

$$\text{cfDNA} = \sum_{\substack{\text{tissue} \\ \text{(including blood)}}} \begin{bmatrix} \text{benign systemic response} \\ \text{tumor systemic response} \\ \text{tumor microenvironment} \\ \text{tumor} \end{bmatrix}$$

FIG. 1A

$$\text{cfDNA} = \sum_{\substack{\text{tissue} \\ \text{(including blood)}}} \begin{bmatrix} \text{benign systemic response} \times \text{benign clearance} \\ \text{tumor systemic response} \times \text{inflammation clearance} \\ \text{tumor microenvironment} \times \text{TM clearance} \\ \text{tumor} \times \text{tumor clearance} \end{bmatrix}$$

FIG. 1B

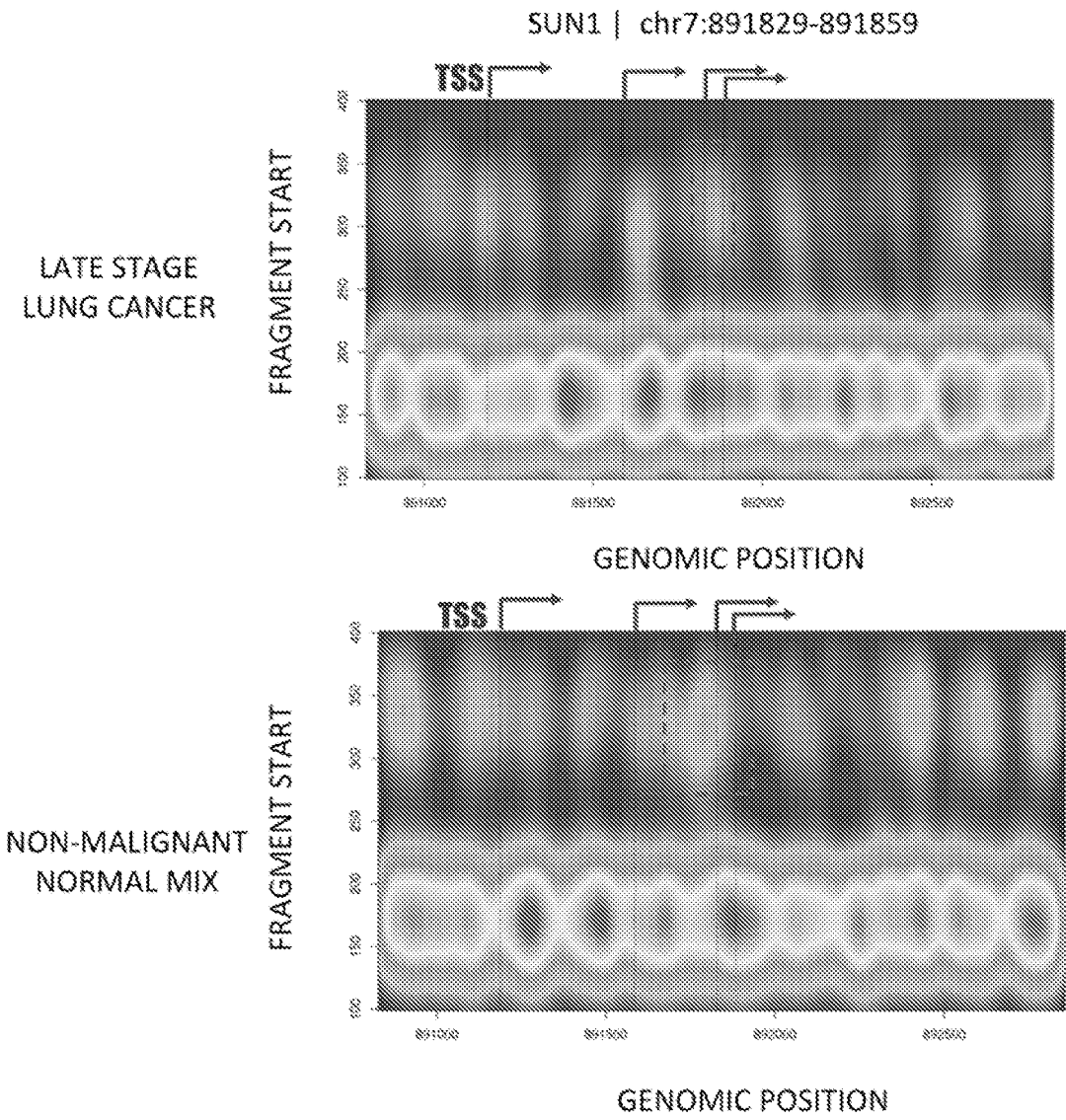


FIG. 1C

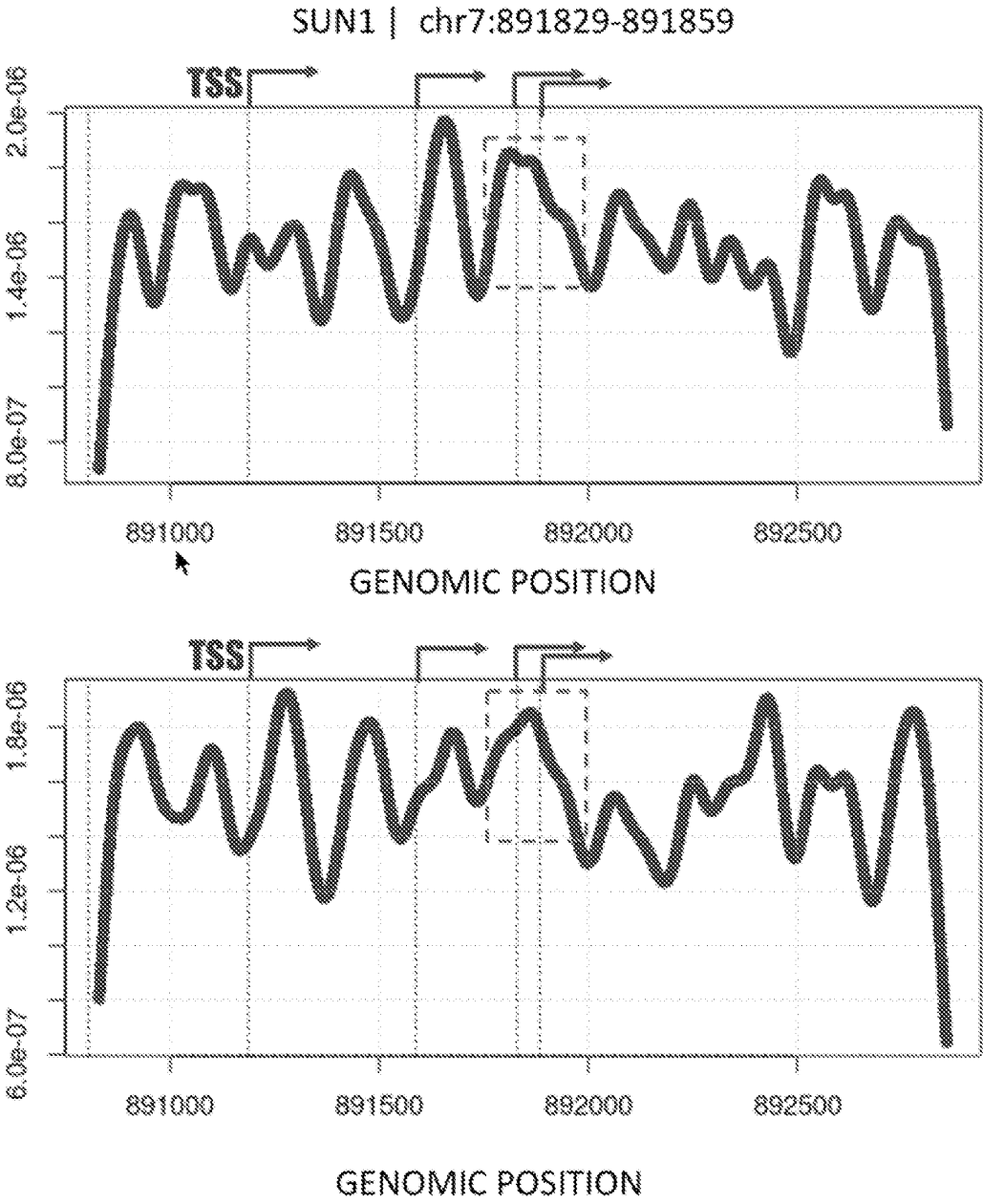


FIG. 1D

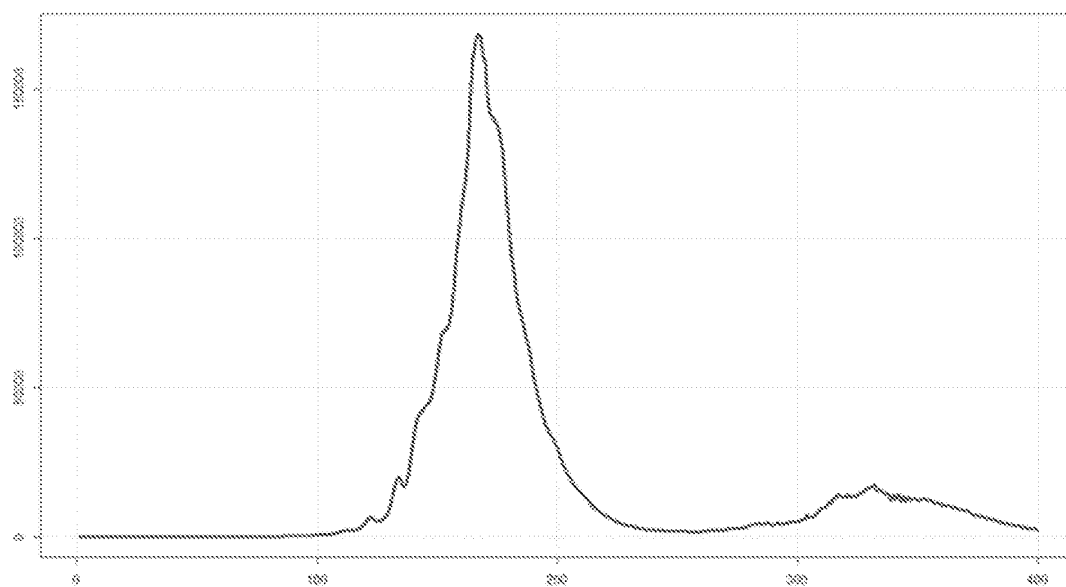


FIG. 1E

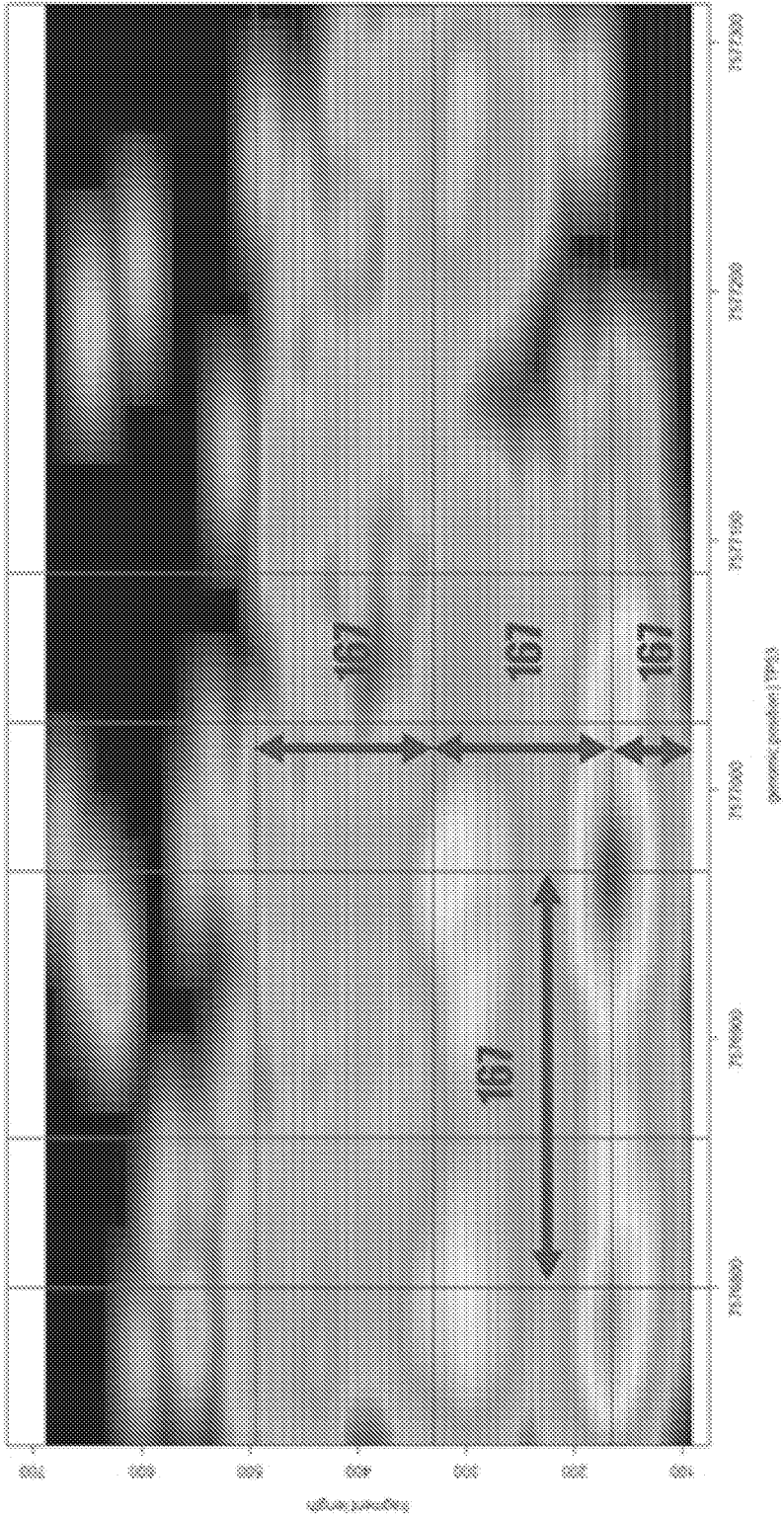


FIG. 2

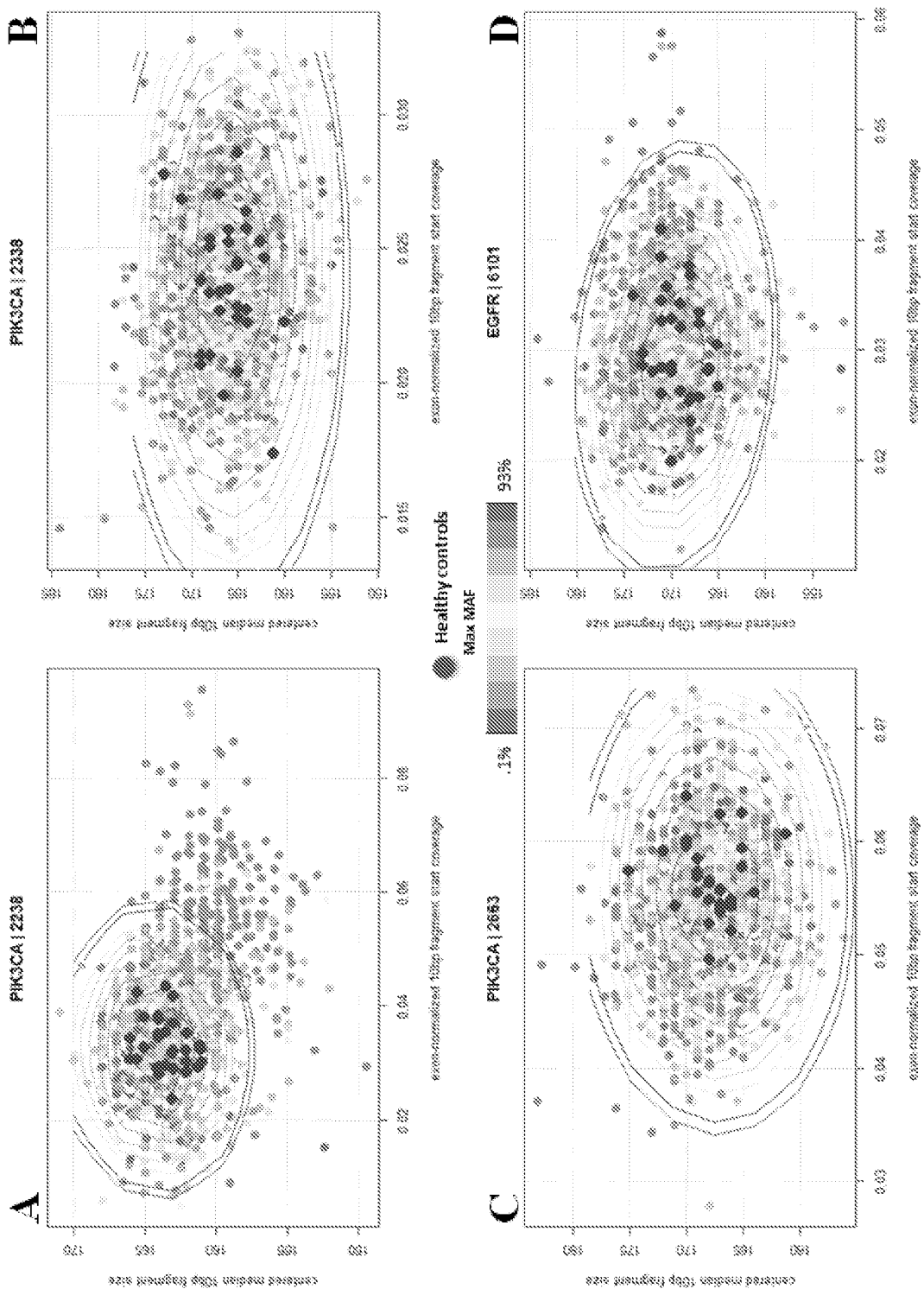


FIG. 3

|       | sampled    | gene   | alteration | percentage | copynumber | type | mut_type   | cancerType                |
|-------|------------|--------|------------|------------|------------|------|------------|---------------------------|
