>A | 25.000 |
| | | 3 | Q61L | | c.182A>T | 25.000 |
| | | 3 | Q61P | | c.182A>C | 25.000 |
| | | 3 | Q61R | | c.182A>G | 25.000 |
| | | 4 | A146P | | c.436G>C | 25.000 |
| | | 4 | A146T | | c.436G>A | 25.000 |
| | | 4 | A146V | | c.437C>T | 25.000 |
| | | 4 | K117N | | c.351A>C | 25.000 |
| | | 4 | K117N | | c.351A>T | 25.000 |

| | | | | | | | |
|------------------|------------------------|-----------|-----------------------------------|-----------------------------------|----------------------------------|----------------------------|-----------------------|
| NM_001127 500 | MET | 18 | L1213V | c.3637 C>G | 70.000 | | |
| | | 18 | V1206L | c.3616 G>T | 70.000 | | |
| NM_002524 | NRAS | 2 | G12A | c.35G>C | 60.000 | | |
| | | 2 | G12C | c.34G>T | 60.000 | | |
| | | 2 | G12D | c.35G>A | 60.000 | | |
| | | 2 | G12R | c.34G>C | 60.000 | | |
| | | 2 | G12S | c.34G>A | 60.000 | | |
| | | 2 | G12V | c.35G>T | 60.000 | | |
| | | 2 | G13A | c.38G>C | 60.000 | | |
| | | 2 | G13C | c.37G>T | 60.000 | | |
| | | 2 | G13D | c.38G>A | 60.000 | | |
| | | 2 | G13R | c.37G>C | 60.000 | | |
| | | 2 | G13V | c.38G>T | 60.000 | | |
| | | 3 | Q61E | c.181C>G | 60.000 | | |
| | | 3 | Q61H | c.183A>C | 60.000 | | |
| | | 3 | Q61H | c.183A>T | 60.000 | | |
| | | 3 | Q61H | c.183A>T | 60.000 | | |
| | | 3 | Q61K | c.181C>A | 60.000 | | |
| | | 3 | Q61L | c.182A>T | 60.000 | | |
| | | 3 | Q61L | c.182_183delAAinsTG | 60.000 | | |
| | | 3 | Q61P | c.182A>C | 60.000 | | |
| | | 3 | Q61R | c.182A>G | 60.000 | | |
| | | 3 | Q61R | c.182_183delAAinsGG | 60.000 | | |
| | | 12 | Y555C | c.1664 A>G | 100.000 | | |
| | | 12 | c.1679_1693delGGGTC ATTGAATCAA | c.1679_1693delGGGTCATTGAATCA A | 100.000 | | |
| | | 12 | c.1681_1682insAGAGG G | c.1681_1682insAGAGGG | 100.000 | | |
| | | 12 | V561D | c.1682 T>A | 100.000 | | |
| | | 12 | c.1696_1713del18 | c.1696_1713del18 | 100.000 | | |
| | | NM_006206 | PDGFRA | 14 | c.2526_2537delCATCAT GCATGA | c.2526_2537delCATCATGCATGA | 70.000 |
| | | | | 14 | c.2533_2544delCATGATT CGAAC | c.2533_2544delCATGATTCGAAC | 70.000 |
| | | | | 18 | D842V | c.2525 A>T | 70.000 |
| | | | | 18 | D846Y | c.2536 G>T | 70.000 |
| | | | | 12 | Exon 12 Mutation | | 100.000 |
| | | | | 14 | Exon 14 Mutation | | 100.000 |
| | | | | 18 | Exon 18 Mutation | | 70.000 |
| | | | | NM_006218 | PIK3CA | 9 | D549N |
| | | 9 | E542K | | | c.1624G>A | 110.000 |
| | | 9 | E545G | | | c.1634A>G | 110.000 |
| | | 9 | E545K | | | c.1633G>A | 110.000 |
| | | 9 | E545Q | | | c.1633G>C | 110.000 |
| 9 | E545V | c.1634A>T | 110.000 | | | | |
| 9 | Q546E | c.1636C>G | 110.000 | | | | |
| 9 | Q546K | c.1636C>A | 110.000 | | | | |
| 9 | Q546L | c.1637A>T | 110.000 | | | | |
| 9 | Q546P | c.1637A>C | 110.000 | | | | |
| 9 | Q546R | c.1637A>G | 110.000 | | | | |
| 20 | H1047R | c.3140A>G | 110.000 | | | | |
| 20 | H1047L | c.3140A>T | 110.000 | | | | |
| 20 | H1047Y | c.3139C>T | 110.000 | | | | |
| 20 | M1043I | c.3129G>A | 110.000 | | | | |
| NM_020975 | RET | 16 | M918I | c.2753 T>C | 350.000 | | |
| NM_000546 | TP53 | | Intera codificante | regione | 30.000 – 380.000 | | |