

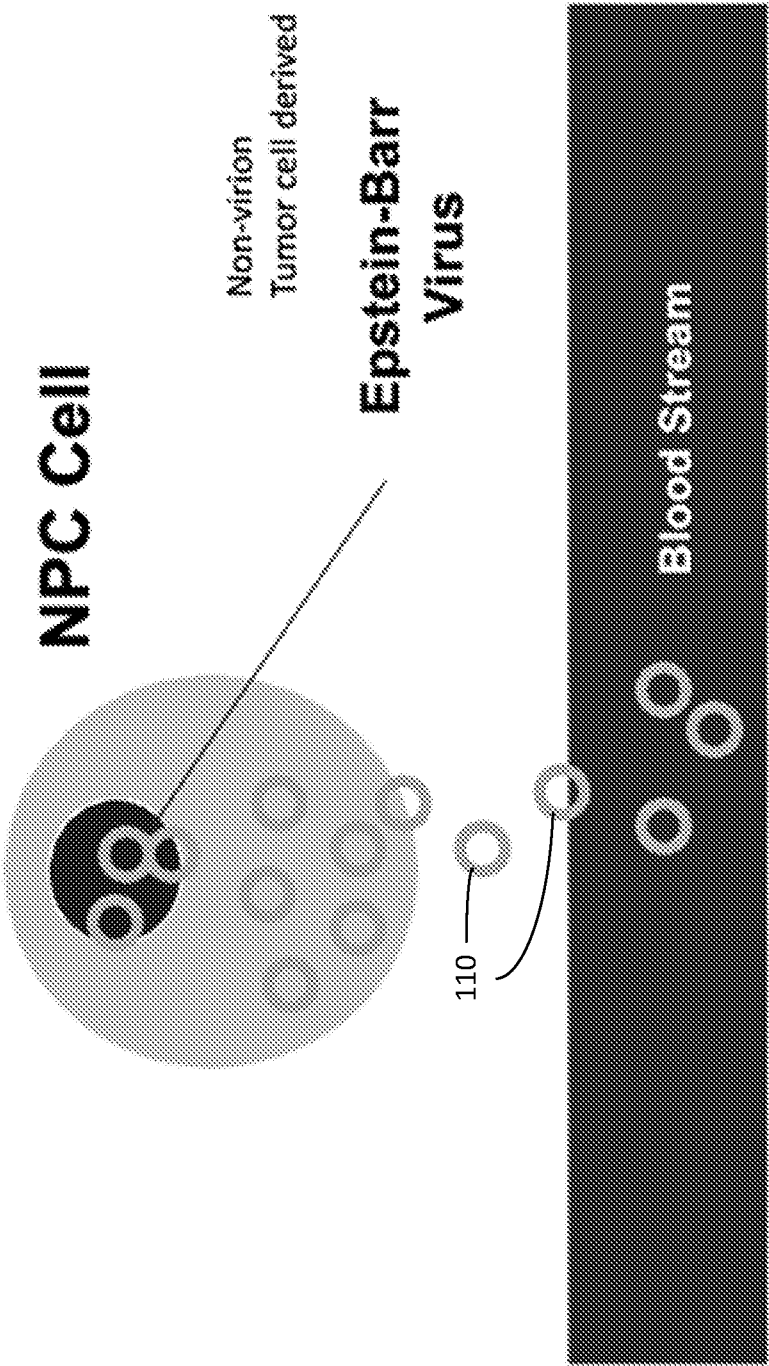
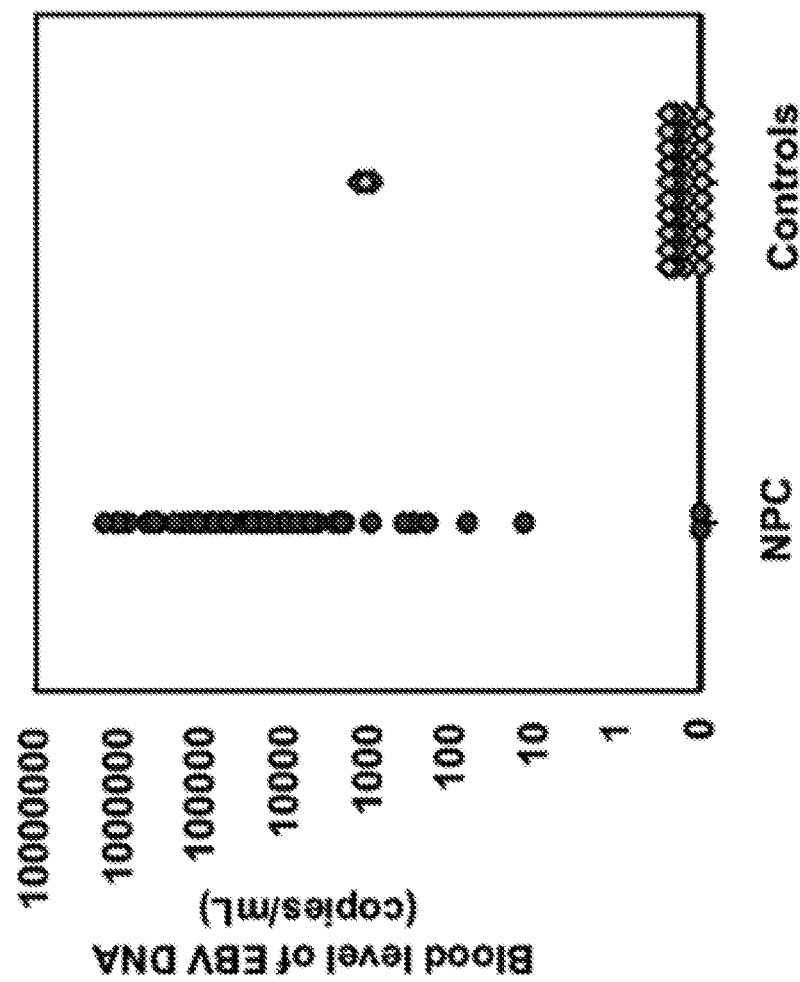


FIG. 1



Lo, Y. M. Dennis, et al. "Quantitative Analysis of Cell-free Epstein-Barr Virus DNA in Plasma of Patients with Nasopharyngeal Carcinoma." Cancer Research, March 1999.