| 59791 | A2570201_1 | RB1    | E209*      | 63.88      | NA         | SNV  | non-sense  | Small Cell Lung Carcinoma |
| 59792 | A2570201_1 | PRKCA  | AMP        | 0.00       | 3.621532   | CNV  | amp        | Small Cell Lung Carcinoma |
| 59794 | A2570201_1 | CCND2  | AMP        | 0.00       | 2.670914   | CNV  | amp        | Small Cell Lung Carcinoma |
| 59795 | A2570201_1 | MYC    | AMP        | 0.00       | 2.598296   | CNV  | amp        | Small Cell Lung Carcinoma |
| 59797 | A2570201_1 | CCND1  | AMP        | 0.00       | 2.595395   | CNV  | amp        | Small Cell Lung Carcinoma |
| 59798 | A2570201_1 | CDK4   | AMP        | 0.00       | 2.469875   | CNV  | amp        | Small Cell Lung Carcinoma |
| 59793 | A2570201_1 | ERBB2  | AMP        | 0.00       | 2.425024   | CNV  | amp        | Small Cell Lung Carcinoma |
| 59796 | A2570201_1 | KRAS   | AMP        | 0.00       | 2.394474   | CNV  | amp        | Small Cell Lung Carcinoma |
| 59799 | A2570201_1 | CDKN2A | G23G       | 0.28       | NA         | SNV  | synonymous | Small Cell Lung Carcinoma |

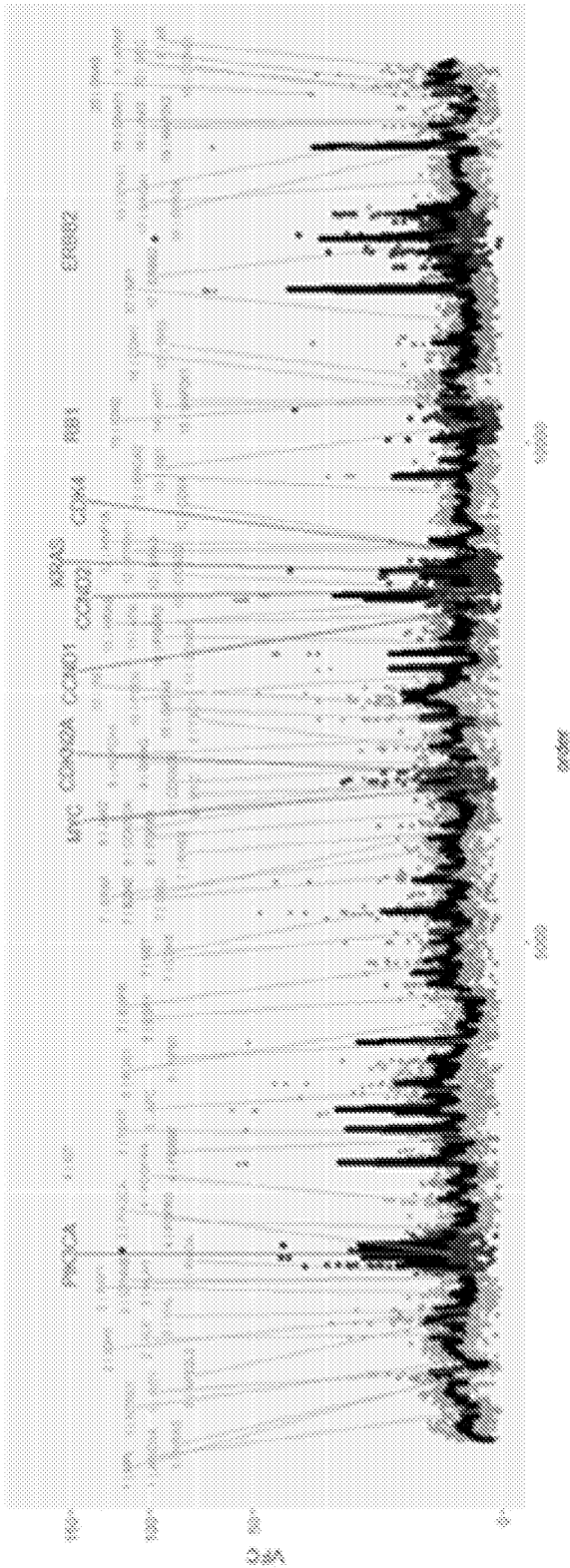


FIG. 4

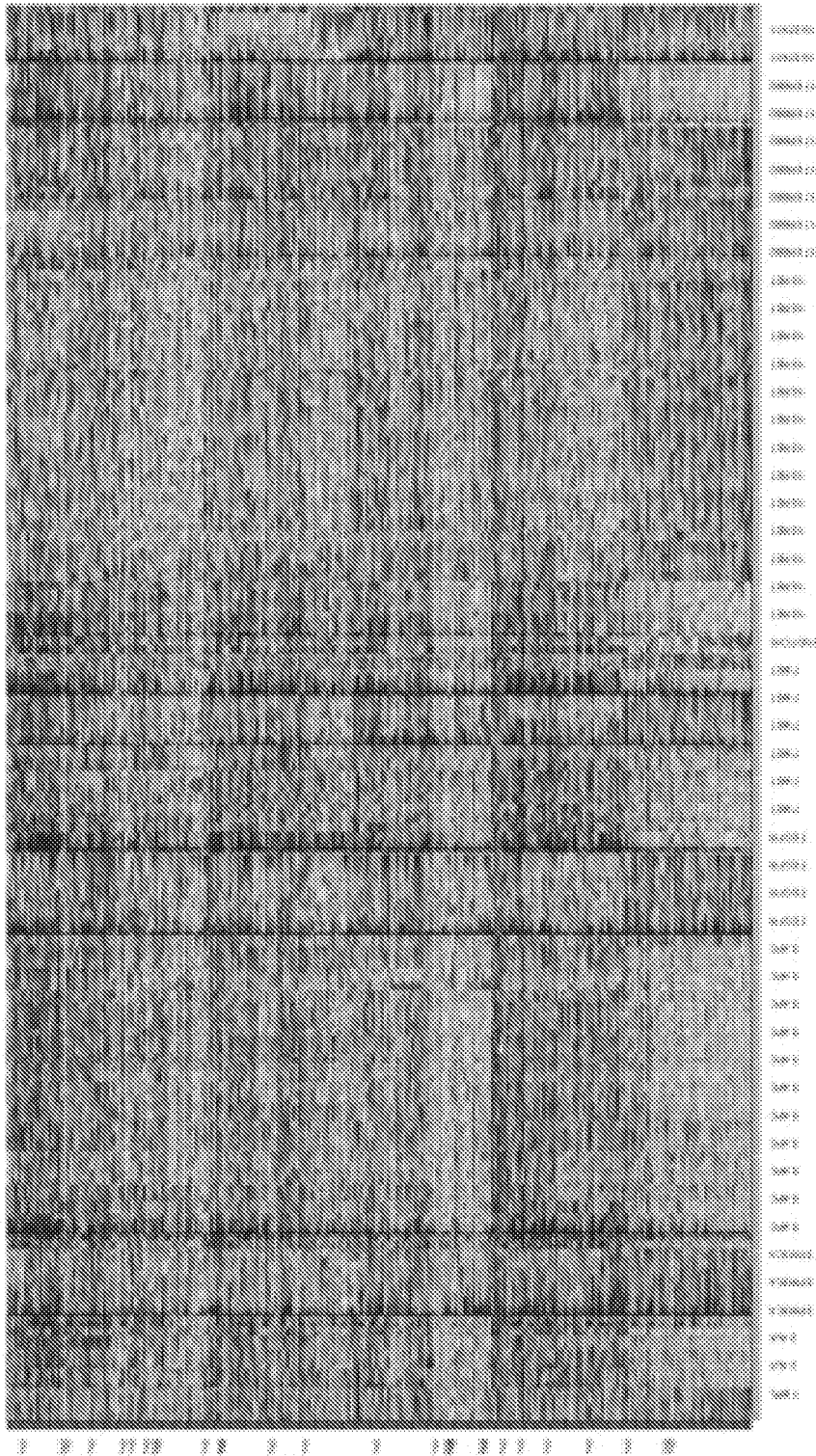
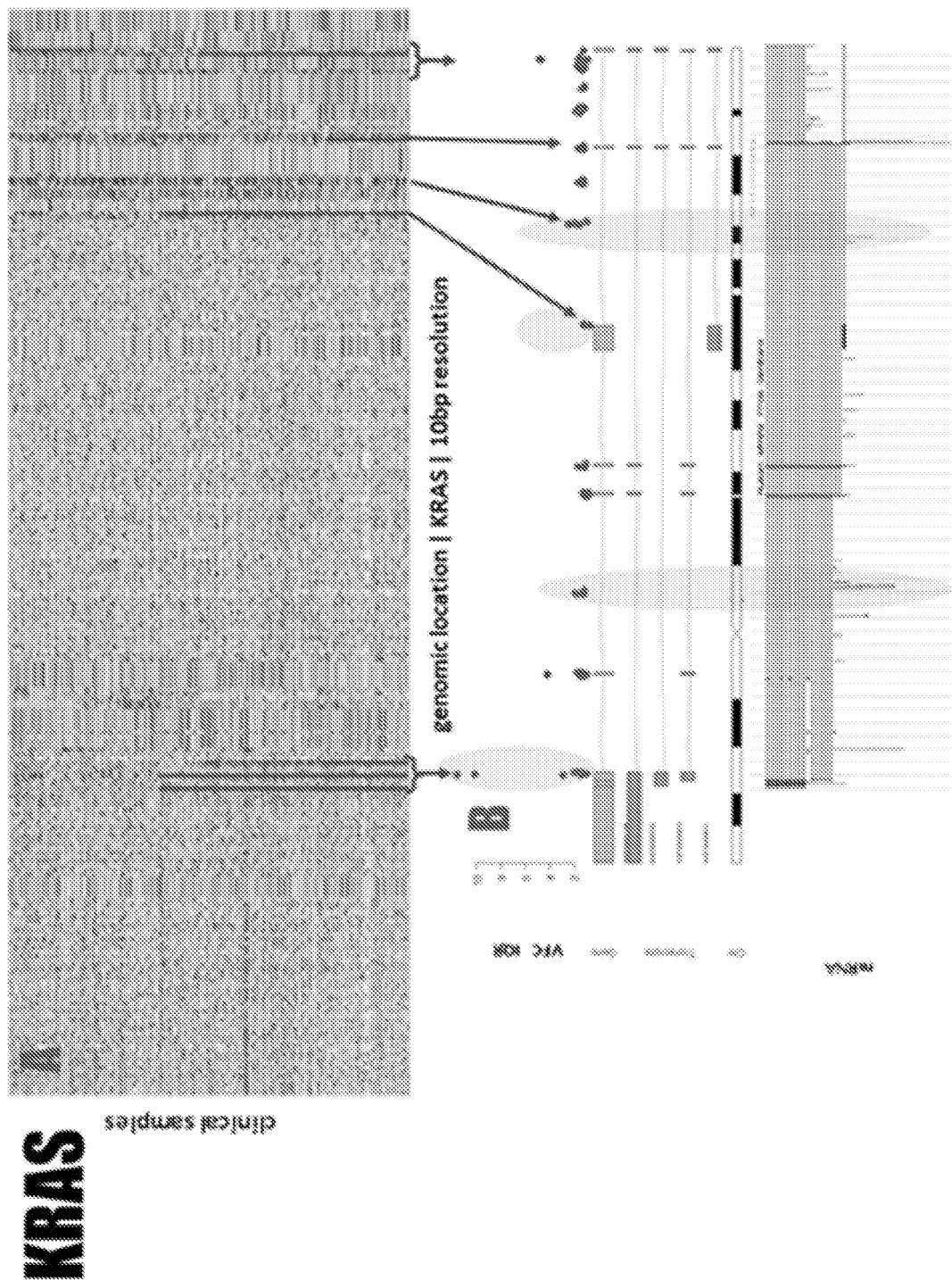


