Breast Cancer Gene Heterogeneity Case Study by NGS(next generation sequence)

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Cancer and tumor gene heterogeneity play a significant role in affecting treatment strategies and outcomes

Cancer cells within a tumor can vary genetically due to mutations, alterations, and changes over time, leading to treatment resistance . Advances in genomic sequencing, bioinformatics, and molecular profiling have improved our ability to characterize tumor heterogeneity and tailor treatments accordingly, which not only can provide specific personalized treatment, targeted therapies, but also can monitor treatment response.

In this case study, NGS data was downloaded from NCBI ,with ID at SRR13268273 . The sample was a breast cancer tissue from a patient with invasive ductal carcinoma.

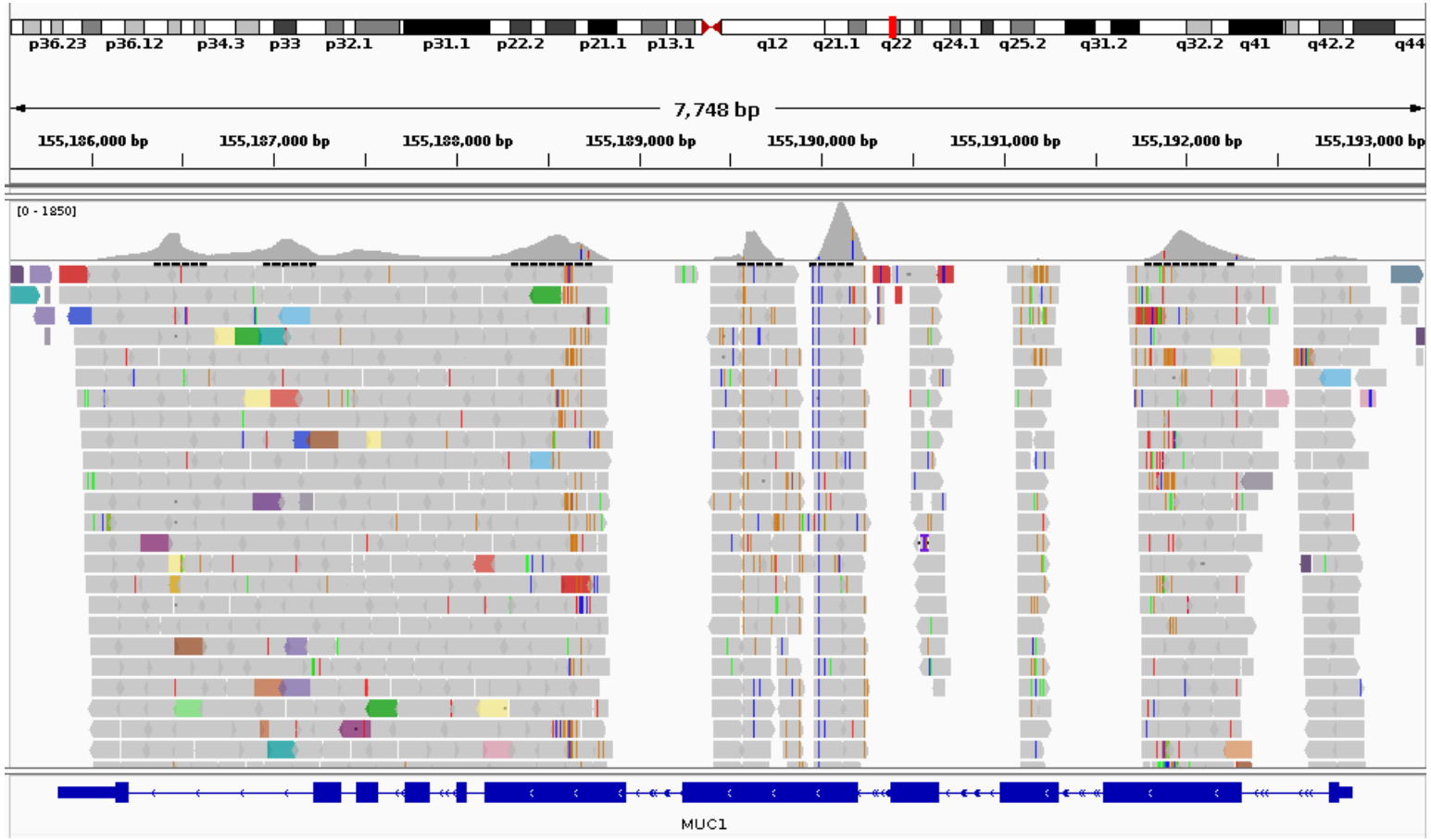
Results show multiple genes have been involved in gene mutations, some genes are known to be associated tumor metastasis, some genes are not known functions and still under ongoing research.