FIG. 2

FIG. 3A

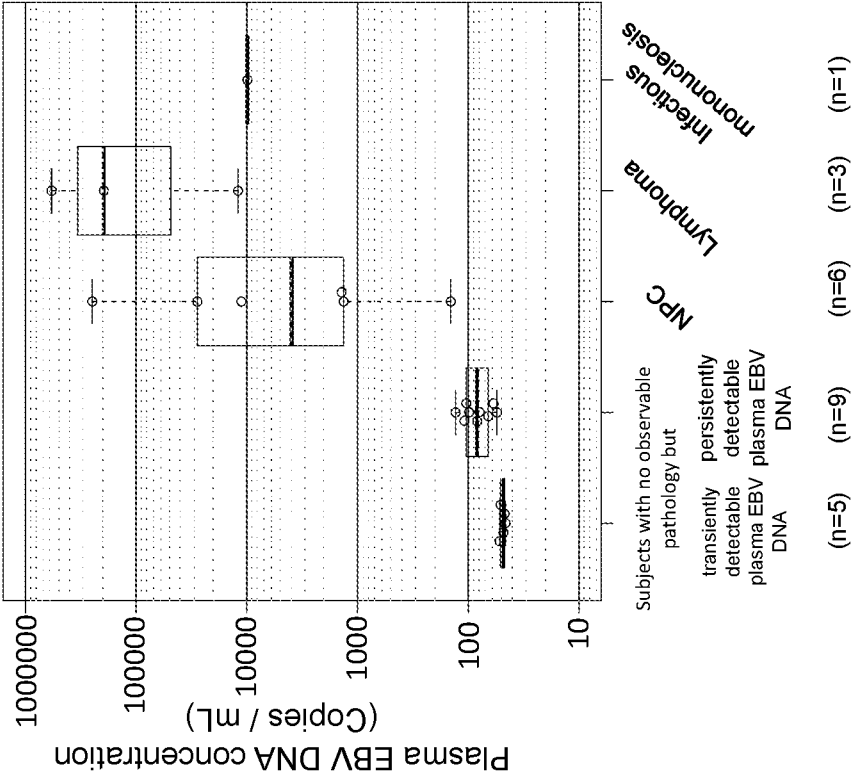
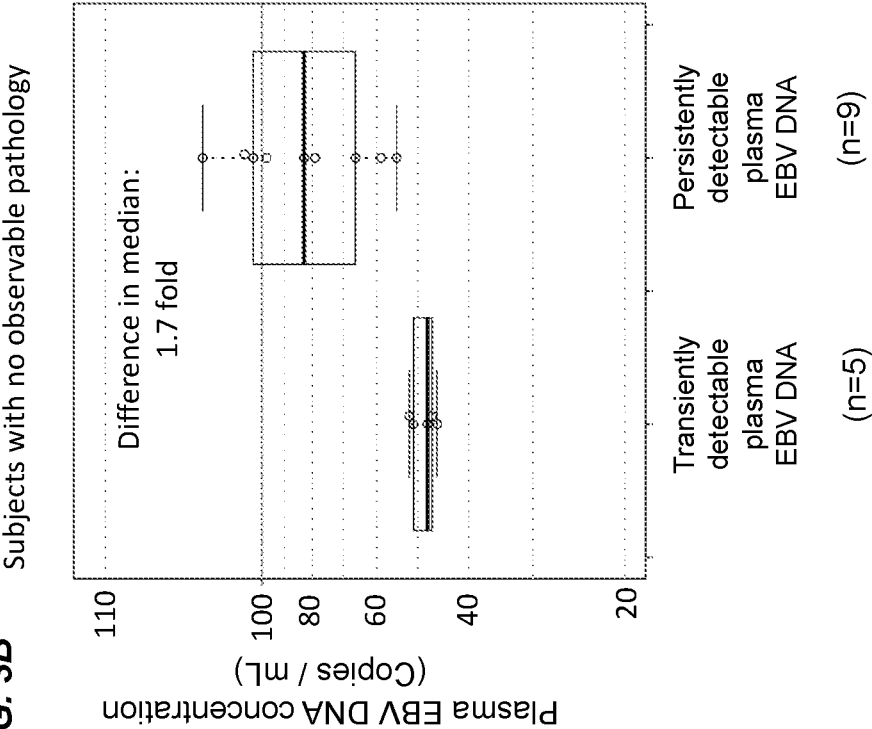
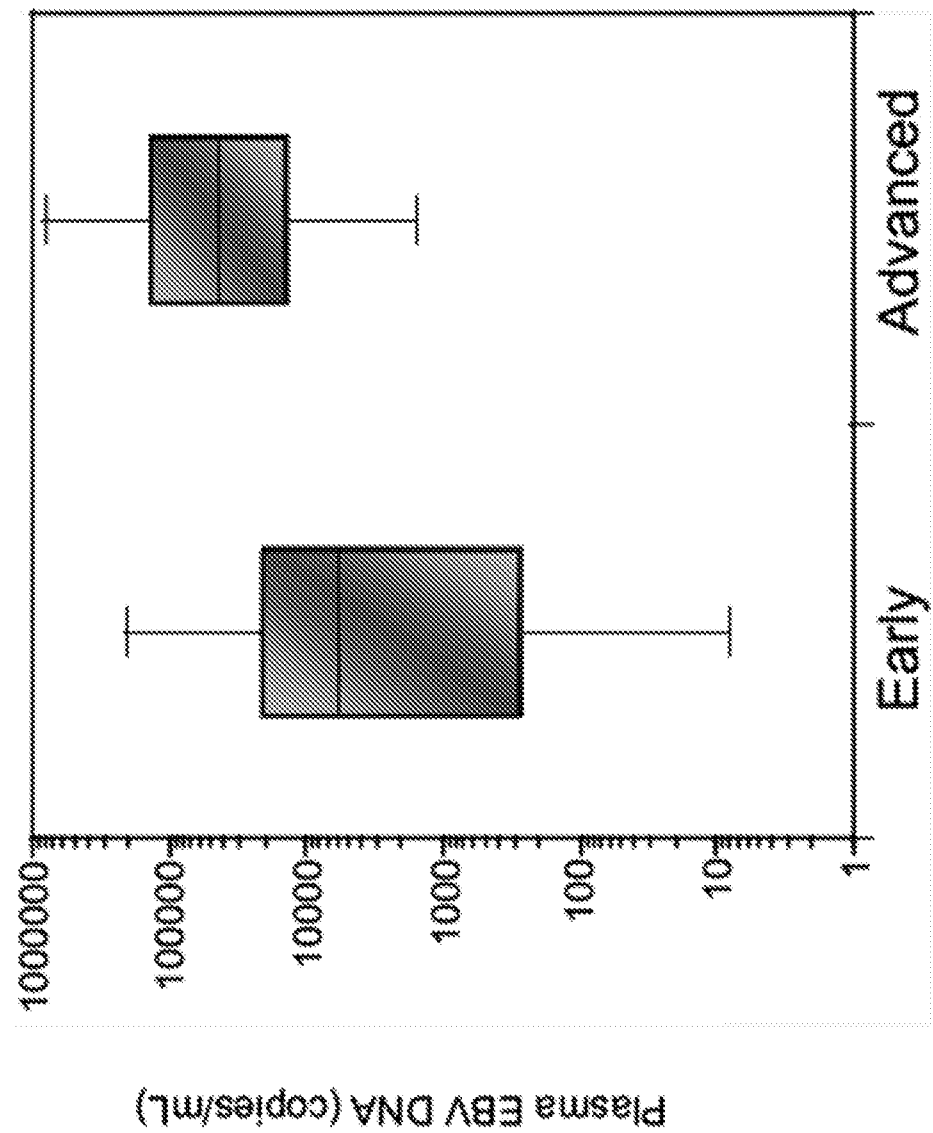


FIG. 3B





Lo, Y. M. Dennis, et al. "Quantitative Analysis of Cell-free Epstein-Barr Virus DNA in Plasma of Patients with Nasopharyngeal Carcinoma." *Cancer Research*, March 1999.