FIG. 5



**FIG. 6**

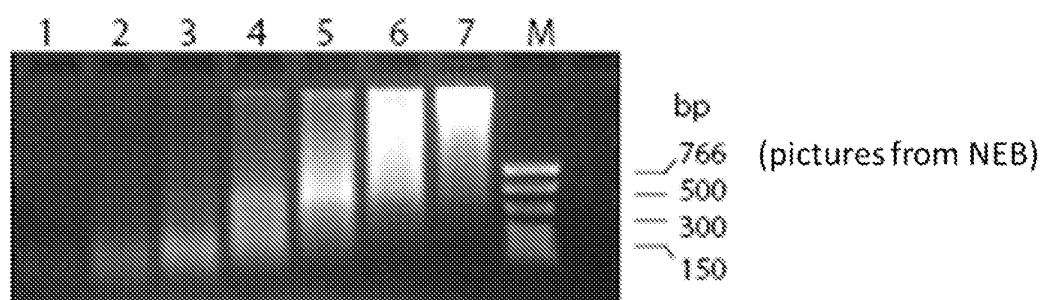
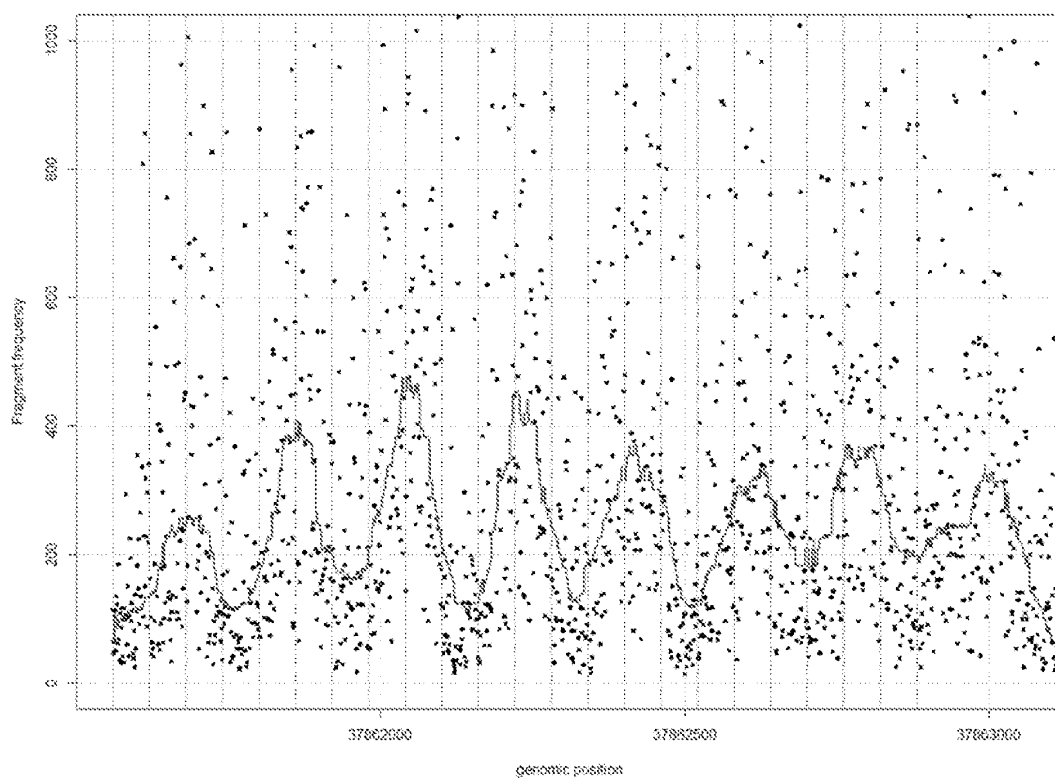
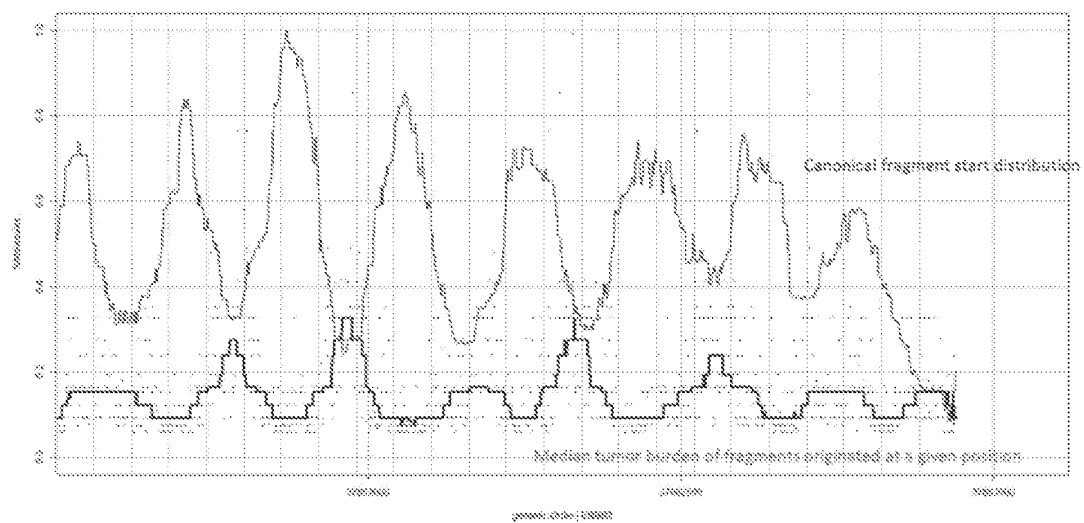


