

NONINVASIVE DIAGNOSIS OF FETAL ANEUPLOIDY BY SEQUENCING

Abstract

5 Disclosed is a method to achieve digital quantification of DNA (i.e., counting
differences between identical sequences) using direct shotgun sequencing followed by
mapping to the chromosome of origin and enumeration of fragments per chromosome. The
preferred method uses massively parallel sequencing, which can produce tens of millions of
short sequence tags in a single run and enabling a sampling that can be statistically evaluated.
10 By counting the number of sequence tags mapped to a predefined window in each
chromosome, the over- or under- representation of any chromosome in maternal plasma DNA
contributed by an aneuploid fetus can be detected. This method does not require the
differentiation of fetal versus maternal DNA. The median count of autosomal values is used
as a normalization constant to account for differences in total number of sequence tags is
15 used for comparison between samples and between chromosomes.

Figure 1A