Here, five genes of them are exampled, the bam file was viewed by IGV, showing variants including insertion on exons and introns.
The five genes are:

MUC1
BRCA1
VIRMA
Angiopoietin 1
DPY19L4

MUC1 variants : diagnostic marker for breast cancer

Overall view of gene mutations/variants in the MUC1 gene exons and introns

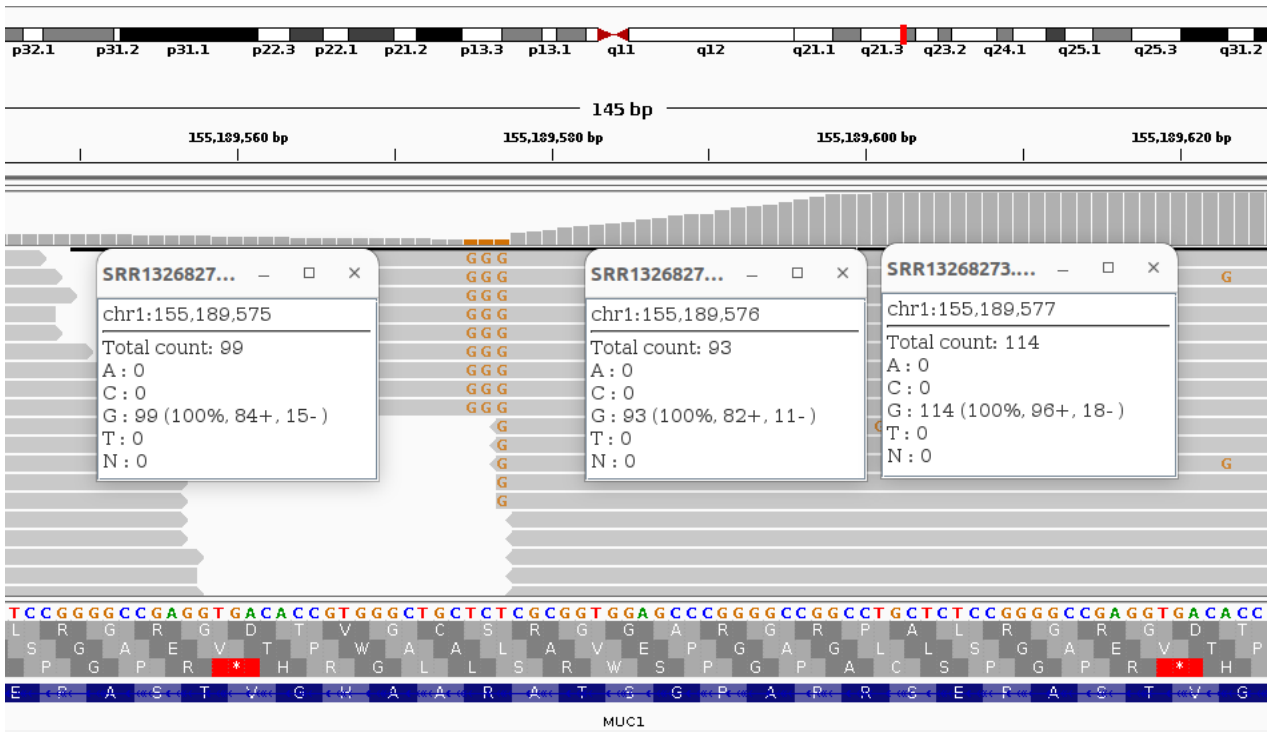


Mucin 1 (MUC1) is a glycoprotein that has been demonstrated to be involved in the metastasis and invasion of multiple tumor types.