FIG. 7

**FIG. 8**

**FIG. 9**

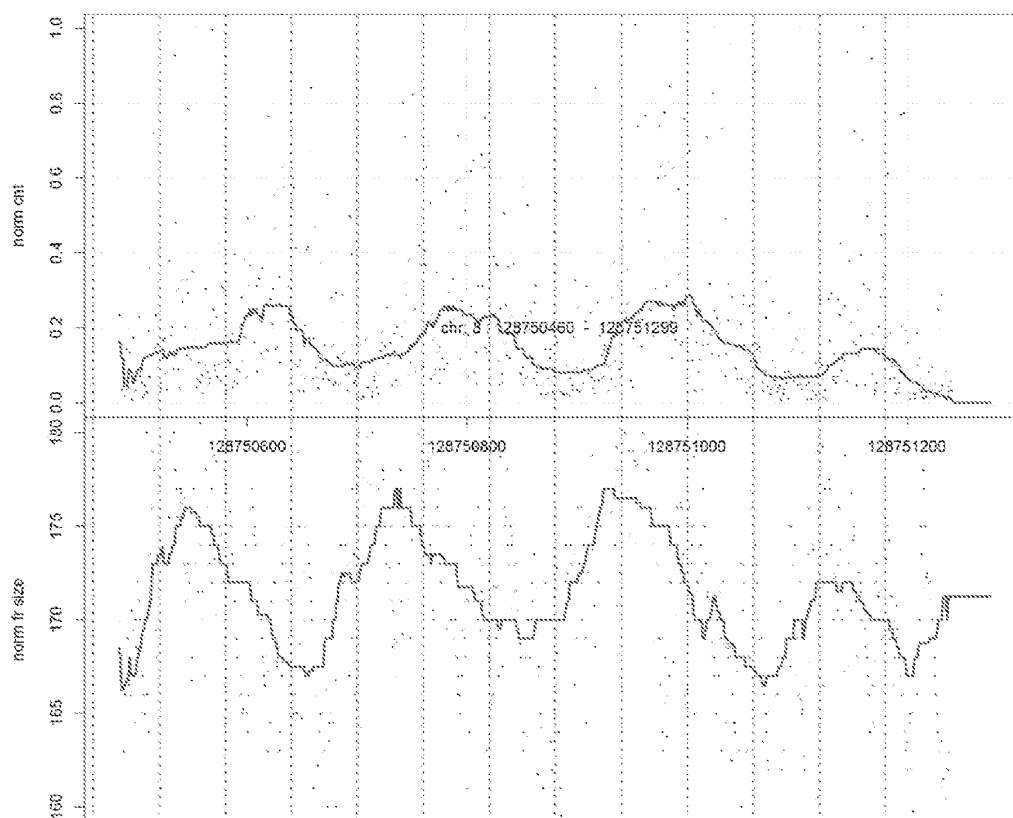


FIG. 10

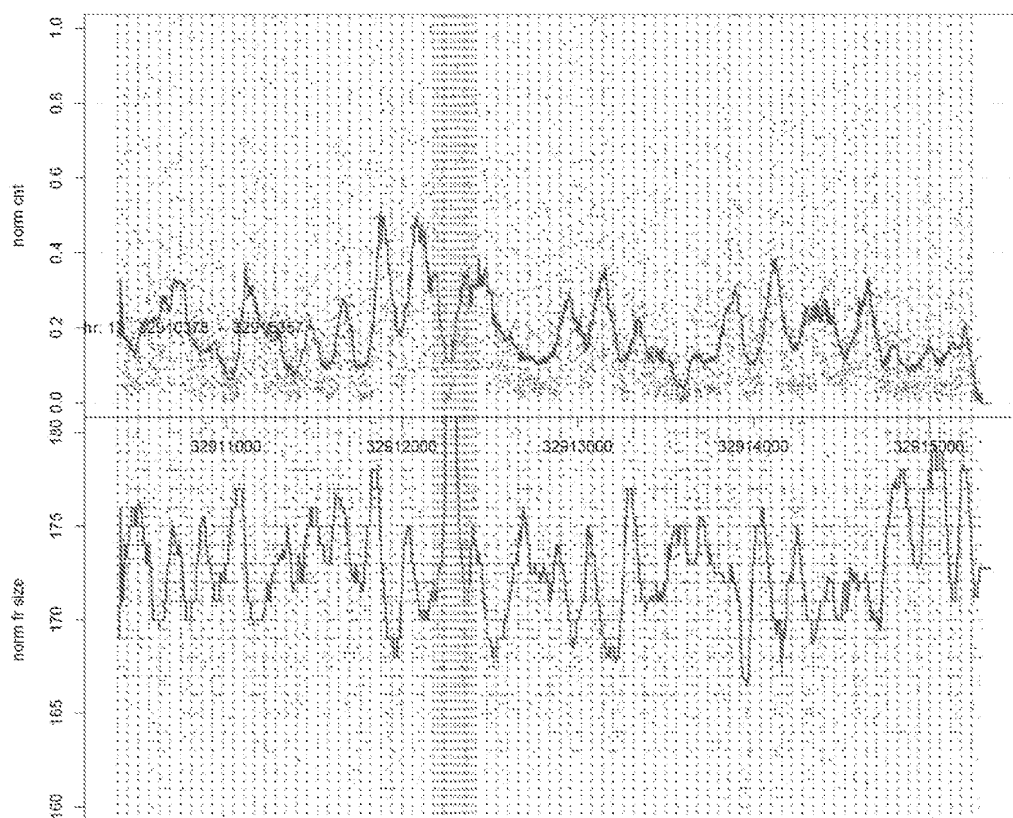


FIG. 11

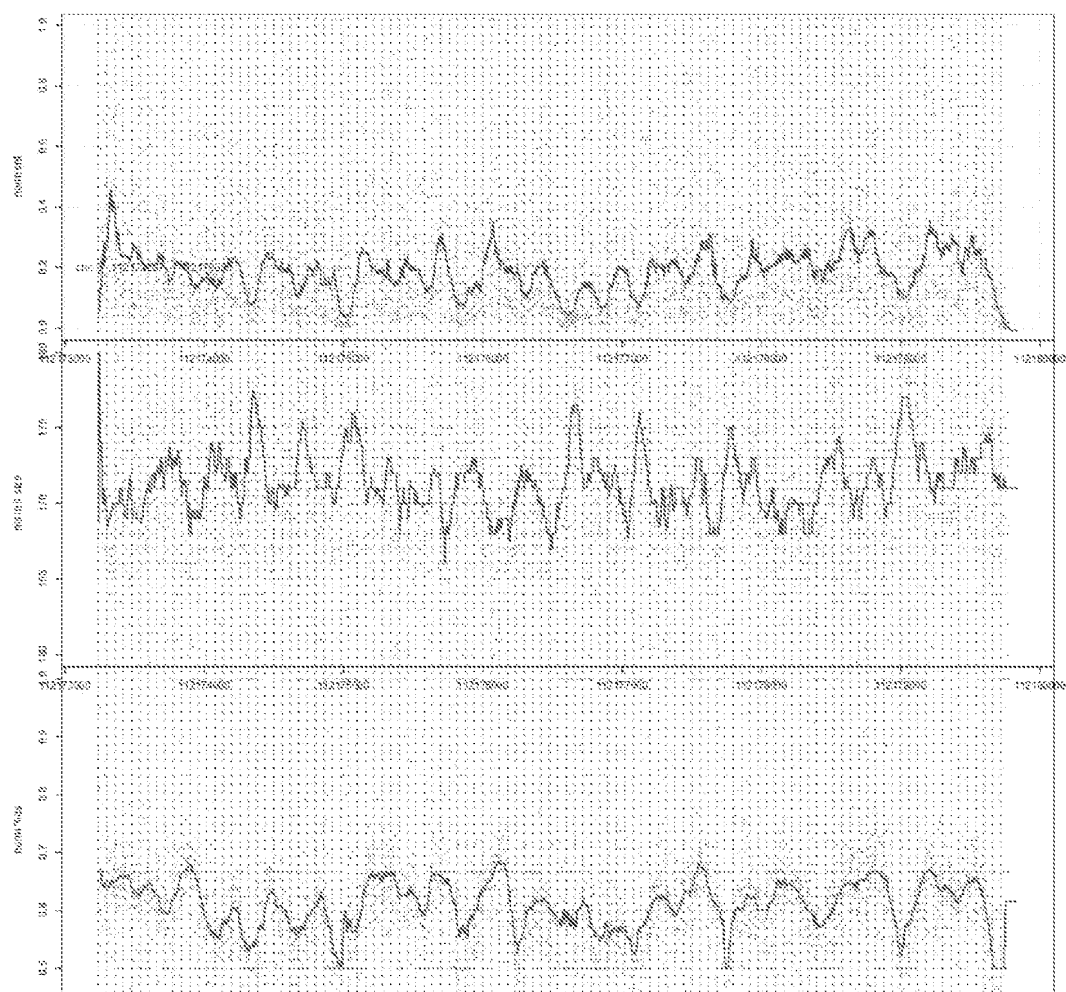


FIG. 12

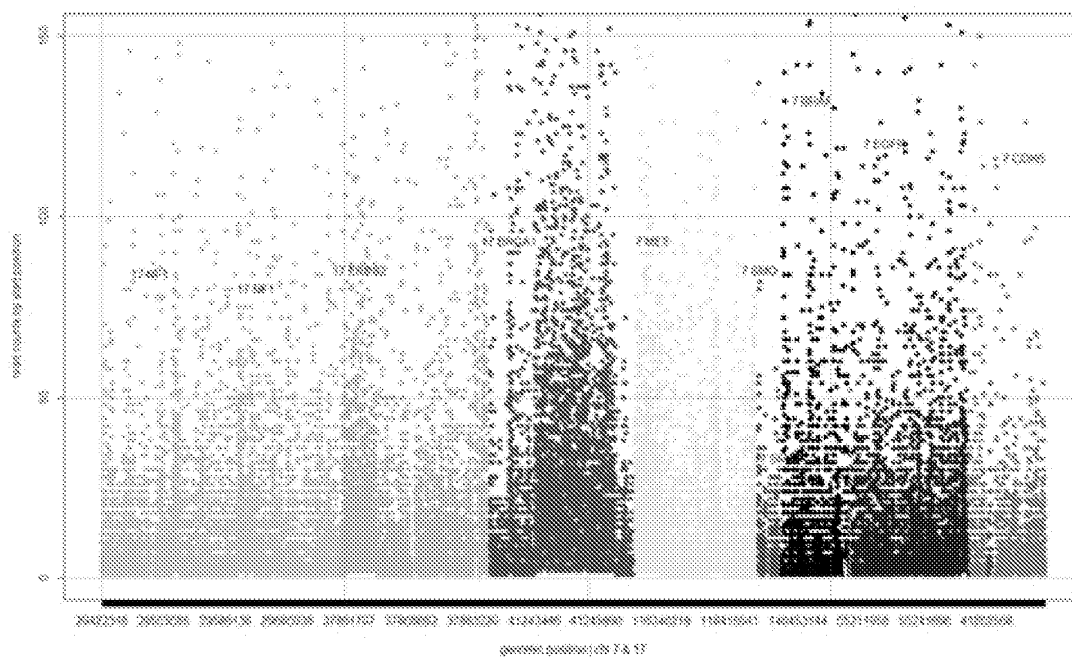


FIG. 13

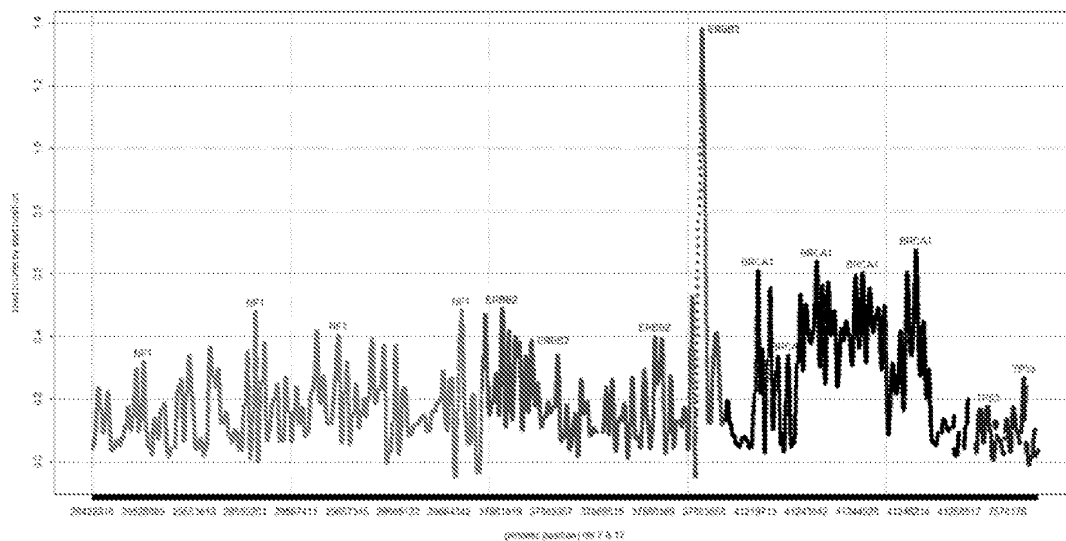


FIG. 14

# TP53

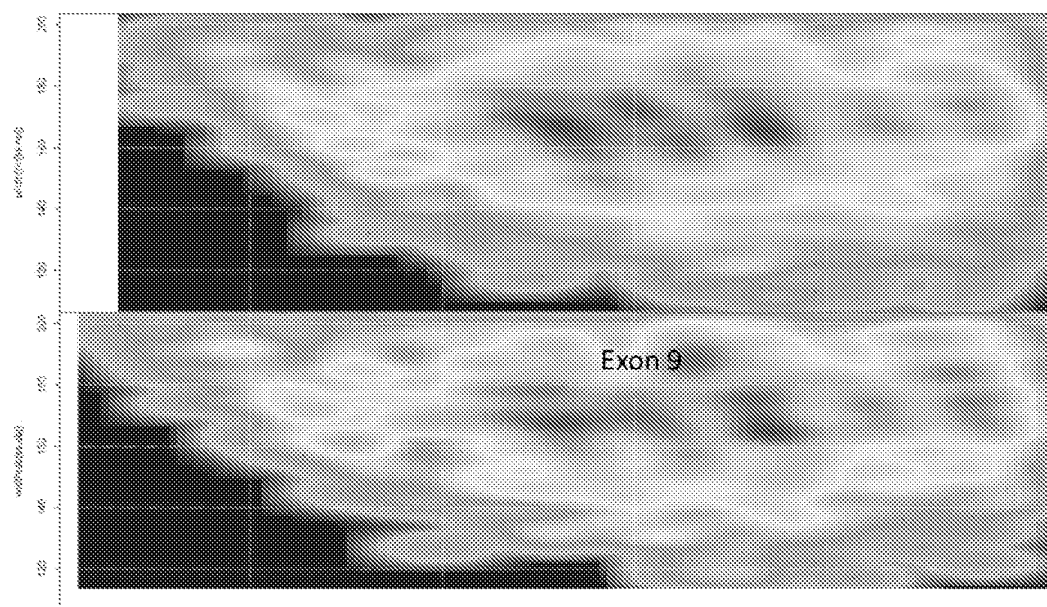
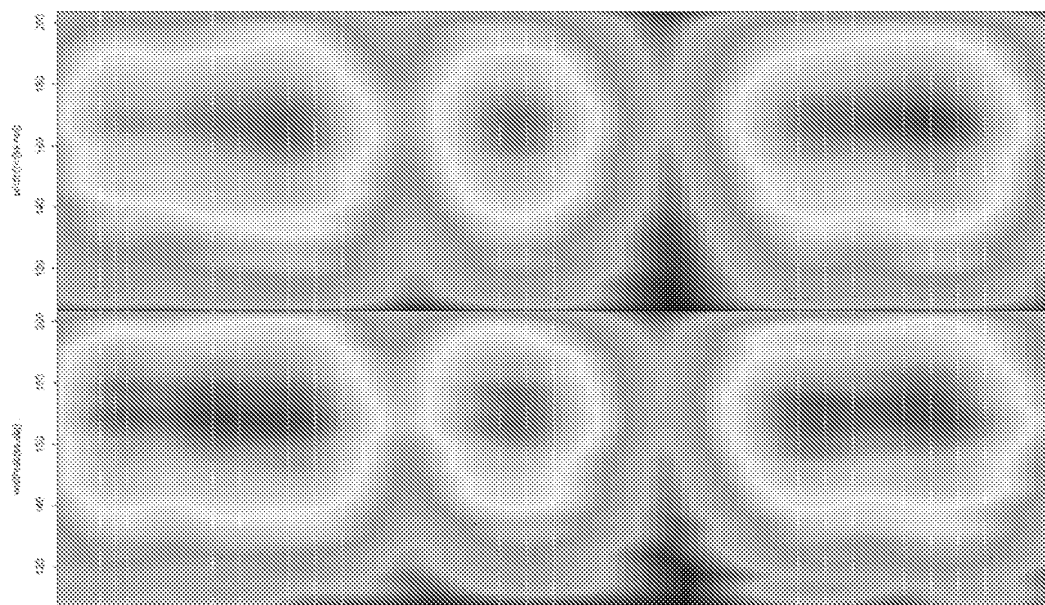