FIG. 4

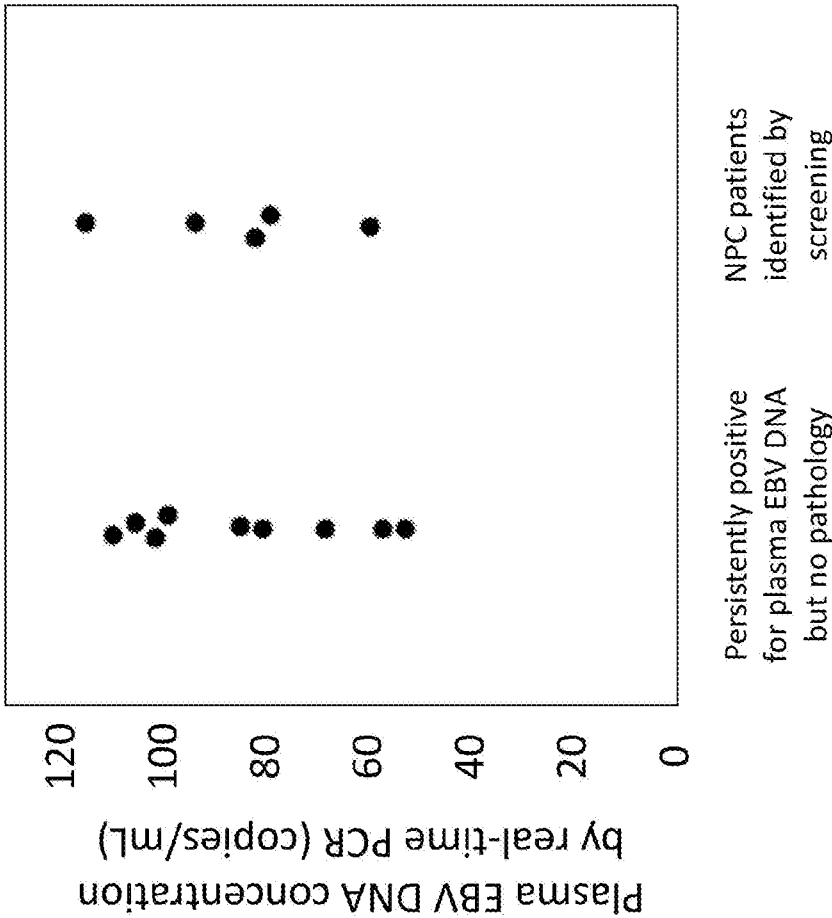


FIG. 5

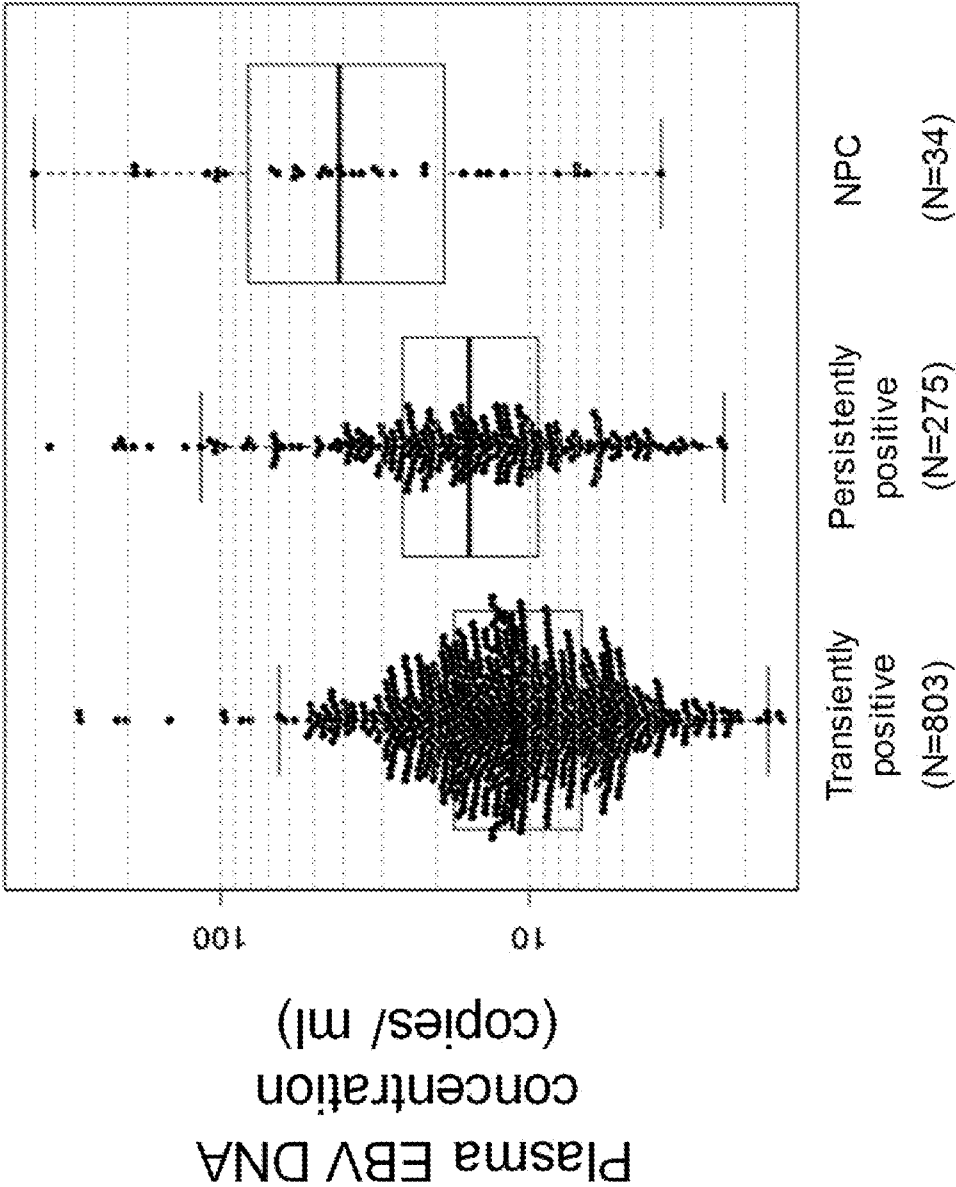


FIG. 6