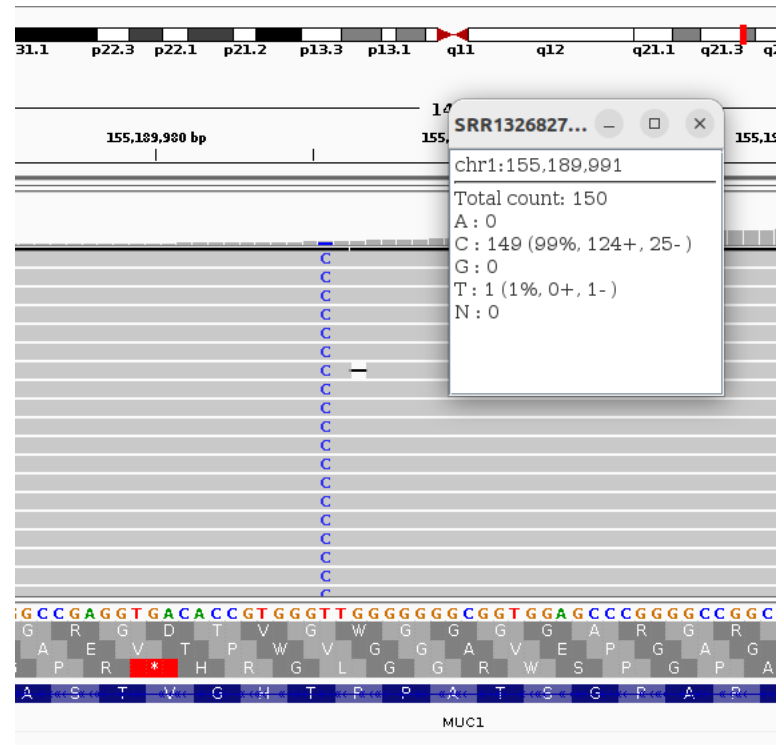
MUC1

1:155188583:G,
1:155188589:G,
1:155188597:G,
1:155188613:G,
1:155188623:C,
1:155188631:G,
1:155188633:G,
1:155188640:C,
1:155188643:GG,
1:155188649:G,
1:155188663:G,
1:15518873:G,
1:155188692:G,
1:155188733:G,
1:155188847:G,
1:155188868:G,
1:155189416:G,
1:155189452:G,
1:155189463:G,
1:155189483:C,
1:155189485:C,
1:155189514:CGGGC,
1:155189575:GGG,
1:155189634:CGGGC,
1:155189663:C,
1:155189665:C,
1:155189747:G,
1:155189752:G,
1:155189754:T,
1:155189813:G,
1:155189843:C,
1:155189885:G,
1:155189902:G,
1:155189959:C,
1:155189991:C,
1:155190054:C,
1:155190083:G,
1:155190174:GGGG,
1:155190203:CTC,
1:155190238:G,
1:155190254:G,
1:155190317:C,
1:155190323:GTG,
1:155190591:A,
1:155190606:A,
1:155190614:G,
1:155190674:C,
1:155191101:G,
1:155191105:G,
1:155191143:G,
1:155191154:G,
1:155191159:G,
1:155191167:G,
1:155191170:G,
1:155191173:G,
1:155191177:G,
1:155191183:C,
1:155191191:G,
1:155191201:A,
1:155191210:C,
1:155191230:G,
1:155191237:G,
1:155191726:G,
1:155191784:C,
1:155191844:T,
1:155191881:G,
1:155191904:G,
1:155191982:C,
1:155192276:T,
1:155192958:C,
1:155197672:G