FIG. 15

# NF1

**FIG. 16**

erbb2

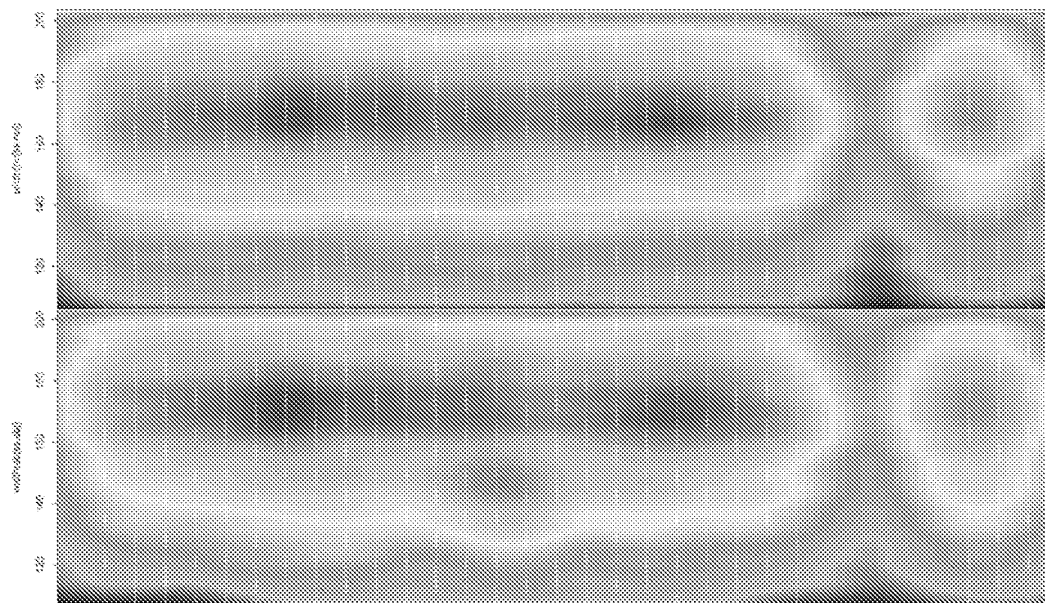


FIG. 17

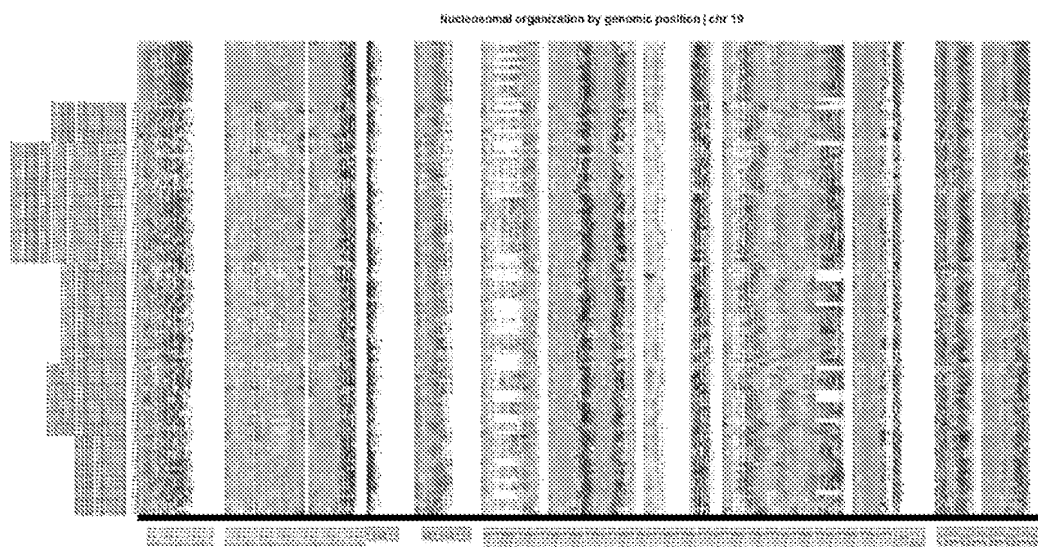


FIG. 18

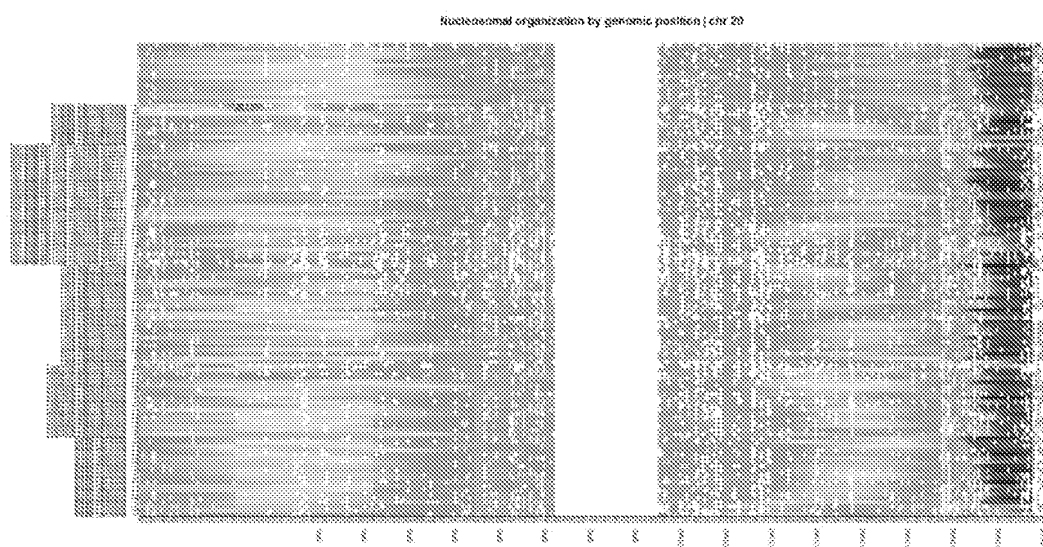
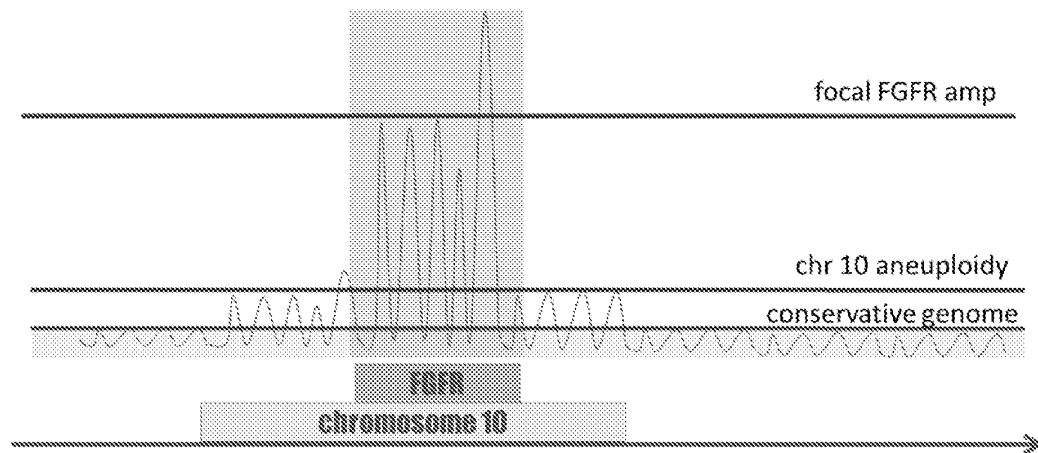


FIG. 19

# Absolute CN



Locate nuc locations and match them to expected in normal cohort

For every nuc window in FGFR

determine a collection of ultraconservative non-chr10 nuc sites (genomeUC)

determine a collection of ultraconservative chr10 nuc sites (ch10UC)

Integrate over pos vs insert size density of FGFR nuc site – (UC)x aneuploidy factor (ch10UC / genomeUC)