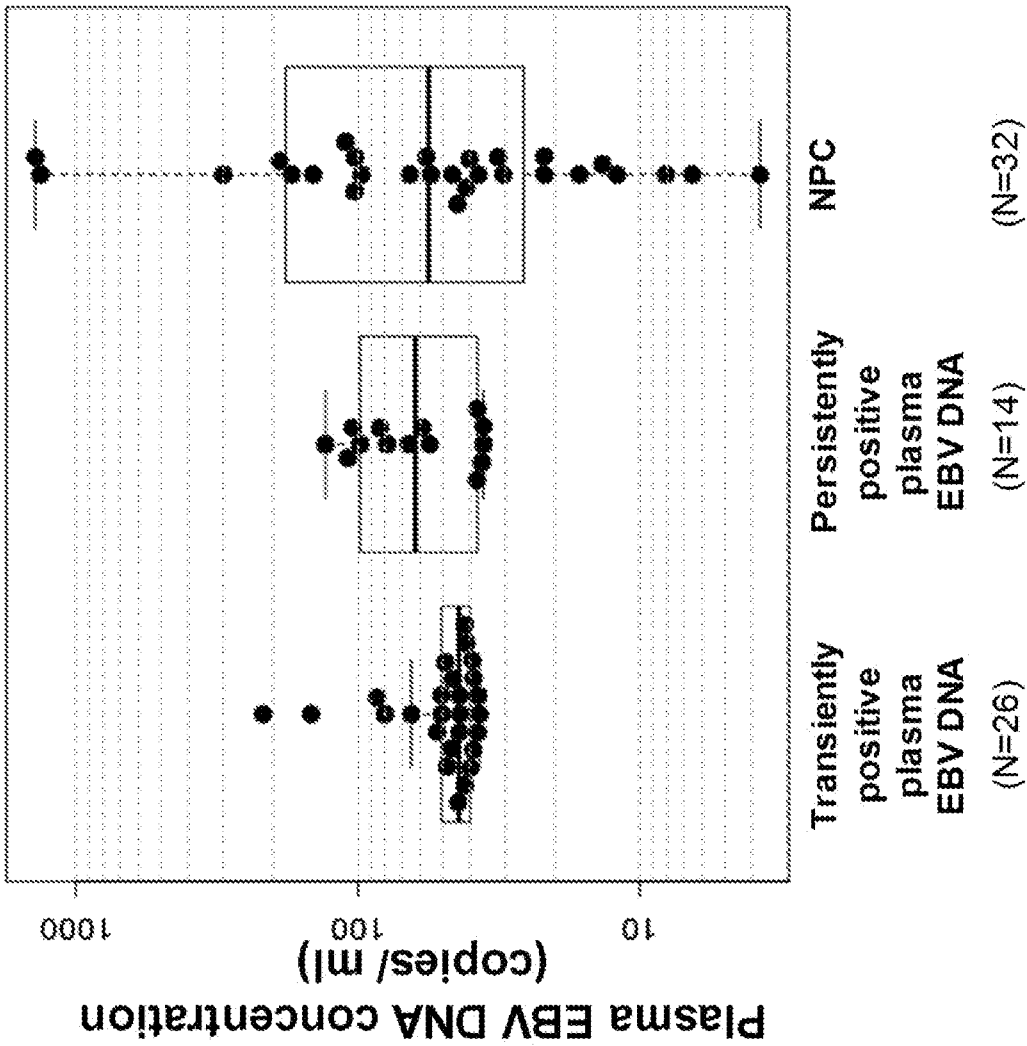


FIG. 7

FIG. 8A

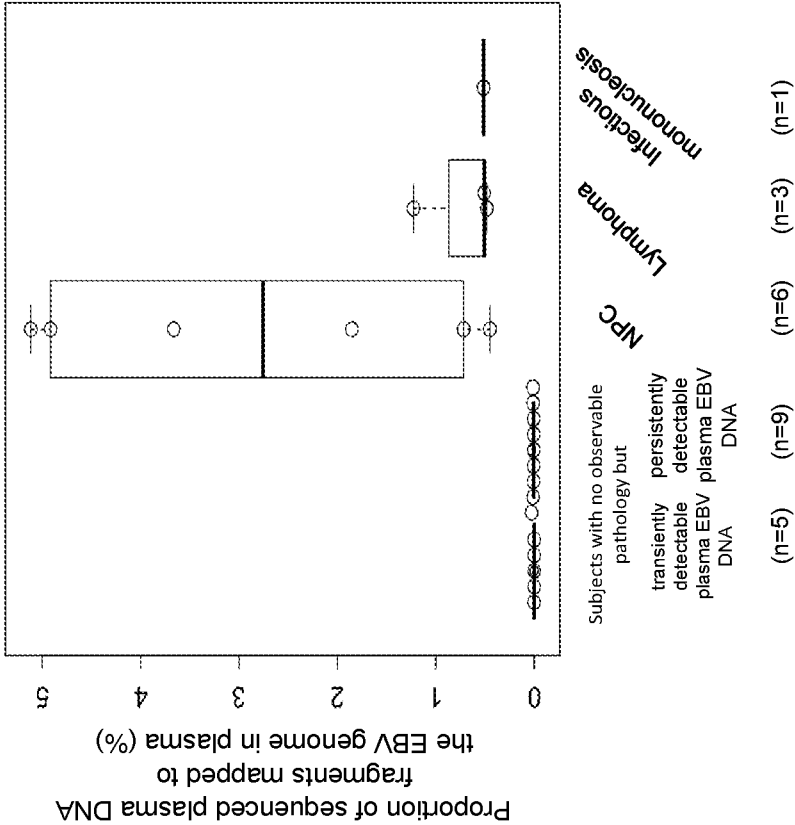
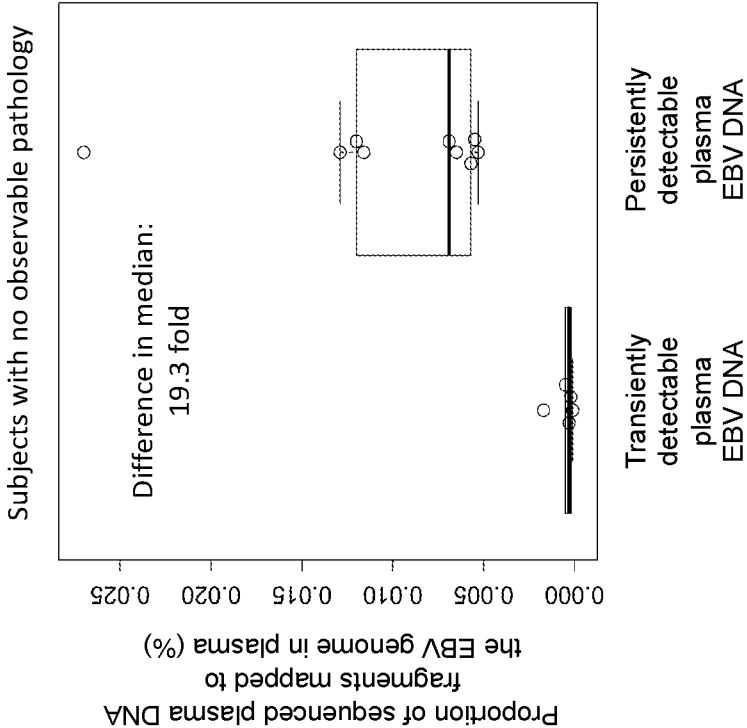


