low pass genome sequencing

测序深度与读长

- 与测序数据量，最少15M reads
- 对于读长单端50bp
- 理论模拟上，对于unique reads至少达到6M

Kucharík M, Budiš J, Hýblová M, et al. Copy Number Variant Detection with Low-Coverage Whole-Genome Sequencing Represents a Viable Alternative to the Conventional Array-CGH[J]. Diagnostics, 2021, 11(4): 708.

Chau M H K, Wang H, Lai Y, et al. Low-pass genome sequencing: a validated method in clinical cytogenetics[J]. Human Genetics, 2020, 139: 1403-1415.

检测算法

- 划动bin大小一般设置50kb
- 步长：5kb
- 解析度：100K

关于拷贝数阈值的设置

- 理论上：

duplication (three copies) $\log_2$ [1.5] = 0.58

a deletion (one copy) is $\log_2$ [0.5] =-1.0

Liang D, Peng Y, Lv W, et al. Copy number variation sequencing for comprehensive diagnosis of chromosome disease syndromes[J]. The Journal of Molecular Diagnostics, 2014, 16(5): 519-526.

关于拷贝数阈值的设置

- 在相关文献中：这个值设为1.2和0.8比如贝瑞发表的文章和dragen：

Zhou X, Chen X, Jiang Y, et al. A Rapid PCR-Free Next-Generation Sequencing Method for the Detection of Copy Number Variations in Prenatal Samples[J]. Life, 2021, 11(2): 98.

- 在华大的文献中：这个值设定为1.15和0.85

Dong Z, Xie W, Chen H, et al. Copy-number variants detection by low-pass whole-genome sequencing[J]. Current protocols in human genetics, 2017, 94(1): 8.17. 1-8.17. 16.

- 为了增加敏感性，华大的另一篇文献里提到设置为：1.1和0.9

Wang H, Dong Z, Zhang R, et al. Low-pass genome sequencing versus chromosomal microarray analysis: implementation in prenatal diagnosis[J]. Genetics in Medicine, 2020, 22(3): 500-510.

华大share的分析代码

- *http://sourceforge.net/projects/increment-ratio-of-coverage/files/*

Dong Z, Zhang J, Hu P, et al. Low-pass whole-genome sequencing in clinical cytogenetics: a validated approach[J]. Genetics in Medicine, 2016, 18(9): 940-948.

Dong Z, Xie W, Chen H, et al. Copy-number variants detection by low-pass whole-genome sequencing[J]. Current protocols in human genetics, 2017, 94(1): 8.17. 1-8.17. 16.