**FIG. 20**

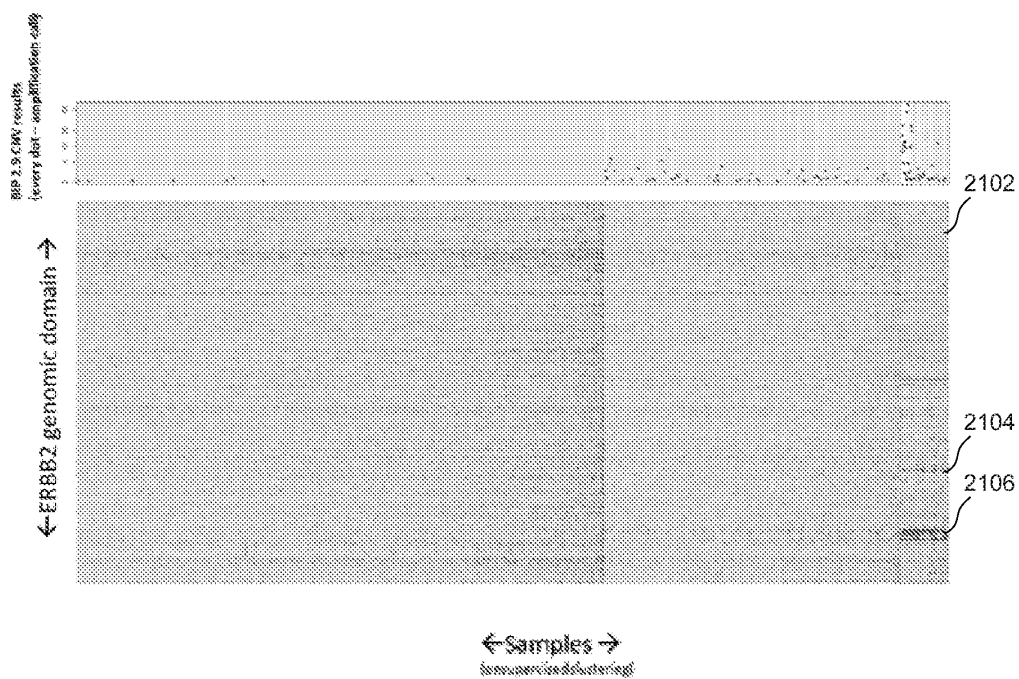


FIG. 21A

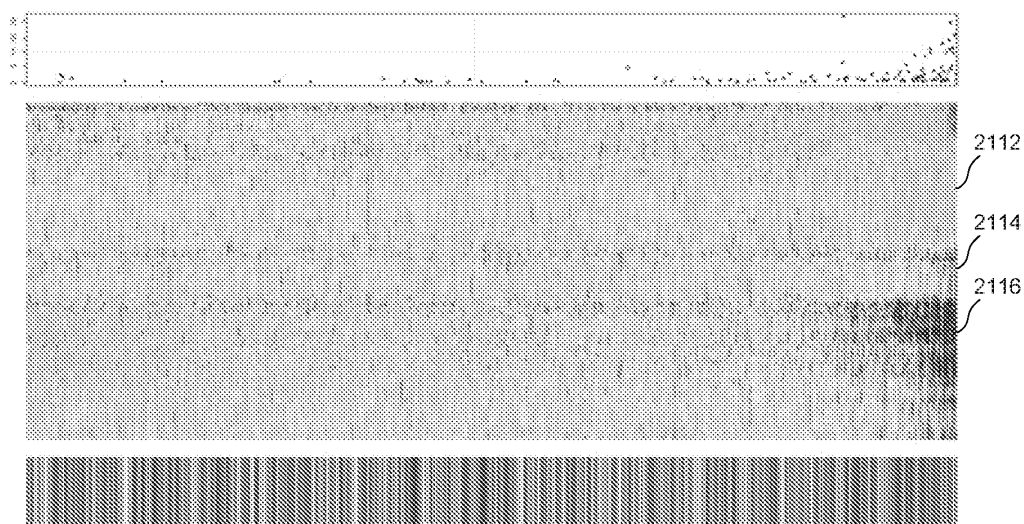


FIG. 21B

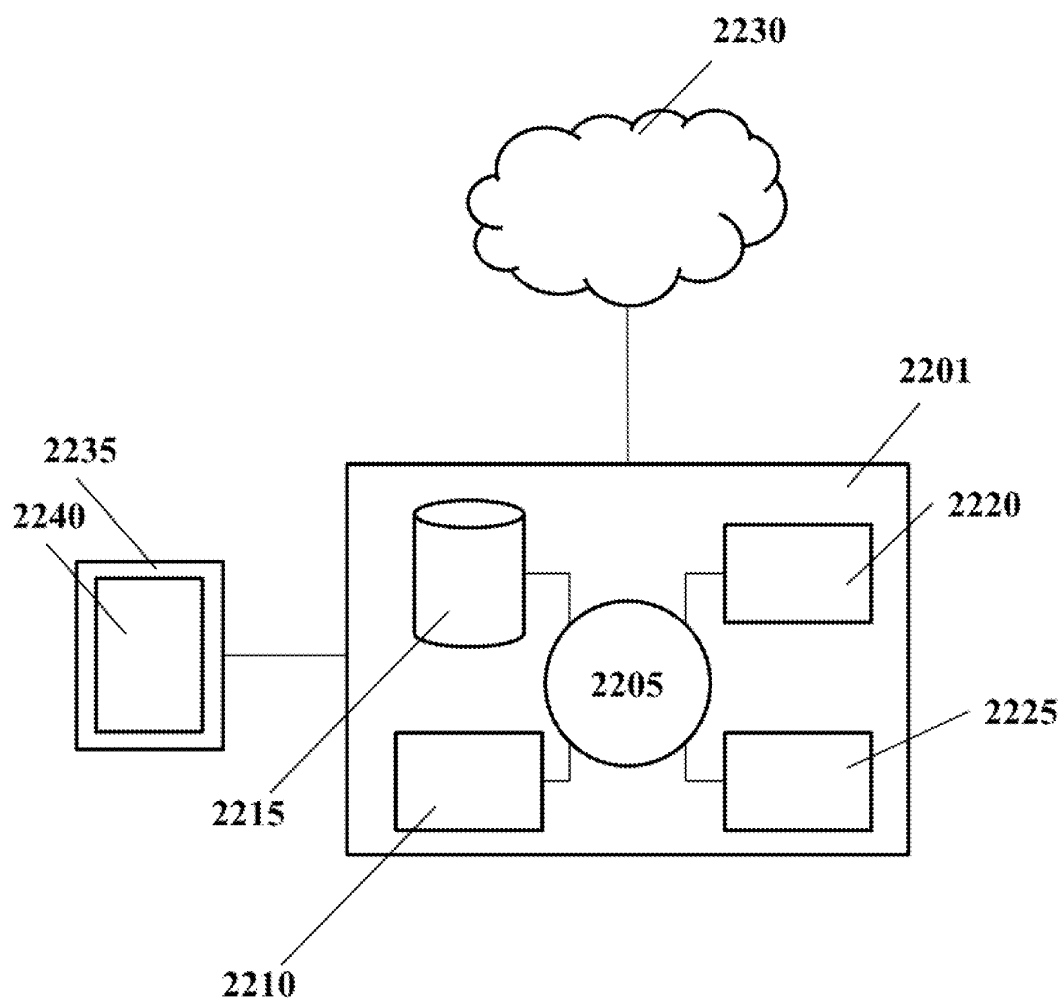


FIG. 22

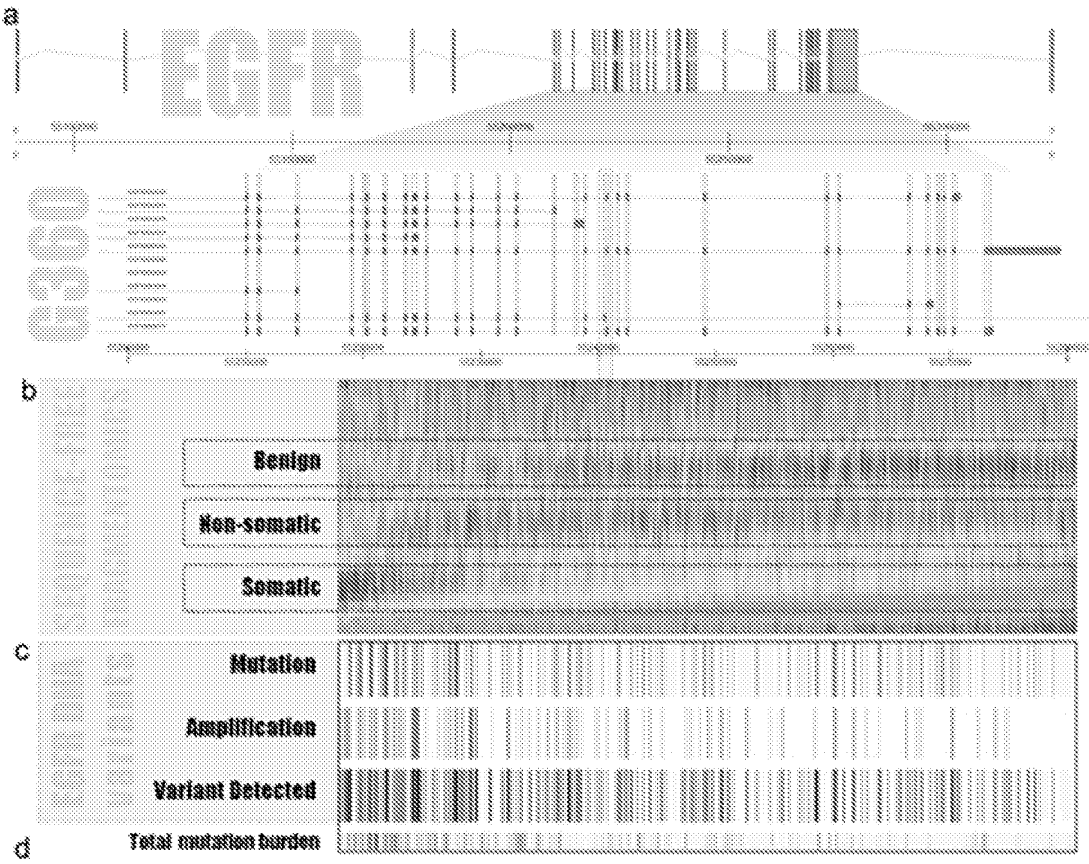


FIG. 23

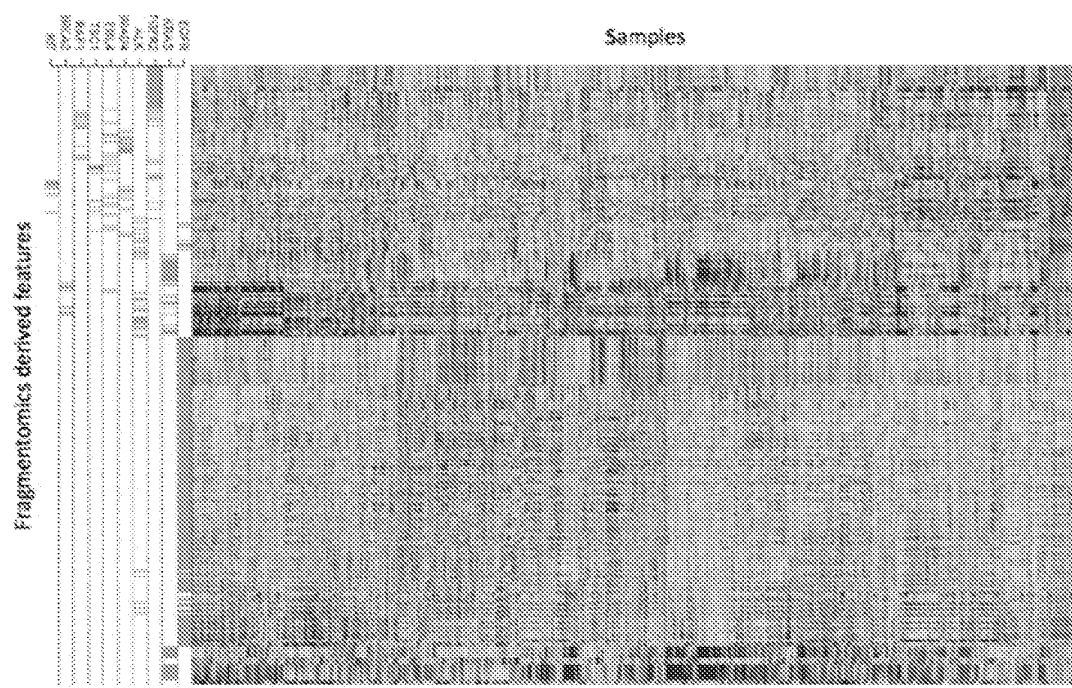


FIG. 24

$$p(\mathbf{X} = \mathbf{x} | \theta) = \sum_{k=1}^K \pi_k p(\mathbf{X} = \mathbf{x} | C = c_k, \theta_k)$$

where:

$\mathbf{X}$  is a multivariate random variable representing individual DNA fragment unit

$C$  is a categorical variable with a values from  $\{c_1 \dots c_K\}$  with one  $c$ 's being possibly cancer

$\pi_k$  is the marginal probability (the weight) of the  $k^{\text{th}}$  class

$\theta_k$  is the parameter estimates of the  $k^{\text{th}}$  class containing the probability distributions for each column/variable