Mutations/variants in Muc1 gene exons



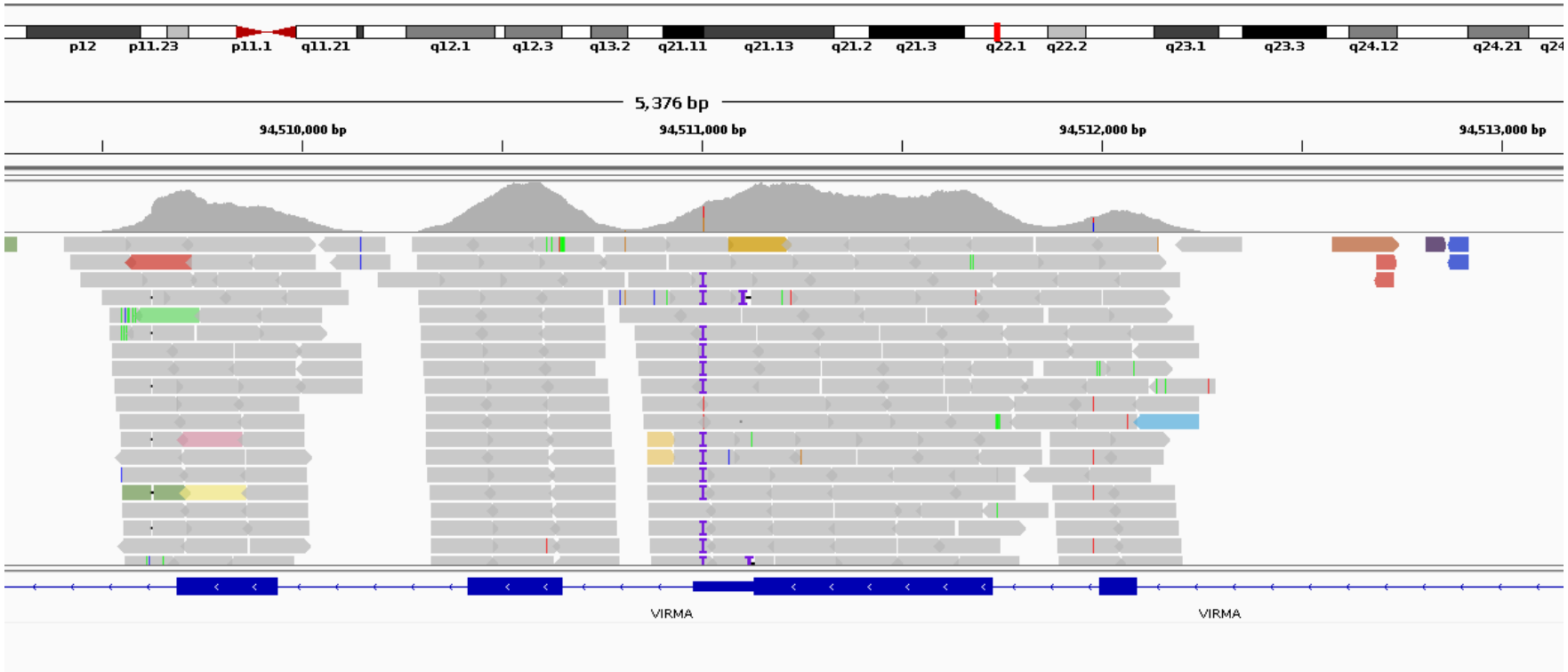
chr1 155180575, 155180575, T to G



Chr1 155189991, T to C

VIRMA mutations/variants

Overall view of gene mutations/variants in the VIRMA gene exons and introns



VIRMA , an oncogenic factor ,is associated with cancer growth and/or metastasis

VIRMA

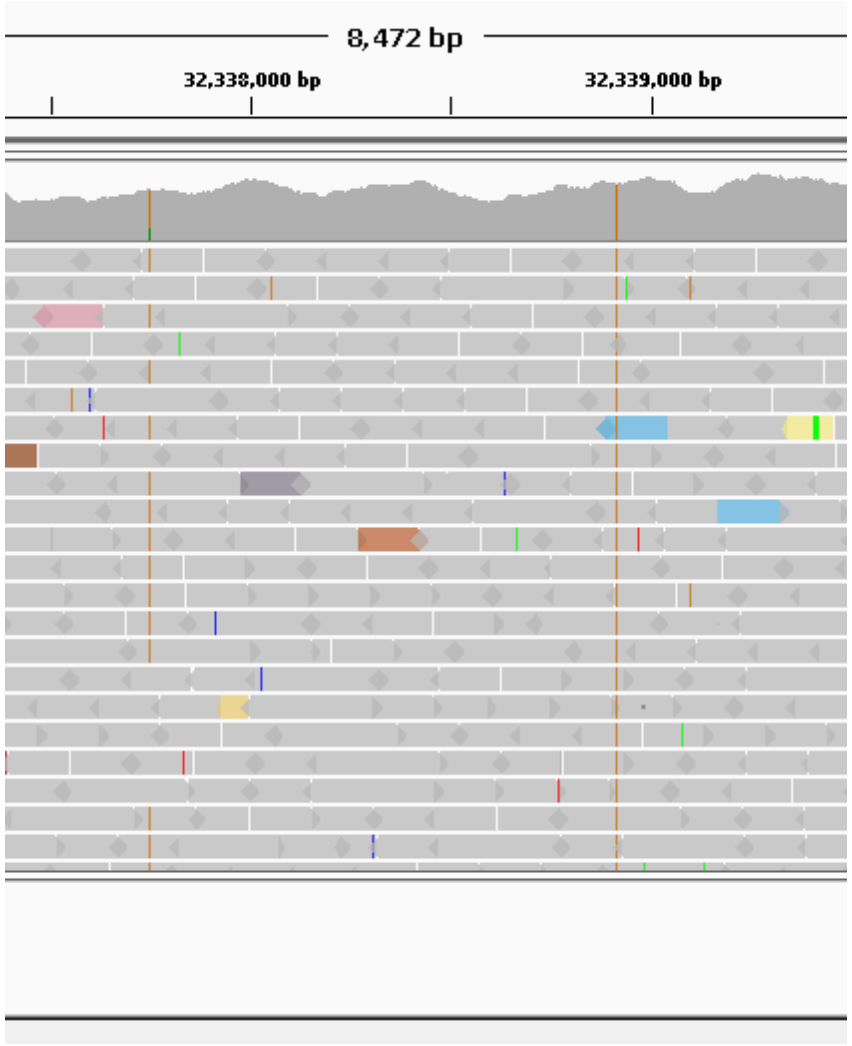
8:94491996:A,