FIG. 8B



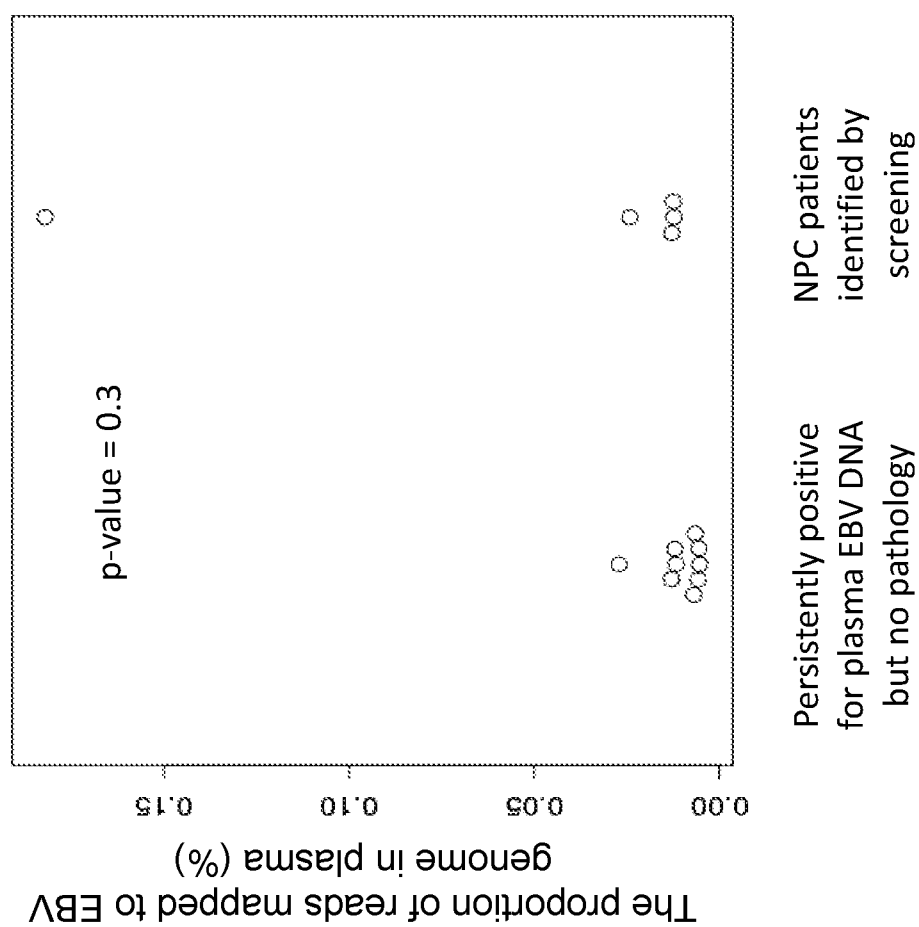
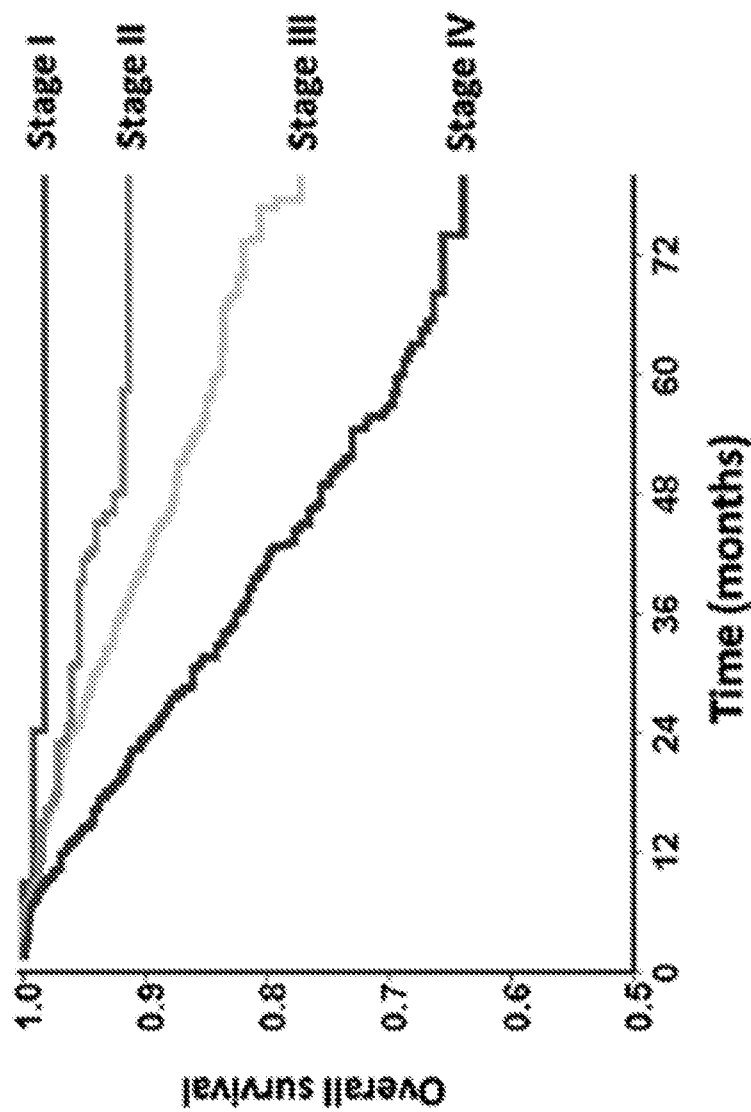
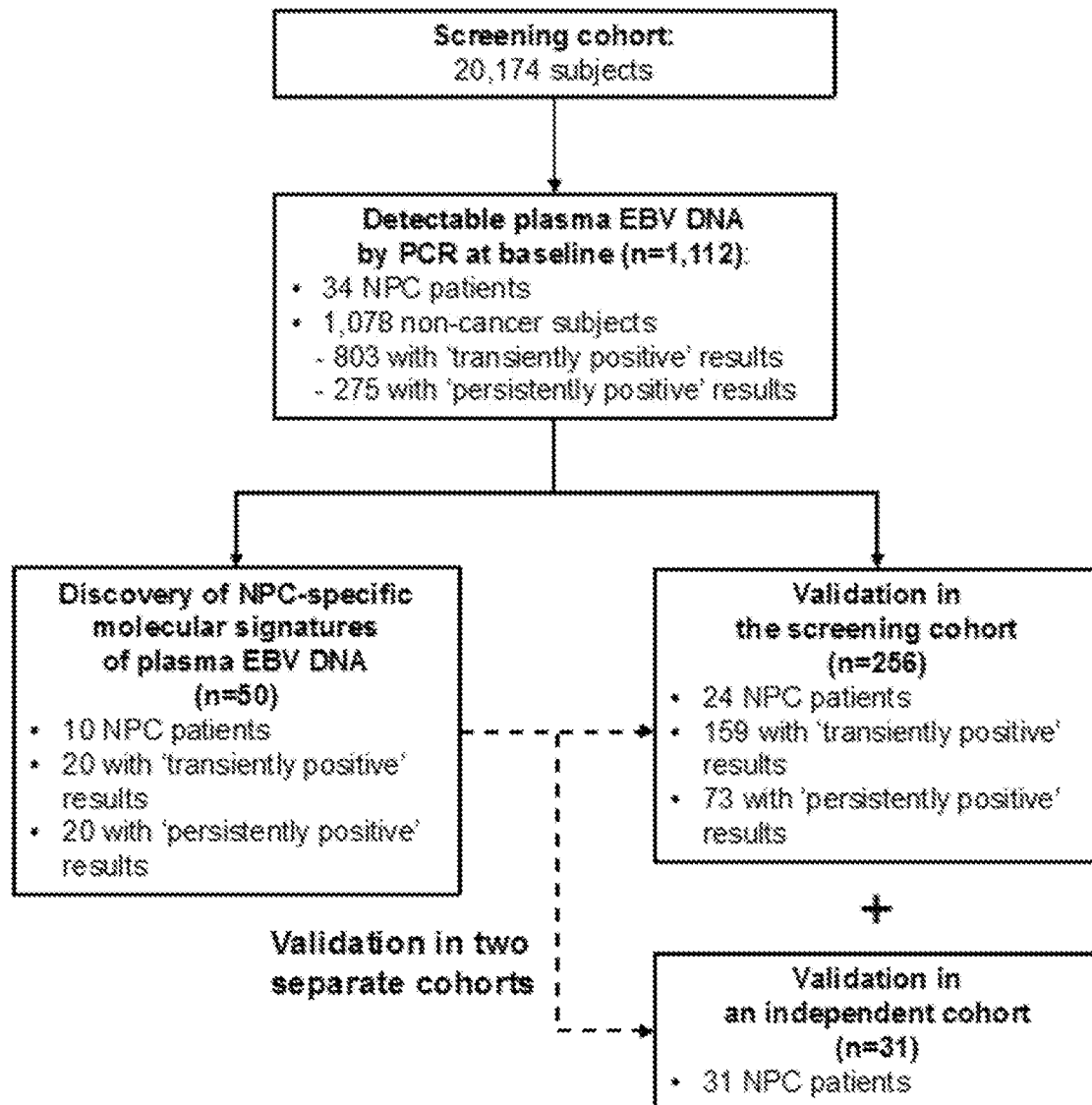


FIG. 9



Li, Jing, et al. "A Comparison between the Sixth and Seventh Editions of the UICC/AJCC Staging System for Nasopharyngeal Carcinoma in a Chinese Cohort." *PLoS One*, December 2014

