Contents

snv+cnv+sv

```
dragen -f -r ${1} -1 ${2} -2 ${3} \
    --RGID Normal_RGID --RGSM Nroma_RGSM \
    --enable-map-align true \
    --enable-map-align-output true \
    --output-format bam --enable-sort true \
    --enable-duplicate-marking true \
    --enable-variant-caller true \
    --enable-vcf-compression true \
    --vc-target-bed ${4} \
    --enable-cnv true \
    --cnv-target-bed ${4} --cnv-normals-list ${5} \
    --enable-sv true --sv-exome true --sv-call-regions-bed ${4} \
    --output-file-prefix ${6} \
    --output-directory ${7}
```

PoN 建立正常样本基线

```
dragen -r ${1} -1 ${2} -2 ${3} \
   --RGSM ${4} --RGID illumina \
   --output-directory ${5} \
   --output-file-prefix ${4} \
   --enable-map-align true --enable-cnv true \
   --cnv-enable-gcbias-correction false \
   --cnv-enable-self-normalization false \
   --cnv-target-bed ${6} --cnv-interval-width 500
```

将 prefix.target.counts.gc-corrected.gz 文件写到 PoN.txt 文本文件中，其内容如下

```
/data/output_trio1/sample1.target.counts.gc-corrected.gz
/data/output_trio1/sample2.target.counts.gc-corrected.gz
/data/output_trio2/sample4.target.counts.gc-corrected.gz
/data/output_trio2/sample5.target.counts.gc-corrected.gz
/data/output_trio3/sample7.target.counts.gc-corrected.gz
/data/output_trio3/sample8.target.counts.gc-corrected.gz
```

附录说明正常样本数量 50 个左右

CNV 分析参数

```
--enable-cnv true
--cnv-filter-copy-ratio 0.2     #   The default value is 0.2, leading to calls less than CR=0.8 or
 ↪  greater than CR=1.2.
--cnv-filter-length 10000       #   Specifies the minimum event length in bases at which a reported
 ↪  event is marked as PASS in the output VCF file. The default is 10000
```

```
--cnv-filter-qual 10            #   PASS in the output VCF file
```

CNV 解析度

WGS_Coverag_per_Sample	Recommended_Resolution(bp)
5X	10000
10X	5000
>=30X	1000

–cnv-interval-width 用来控制解析度，WES 默认是 500，WGS 默认是 1000 该参数在分析是需要设置，如果设置变小会增加分析时间

参考文献

dragen_PoN

Patel B, Parets S, Akana M, et al. Comprehensive genetic testing for female and male infertility using next-generation sequencing[J]. Journal of assisted reproduction and genetics, 2018, 35(8): 1489-1496.

CNV refers to an intermediate scale structural variant, with copy number changes ranging from 1 Kb to 5 Mb of DNA

Kerkhof J, Schenkel L C, Reilly J, et al. Clinical validation of copy number variant detection from targeted next-generation sequencing panels[J]. The Journal of Molecular Diagnostics, 2017, 19(6): 905-920.

CNV size cutoffs were 1 kb for losses and 2kb for gains

Lionel A C, Costain G, Monfared N, et al. Improved diagnostic yield compared with targeted gene sequencing panels suggests a role for whole-genome sequencing as a first-tier genetic test[J]. Genetics in Medicine, 2018, 20(4): 435-443.

high copy number calls expected to have >0.85,and high copy number loss <-1.25

Chaubey A, Shenoy S, Mathur A, et al. Low Pass-Genome Sequencing: Validation and diagnostic utility from 409 clinical cases of low-pass genome sequencing for the detection of copy number variants (CNVs) to replace constitutional microarray[J]. The Journal of Molecular Diagnostics, 2020.