8:94495009:ATTTTTTTTTTTTGAGA,
8:94495100:C,
8:94506725:A,
8:94507280:C,
8:94509625:TACACACACACACACACACAT,
8:94510149:C,
8:94510810:G,
8:94511003:TT,
8:94511981:T,
8:94528860:T,
8:94528995:A,
8:94529074:G,
8:94529143:A,
8:94529435:A,
8:94530872:G,
8:94531178:TT,
8:94534891:G,
8:94543949:A,
8:94544454:CTA,
8:94544466:T,
8:94553597:T

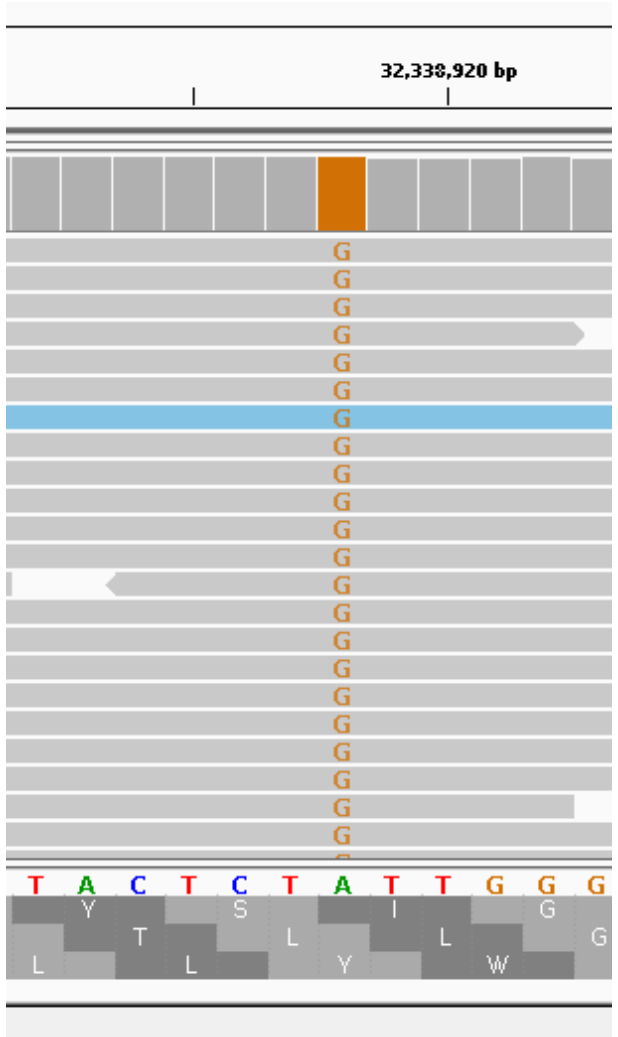
Insertion mutation on VIRMA gene exon 13