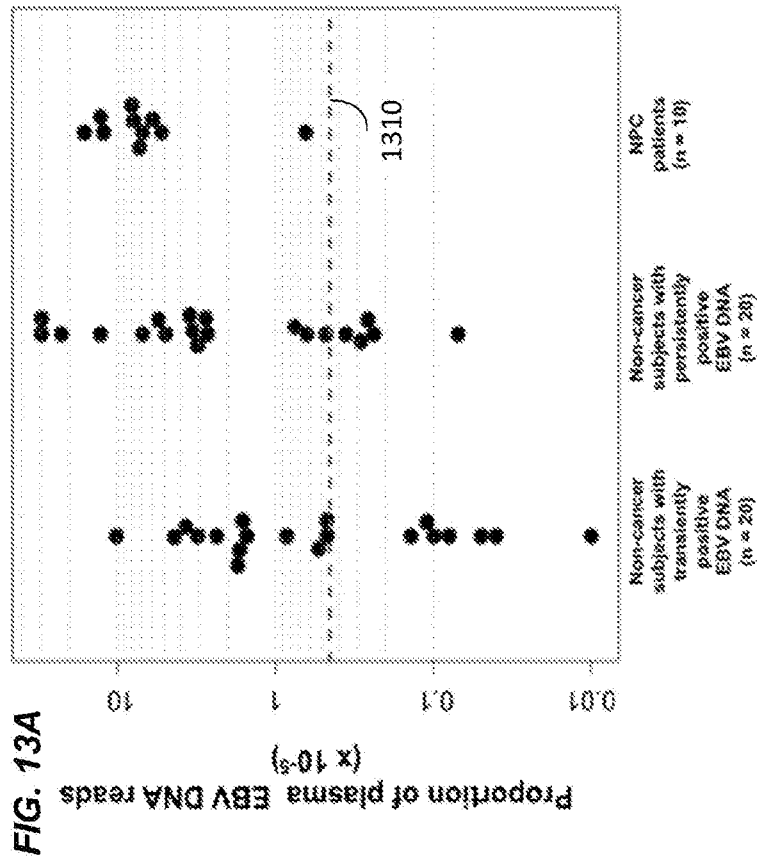
FIG. 10

**FIG. 11**

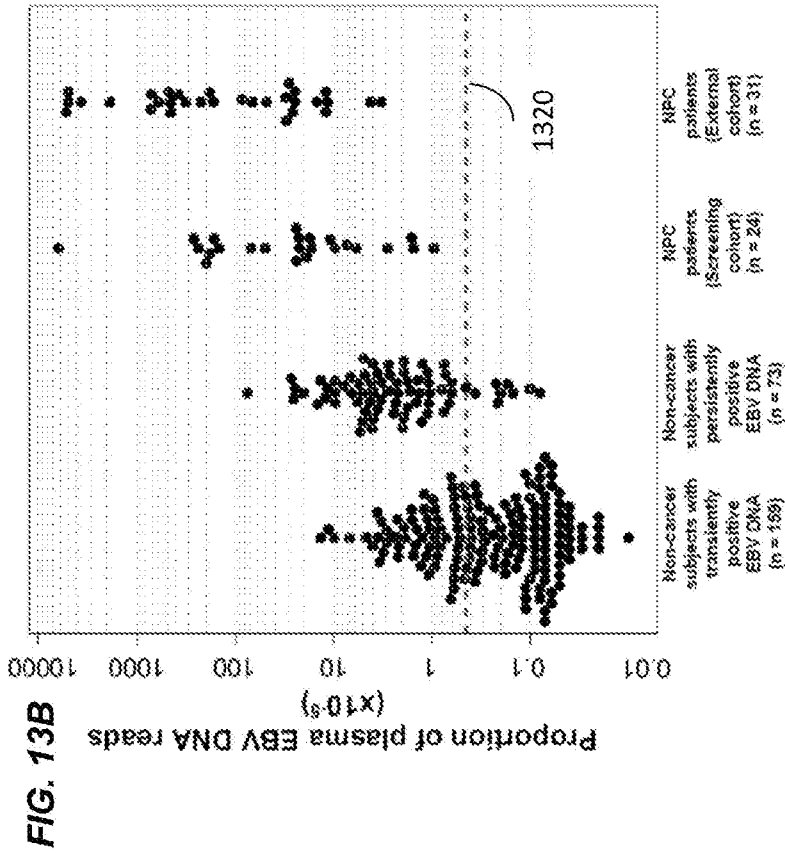
	Exploratory dataset			Validation dataset			
	Non-cancer subjects with transiently positive plasma EBV DNA	Non-cancer subjects with persistently positive plasma EBV DNA	NPC patients from the screening cohort	Non-cancer subjects with transiently positive plasma EBV DNA	Non-cancer subjects with persistently positive plasma EBV DNA	NPC patients from the screening cohort	NPC patients from an external cohort
Number	20	20	10	159	73	24	31
Sex							
M	20	20	10	159	73	24	24
F	0	0	0	0	0	0	7
Median age, year (IQR)	54.5 (50– 56)	55 (50 – 60.5)	54 (47 – 56)	53 (47 – 57)	53 (48 – 59)	50 (43 – 54)	56 (50 – 62)
Tumor stage							
I			5			11	3
II			2			6	2
III			2			6	20
IV			1			1	6