FIG. 25

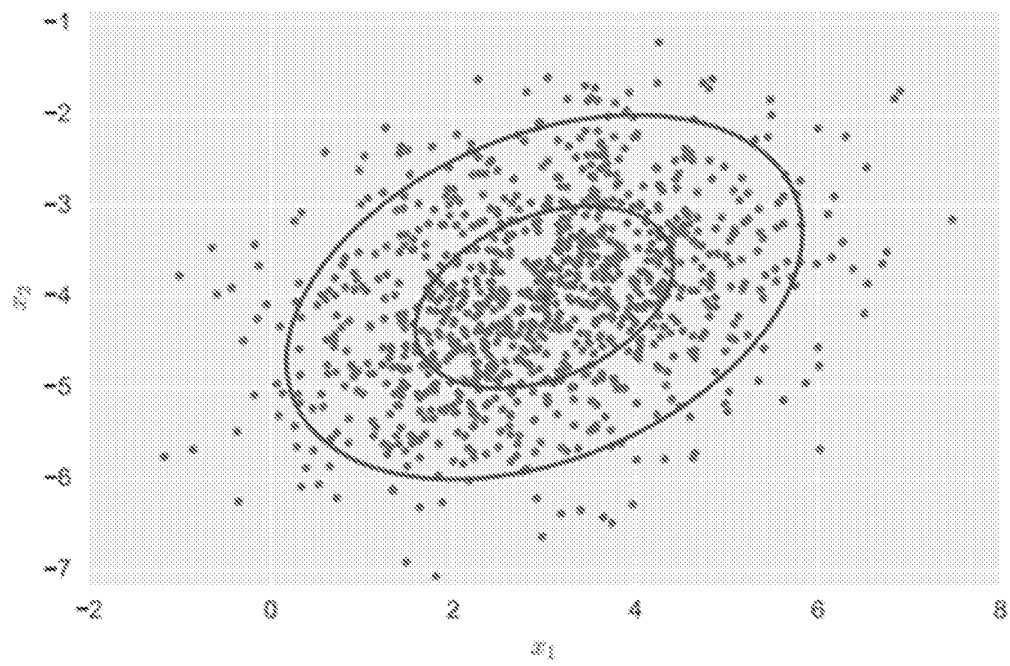


FIG. 26A

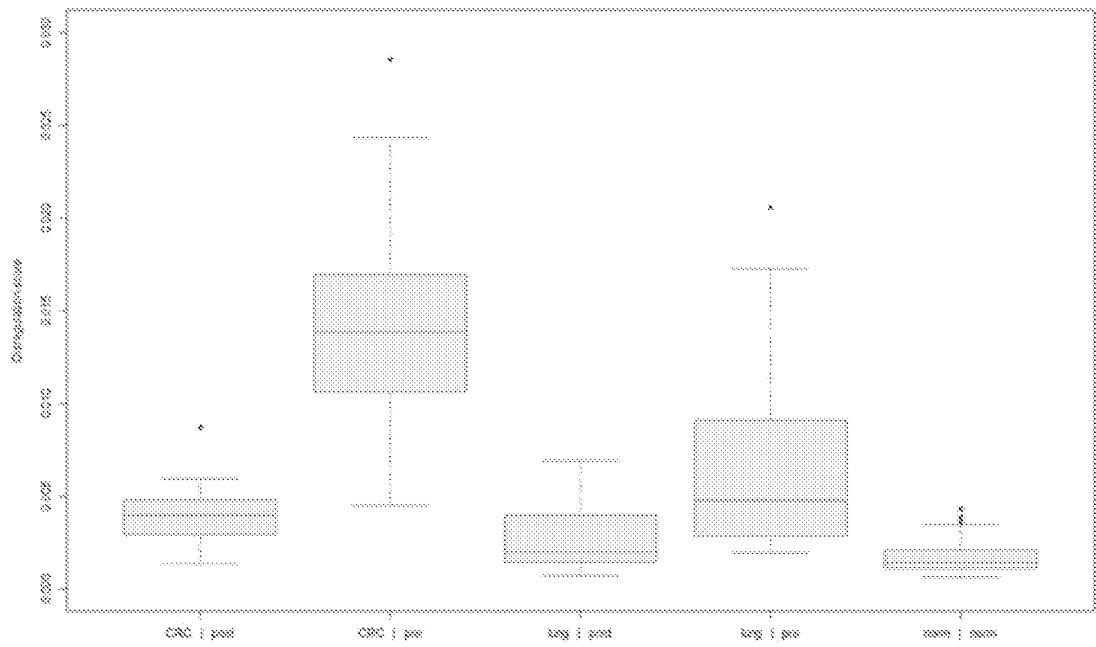


FIG. 26B

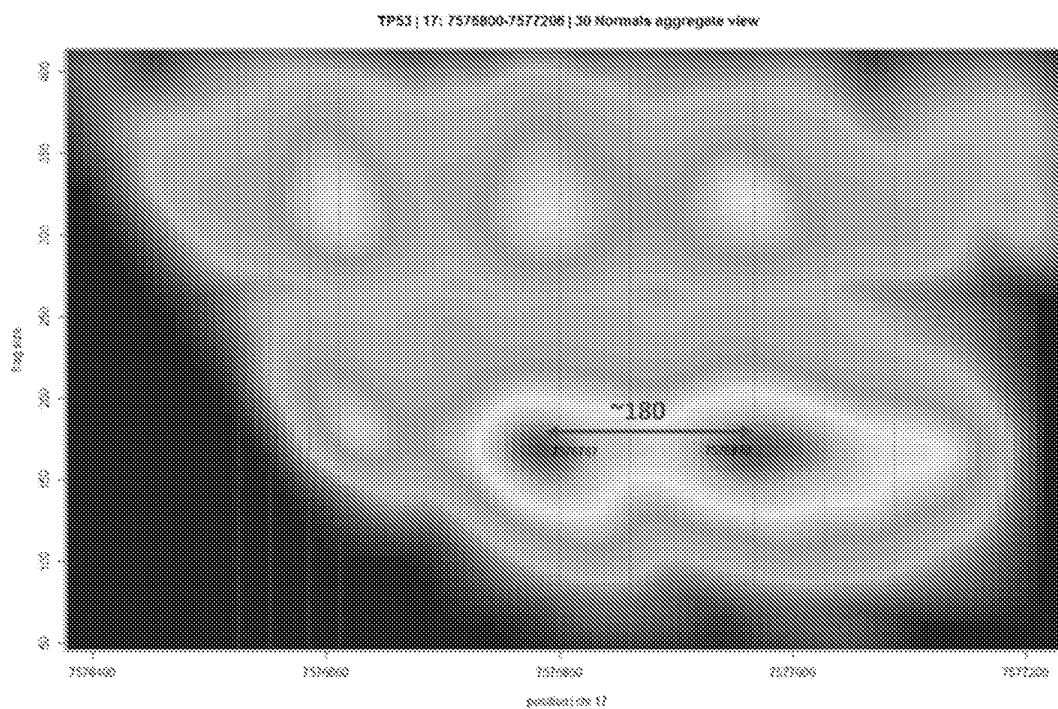


FIG. 27A

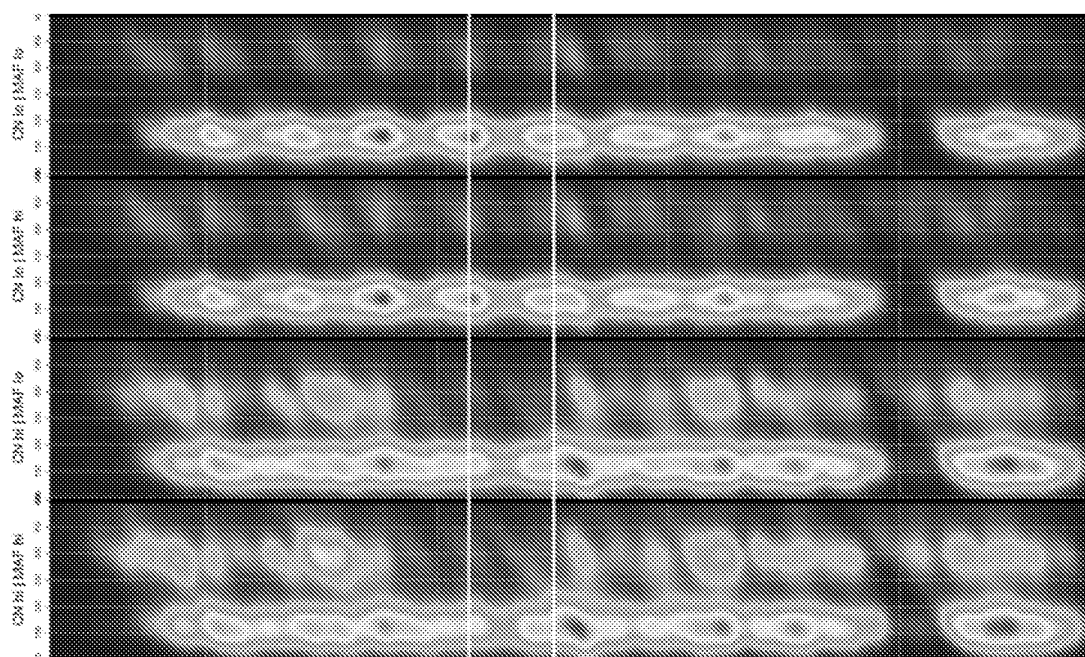


FIG. 27B

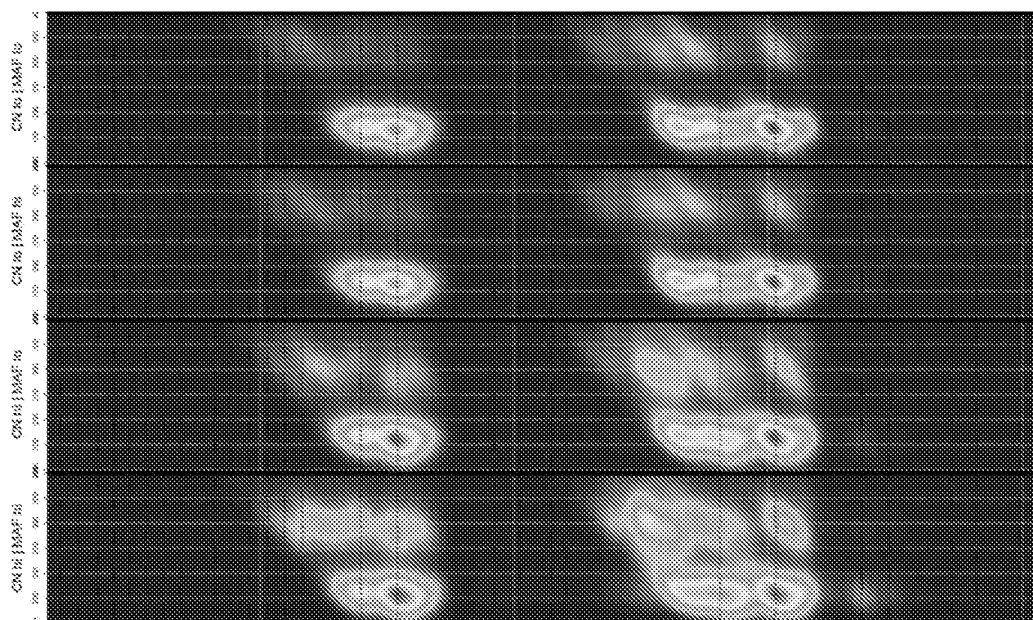


FIG. 27C

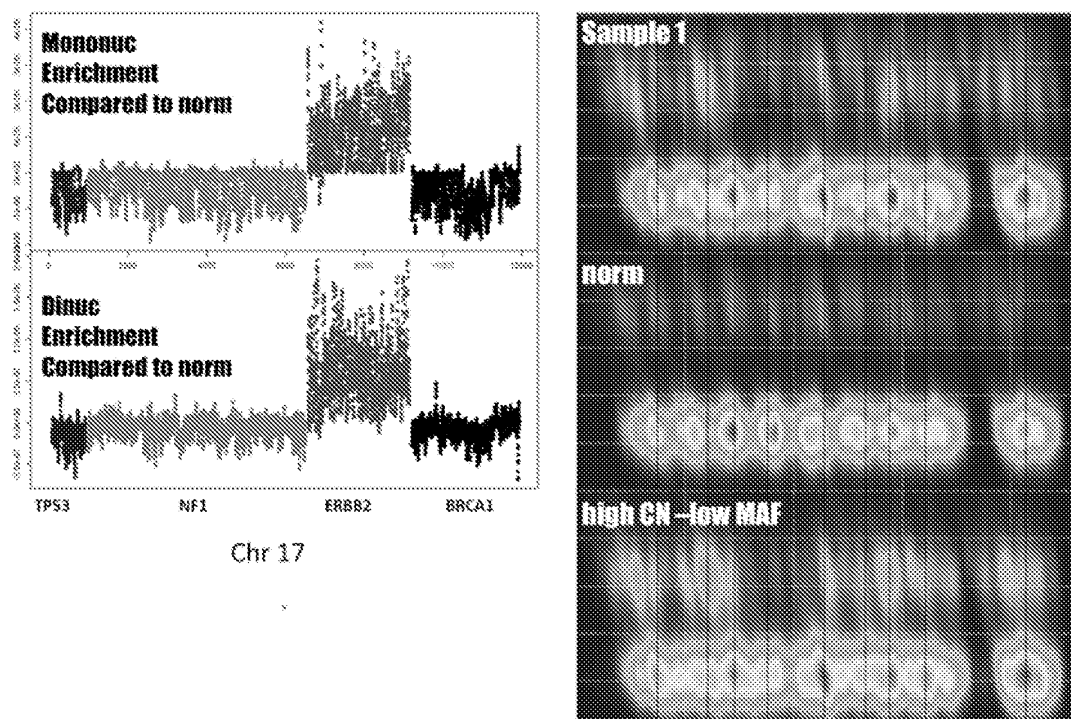


FIG. 28A

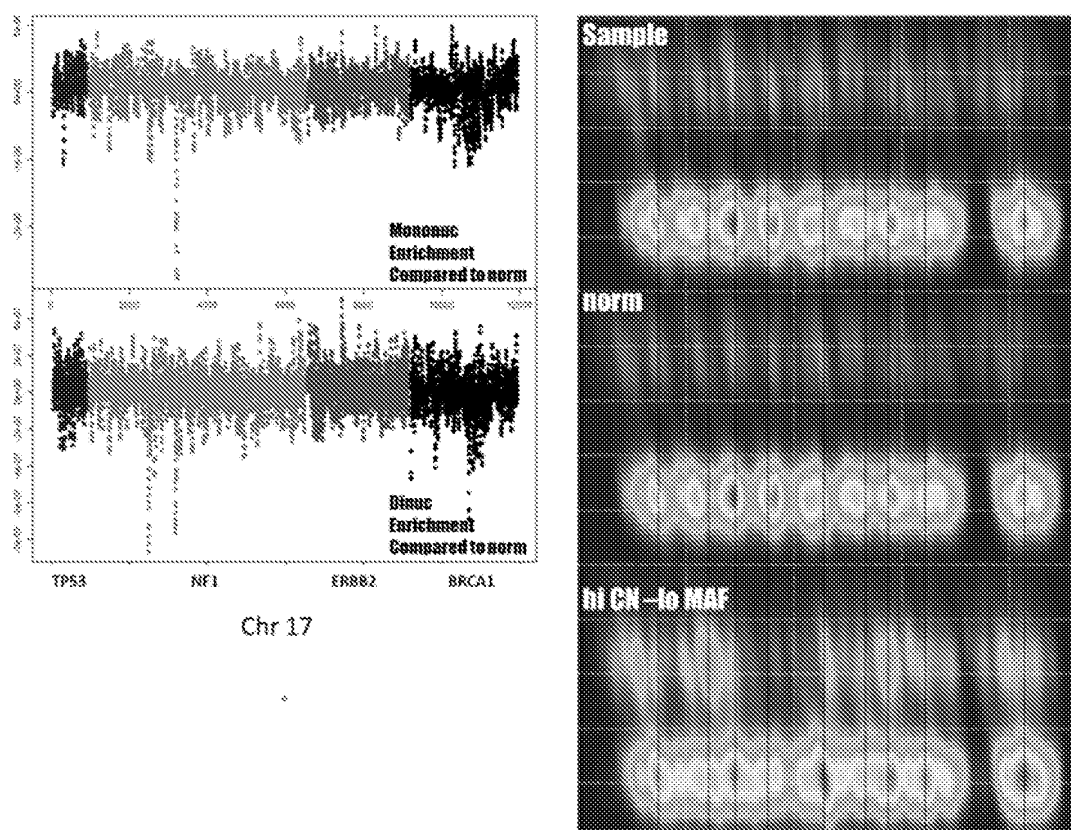


FIG. 28B