Chr8, between 94511003 and 94511004, on VIRMA gene exon13, T was inserted

BRCA2 variants

BRCA2 is a predictive biomarker for treatment of primary peritoneal carcinoma, breast carcinoma, and prostate carcinoma





BRCA2

13:32310516:T,
13:32311074:GTTGGG,
13:32316435:A,
13:32319060:ATTTTTTTTTTAAATAT,
13:32325276:G,
13:32325430:C,
13:32326796:A,
13:32328257:C,
13:32331082:ATTTTTTTTTTGAGG,
13:32331128:A,
13:32332592:C,
13:32333398:CTTTTTTTTTGTAAA,
13:32337751:G,
13:32338918:G,
13:32340868:C,
13:32341273:CA,
13:32341387:A,
13:32343028:A,
13:32346707:C,
13:32354425:TAAAAAGGT,
13:32355095:G,
13:32355250:C,
13:32356333:C,
13:32356799:A,
13:32362509:C,
13:32370664:G,
13:32370669:A,
13:32370670:C,
13:32370731:C,
13:32375245:C,
13:32375531:T,
13:32376974:CTACT,
13:32379251:C,
13:32385062:T,
13:32385103:A,
13:32394454:A,
13:32394470:G,
13:32394681:T,
13:32395944:T,
13:32395952:TTTTTTTTT,13:32395964:C,
13:32395989:T,
13:32396181:C,
13:32396182:CAGG,
13:32396194:A,
13:32396234:A
13:32396239:G,
13:32396245:A,
13:32396791:CTTTTTGGTC,
13:32403208:GAAAAAAAAATGC

ANGPT1 variants

Angiopoietin 1 could be involved in MM-induced angiogenesis, which is related to the cancer metastasis

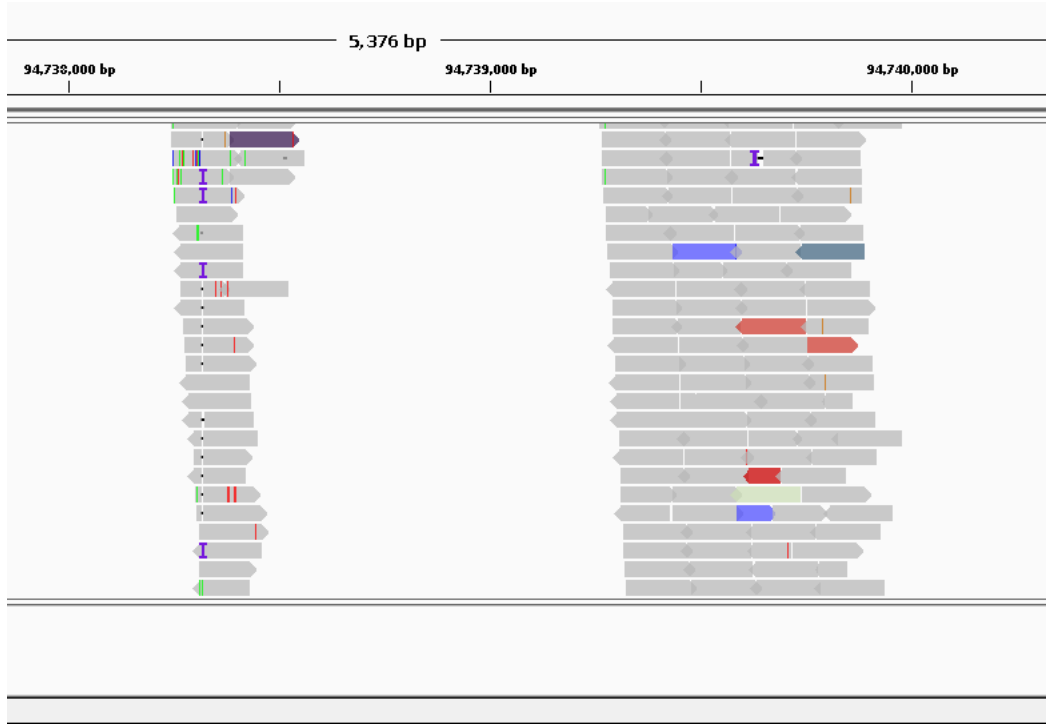
Angiopoietin 1 at 107346889 AA insertion(chromosome 8)