FIG. 12

Exploratory dataset



Validation dataset



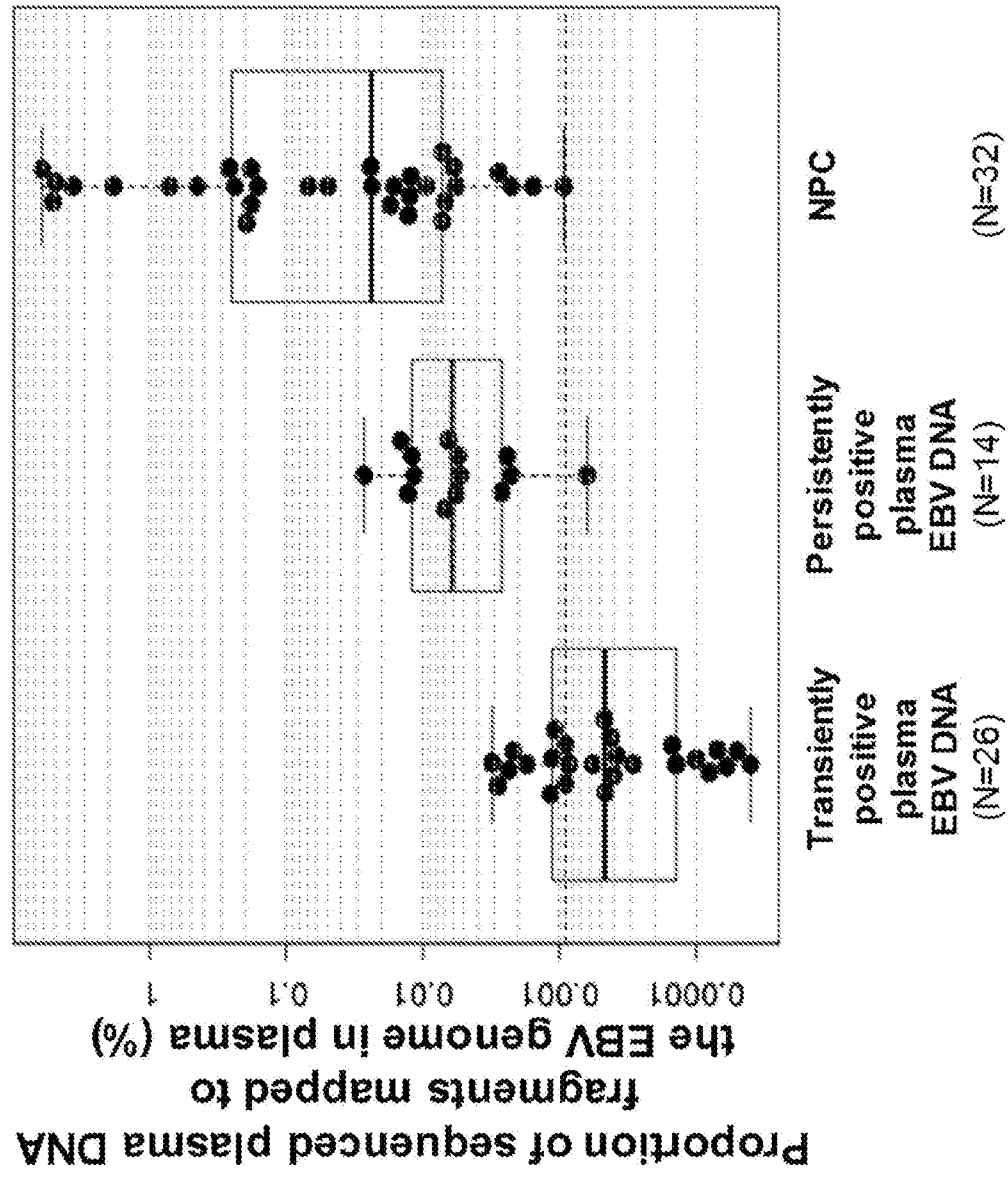


FIG. 14

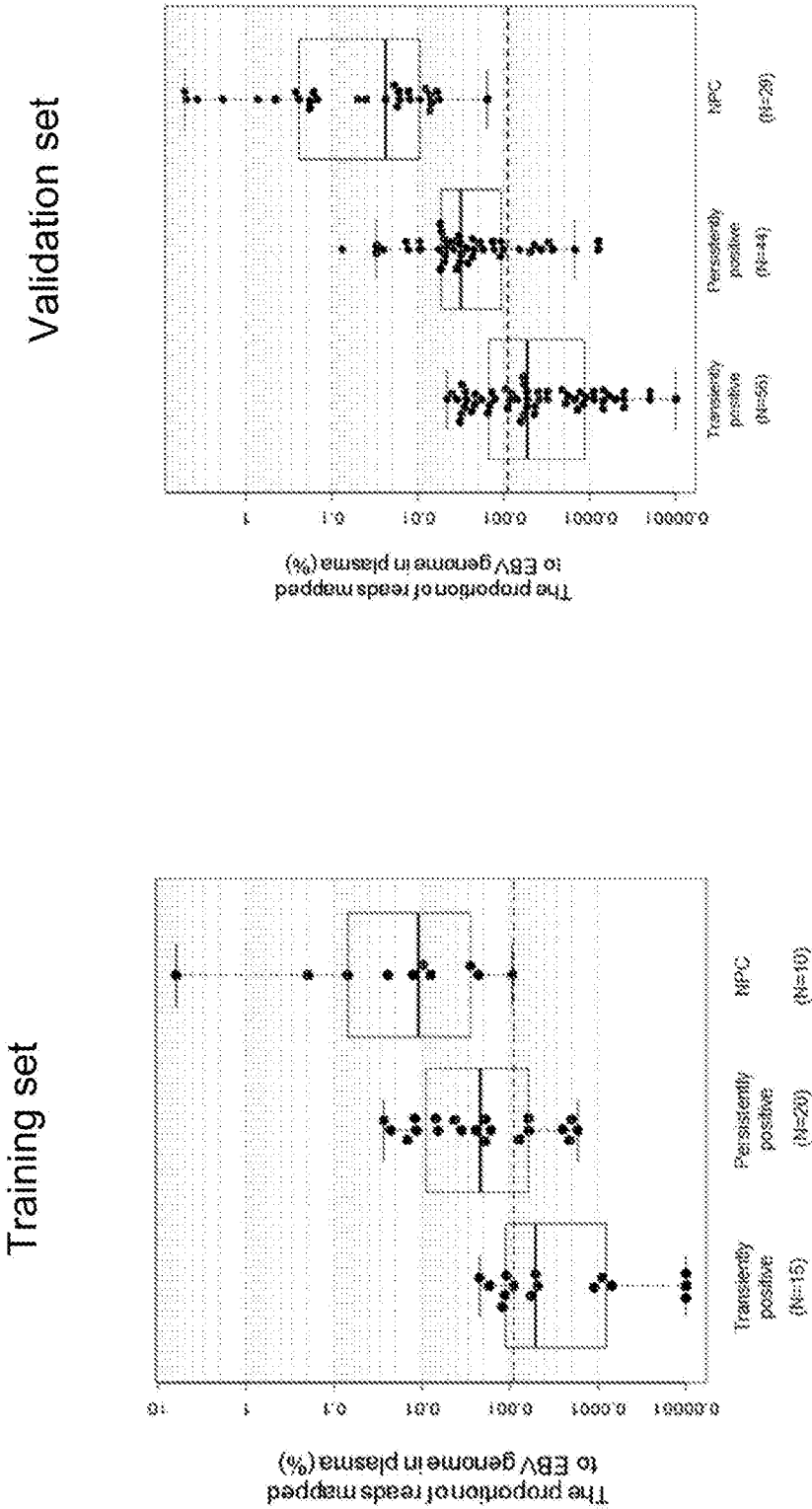


FIG. 15A

FIG. 15B

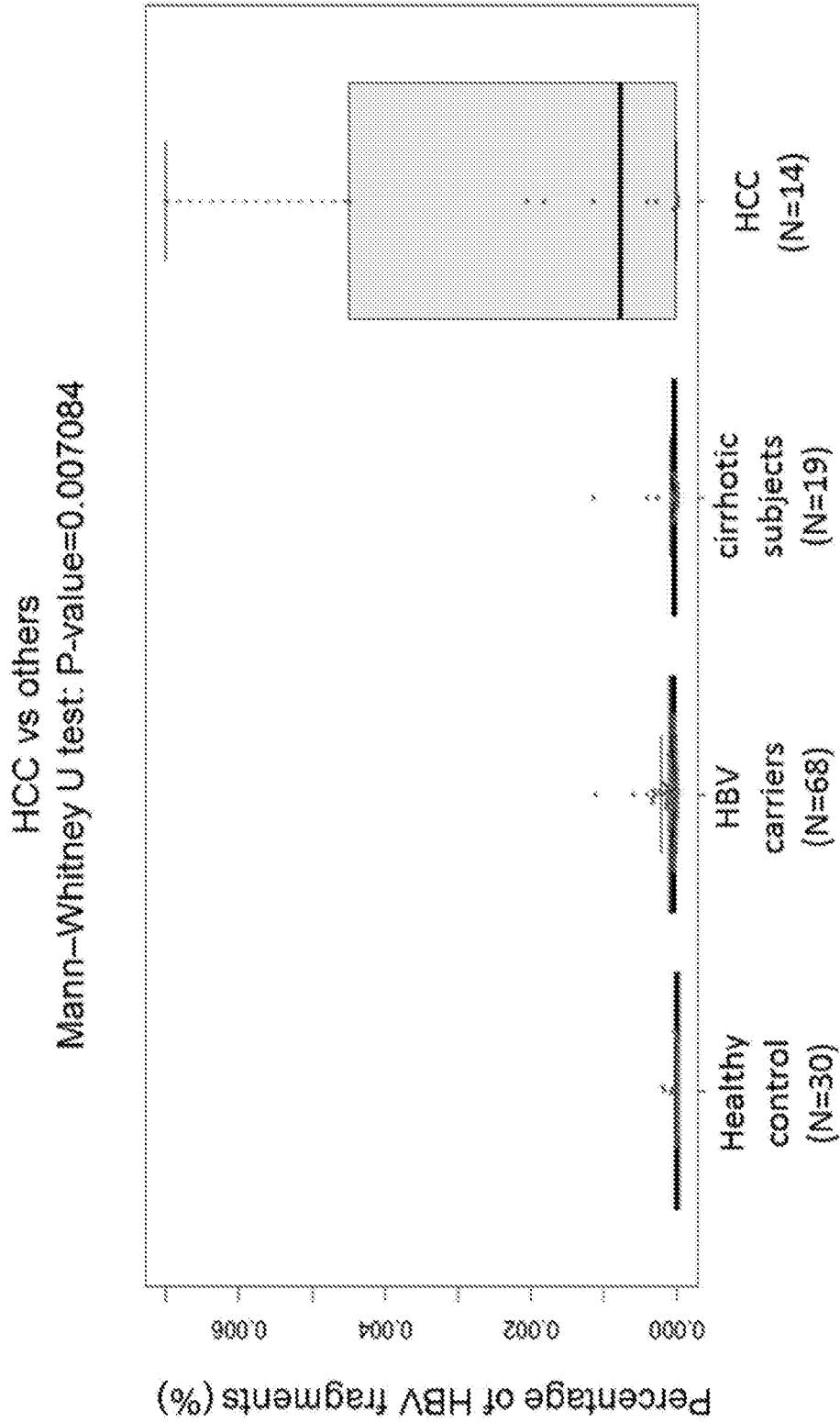


FIG. 16

HPV DNA fragments in patients with Ca cervix

Type	Sample	Stage	Mapped fragments	Fragments mapped to HPV16	% reads mapped to HPV16	Fragments mapped to HPV18	% reads mapped to HPV18	Fragments mapped to HPV33	% reads mapped to HPV33	Fragments mapped to HPV32	% reads mapped to HPV32	Fragments mapped to HPV38	% reads mapped to HPV38
Ca cervix	C-788	N/A	13137672	7992	0.06083	0	0	0	0	0	0	0	0
Ca cervix	C-801	N/A	4660998	2127	0.04563	0	0	0	0	0	0	0	0
Ca cervix	C-803	N/A	8747442	1316	0.01504	0	0	0	0	0	0	0	0
Ca cervix	C-819	N/A	20372000	1483	0.00731	0	0	0	0	0	0	0	0
Ca cervix	C-872	N/A	13036820	1720	0.0132	0	0	0	0	0	0	0	0
Ca cervix	C-877	N/A	21316598	6773	0.03177	0	0	0	0	0	0	0	0
Ca cervix	CaCx 3276	IIIB	53407760	31	5.80E-05	1375	0.0026	0	0	0	0	0	0
Ca cervix	CaCx 3485	IIB	64175765	143505	0.2236	1	1.56E-06	0	0	0	0	0	0
Ca cervix	CaCx 3499	IIB	41596564	36	8.65E-05	0	0	0	0	0	0	0	0
Ca cervix	CaCx 3542	IIIA	60513865	24	3.9E-05	0	0	7	0.000012	0	0	0	0
Ca cervix	CaCx 3581	IIB	46051601	39	8.46E-05	0	0	0	0	1	2.17E-06	152	0.00033

FIG. 17

HPV DNA fragments in patients with CIN

Type	Sample	Stage	Mapped fragments	Fragments mapped to HPV18	% reads mapped to HPV18	Fragments mapped to HPV18	% reads mapped to HPV18	Fragments mapped to HPV33	% reads mapped to HPV33	Fragments mapped to HPV33	% reads mapped to HPV33	Fragments mapped to HPV52	% reads mapped to HPV52	Fragments mapped to HPV53	% reads mapped to HPV53
CIN	CIN264	III	96267591	0	0	0	0	19	0.000021	1	1.11E-06	1	1.11E-06	1	1.11E-06
CIN	CIN266	III	65164406	2	2.90E-06	0	0	7	0.00001	0	0	0	0	0	0
