Validation and depth evaluation of low-pass genome sequencing in prenatal diagnosis using 387 amniotic fluid samples

Running title: Validation and depth evaluation of clinical LP GS

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Filtering criteria for Detected CNVs:

After CNV detection using binary segmentation algorithm, the detected CNVs were then filtered according to our previous published article with minor modifications. Detailed filtering criteria was described as follows:

(1) U-test (ST) was used to evaluate the significance of each segment as a CNV. Then the Parallelism-test (PT) was used to estimate the reliability of each signal under the consideration of multiplex-related bias. CNVs with a p-value of >= 0.001 in U-test or a p-value of >= 0.1 in Parallelism-test were filtered out.

(2) The standard deviation (SD) of the relative copy ratio (RCR) was calculated for each CNV to evaluate the fluctuation of the CNV. CNVs with a SD of >1 were filtered out.

(3) CNVs with a RCR of >1.2 (for duplication) or <0.8 (for deletion) were collected for further filtering. In these CNVs, the proportion of windows with high RCR (> 1.43 for duplication) or low RCR (< 0.57 for deletion) was calculated. CNVs with a proportion of < 10% were filtered out.

(4) A population-scale control set was used to filter polymorphic CNVs. CNVs detected by LP GS with a reciprocal overlap of >=90% with the CNVs in the population-scale control set were filtered out.

(5) CNVs with a RCR of < 1.3 (duplication) or >0.7 (deletion) were filtered out.

(6) CNVs with a size of < 100 kb were filtered out.

Reference