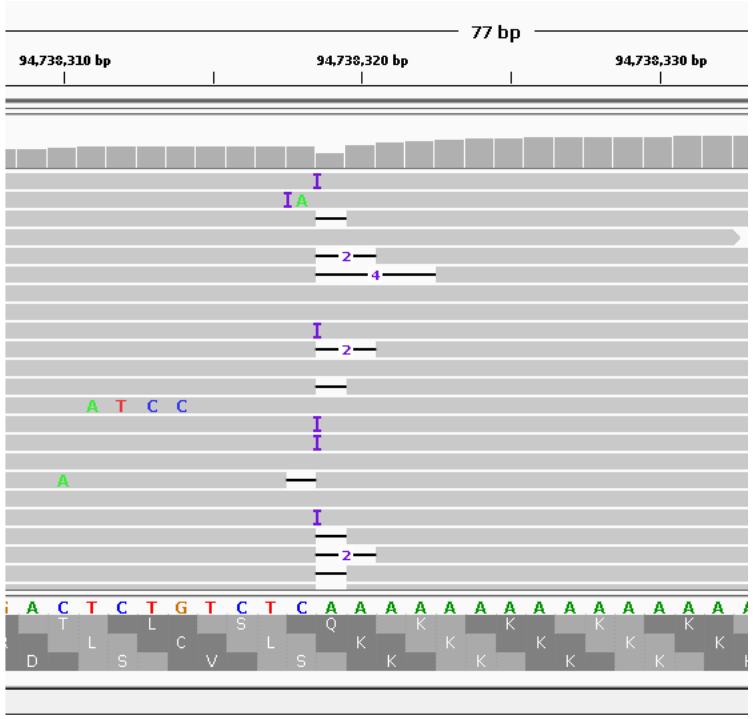
ANGPT1

8:107254136:T,
8:107264365:A,
8:107282089:T,
8:107284560:CAAAAAAAAAGAATT,
8:107303049:G,
8:107303368:A,
8:107303371:AAAAAAAAAAAAAAAAGATTGC,
8:107303450:A,
8:107303451:A,
8:107336440:C,
8:107336455:G,
8:107336476:C,
8:107341899:T,
8:107341983:GG,
8:107342782:TACACACACACACACACACACACACACACACACACACACACACACAAG,
8:107346798:A,
8:107346889:GAAAAAAAAAAAATTTTTC,
8:107376661:G,
8:107392929:ATTCT,
8:107393561:T,
8:107393654:G,
8:107419950:T,
8:107449400:GCACACACACACACACACAG

DPY19L4 variants

How DPY1914 affects breast cancer is unknown





DPY19L4

8:94715513:C,
8:94715551:A,
8:94720055:C,
8:94724749:A,
8:94726489:G,
8:94733565:GGG,
8:94733572:C,
8:94733643:A,
8:94734605:G,
8:94738251:A,
8:94738318:AAAA
AAAAAAAAAAAAT
TAAATTTAAATAA
TAATTTC,
8:94739274:A,
8:94751367:T,
8:94755929:T,
8:94756588:A,
8:94757992:A,
8:94758087:G,
8:94758105:T,
8:94761658:TAGT,
8:94765350:ATTTT
TTTTTTGAAG,
8:94765398:G,
8:94766525:T,
8:94768635:C,
8:94770636:G,
8:94770675:A,
8:94770685:G,
8:94776780:G,
8:94777857:C,
8:94778028:T,
8:94778037:C,
8:94778050:A,
8:94780246:T,
8:94780247:T,
8:94780248:TTTTTT,
:94780651:G,
8:94781006:C,
8:94781017:T,
8:94781024:T,
8:94781041:T,
8:94781056:TTTTTTTTTTTTTT
TTTTGCATTTTAGTTTTTTCC,
8:94781287:A,8
:94783479:CAGT,
8:94783882:C,
8:94783949:A,
8:94784279:T,
8:94784296:C

Conclusions

Gene variants data produced by NGS could provide key gene variants panel for specific patient, not only can provide treatment targets , but also can monitor therapeutic effects from time to time