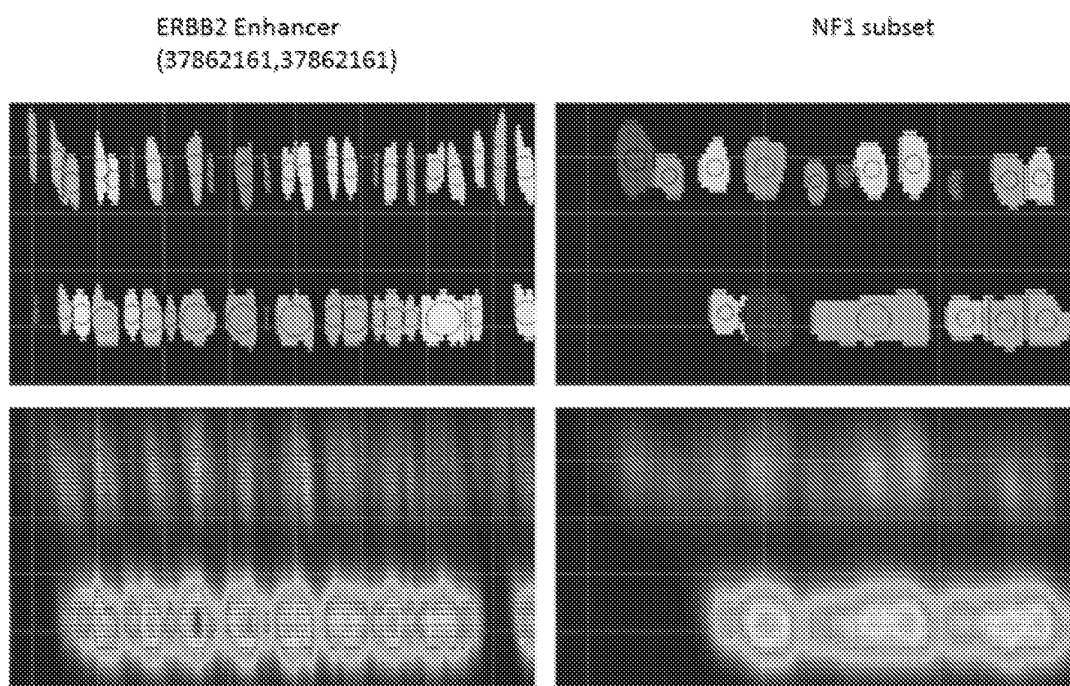


FIG. 29A

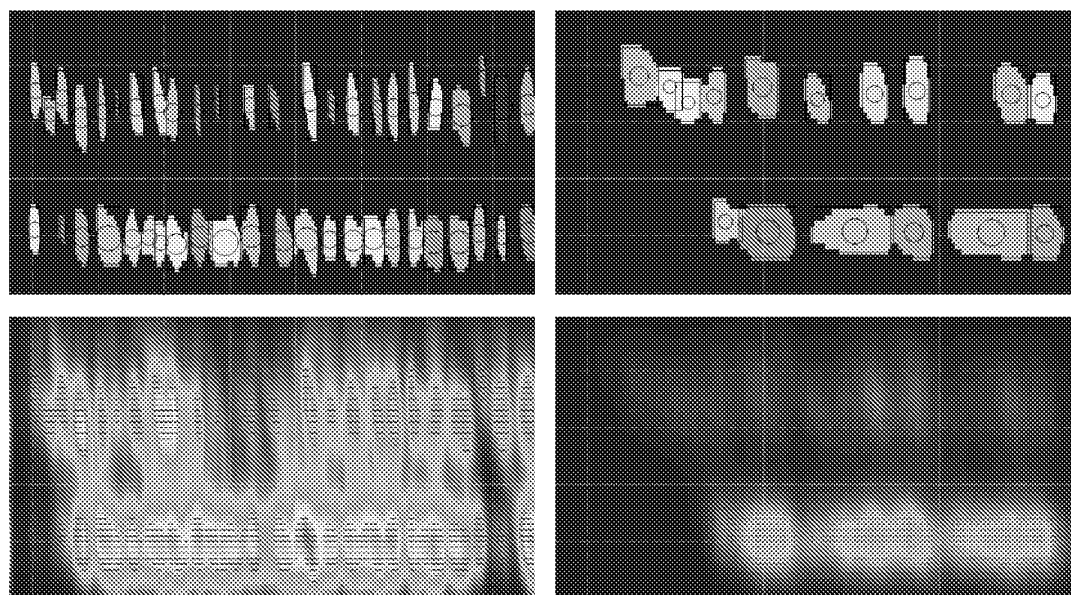


FIG. 29B

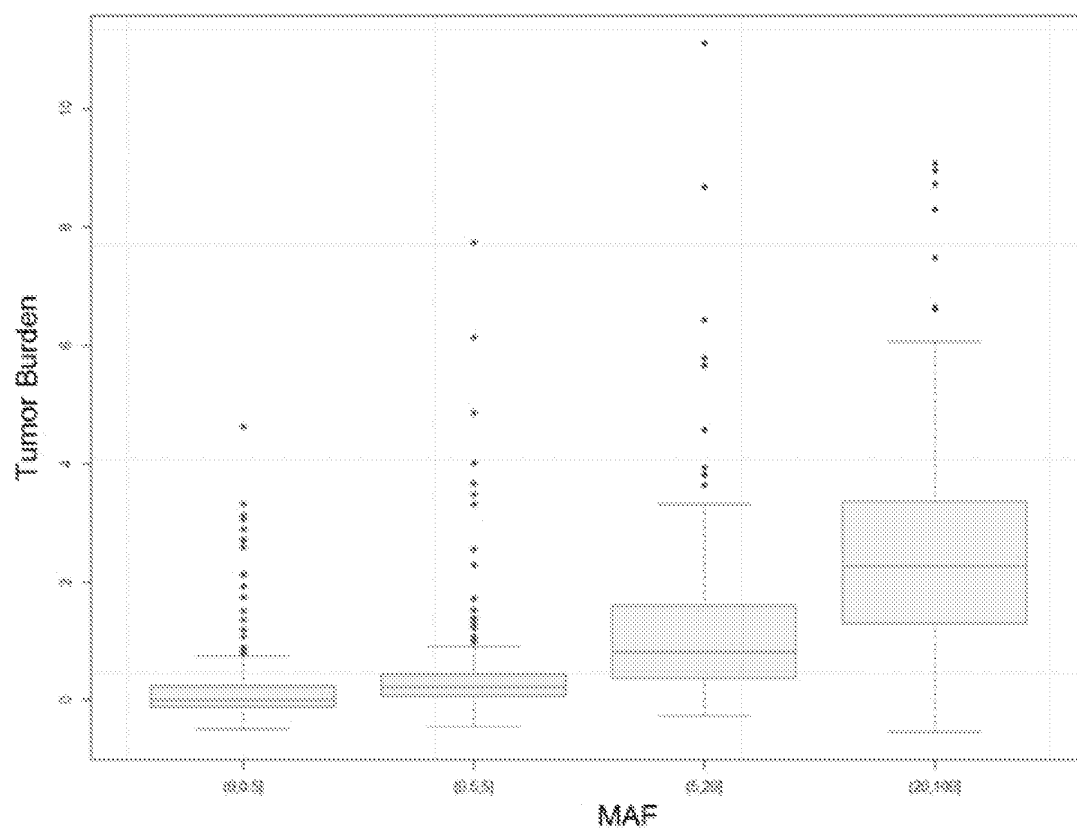


FIG. 30

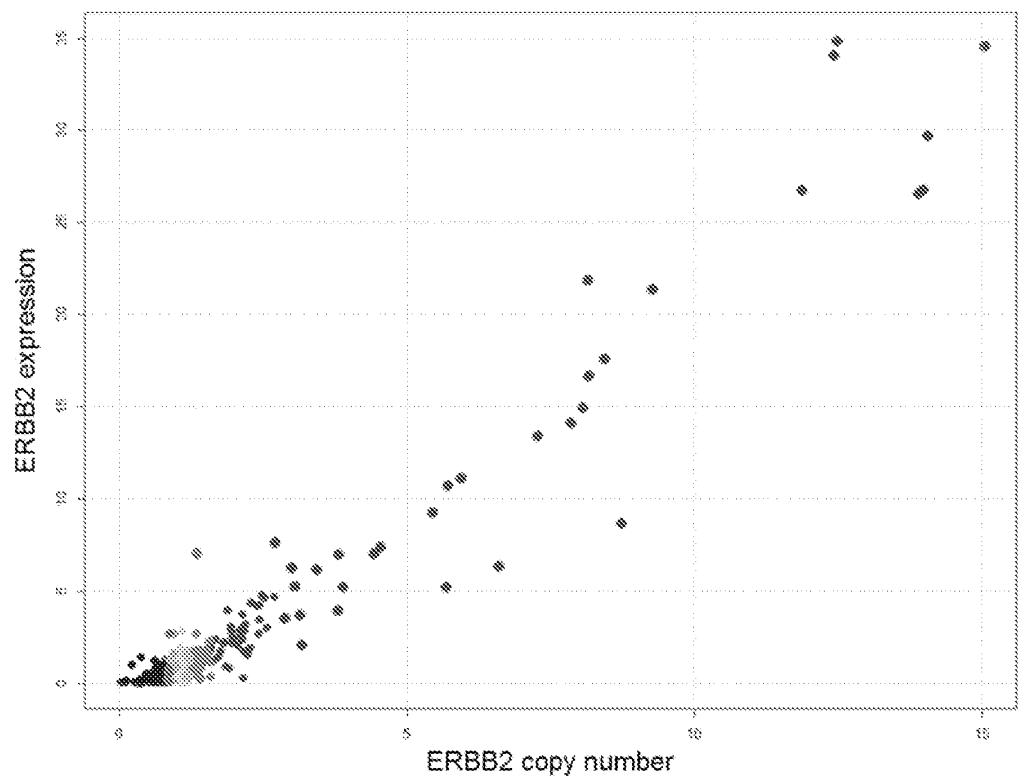
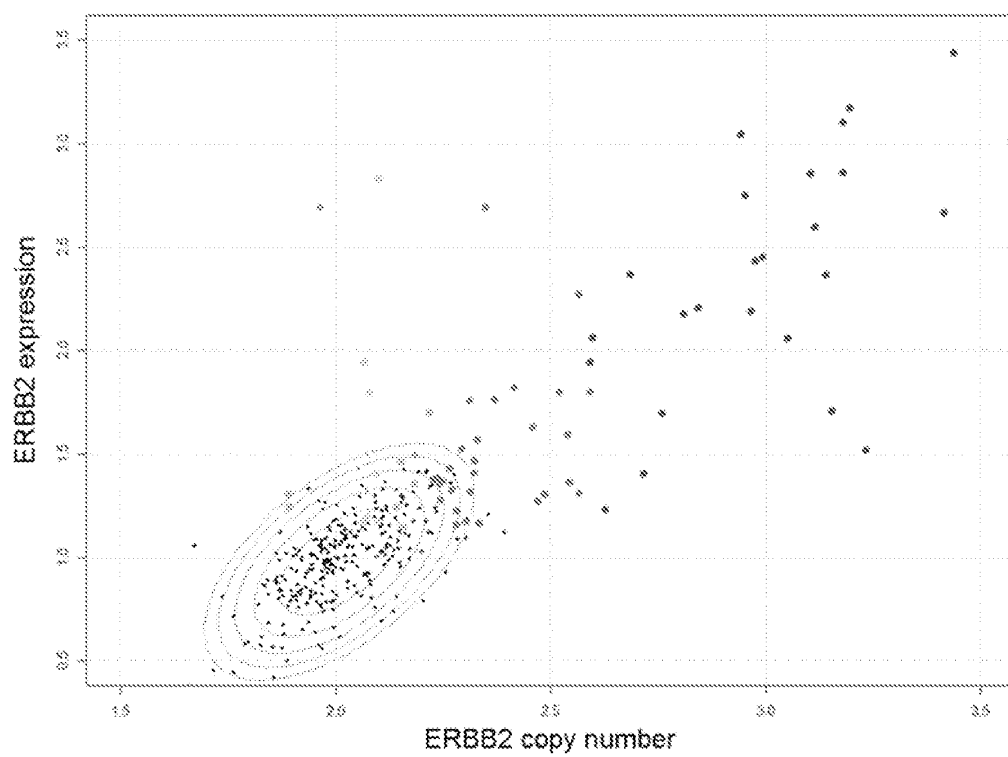


FIG. 31A

**FIG. 31B**

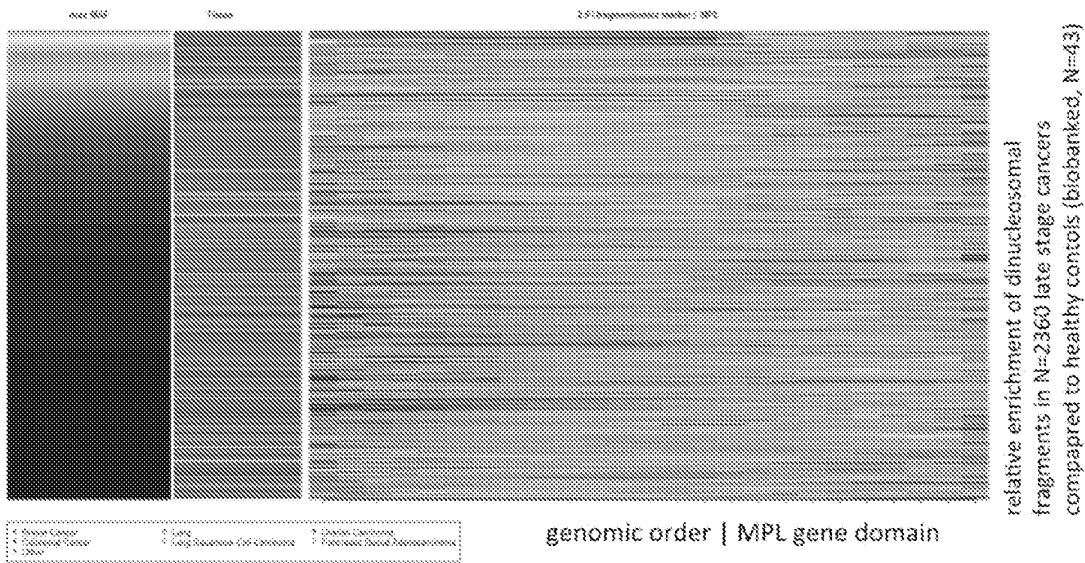


FIG. 32A

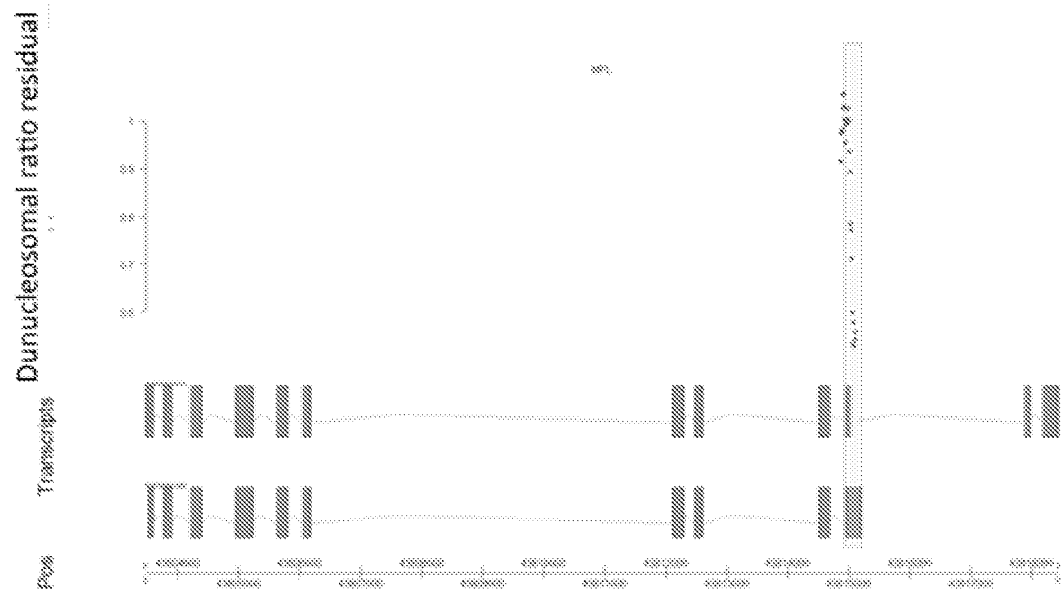


FIG. 32B

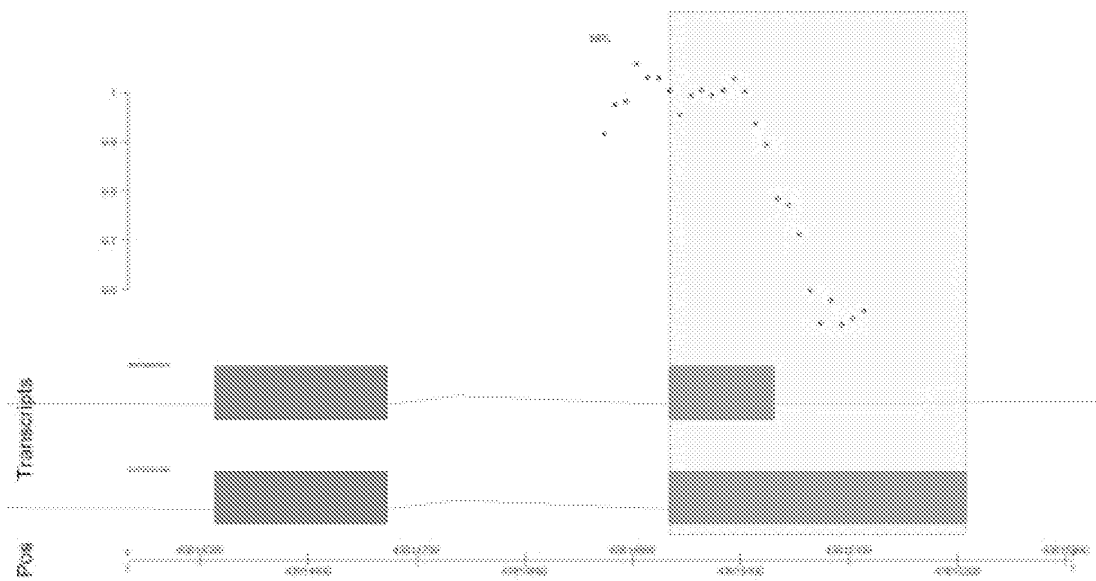


FIG. 32C