CIN	CIN270	III	23521018	0	0	0	0	0	0	0	0	0	0	0	0
CIN	CIN272	III	52110686	0	0	0	0	0	0	0	0	0	0	0	0
CIN	CIN306	III	79970503	0	0	0	0	0	0	0	0	0	0	0	0
CIN	CIN313	III	49674122	0	0	0	0	0	0	0	0	0	0	0	0
CIN	CIN346	III	47867453	1	2.10E-06	0	0	0	0	0	0	0	0	0	0
CIN	CIN347	III	62446833	0	0	0	0	0	0	0	0	0	0	0	0
CIN	CIN351	III	65724902	0	0	0	0	0	0	0	0	0	0	0	0
CIN	CIN362	III	47021676	0	0	0	0	0	0	0	0	0	0	0	0
CIN	CIN_1501	N/A	14094358	0	0	0	0	0	0	0	0	0	0	0	0
CIN	CIN_1502	N/A	15689492	0	0	0	0	0	0	0	0	0	0	0	0
CIN	CIN_1503	N/A	14375461	0	0	0	0	0	0	0	0	0	0	0	0
CIN	CIN_1504	N/A	15580726	0	0	0	0	0	0	0	0	0	0	0	0
CIN	CIN_1506	N/A	14080589	0	0	0	0	0	0	0	0	0	0	0	0
CIN	CIN_1507	N/A	9179781	0	0	0	0	0	0	0	0	0	0	0	0

FIG. 18

HPV DNA fragments in patients with HPV+ve HNSCC

Type	Sample	Stage	Mapped fragments	Fragments mapped to HPV16	N reads mapped to HPV16	Fragments mapped to HPV16	N reads mapped to HPV16	Fragments mapped to HPV18	N reads mapped to HPV18	Fragments mapped to HPV33	N reads mapped to HPV33	Fragments mapped to HPV32	N reads mapped to HPV32	Fragments mapped to HPV35	N reads mapped to HPV35
HNSCC	TBR1019	II	51218367	3287	0.006416	0	0	0	0	0	0	0	0	0	0
HNSCC	TBR1067	III	57211251	53	9.26E-05	0	0	0	0	0	0	0	0	0	0
HNSCC	TBR1245	I	63709771	1715	0.001692	0	0	0	0	0	0	0	0	0	0
HNSCC	TBR1988	I	76580006	1159	0.001513	0	0	0	0	0	0	0	0	0	0
HNSCC	TBR1989	II	60576165	484320	0.800513	0	0	0	0	0	0	0	0	0	0
HNSCC	TBR2002	I	78175347	1949	0.002493	0	0	0	0	0	0	0	0	0	0
HNSCC	TBR2175	II	60128334	4022	0.006889	0	0	0	0	0	0	0	0	0	0

FIG. 19

HPV detection in healthy control

Sample type	Sample number	No. of sample with detectable HPV reads by sequencing	Proportion(%)
Healthy control	270	9	3.3

Type	Sample	HPV type	Number of HPV fragment(s)
Healthy controls	AB155	HPV39	1
Healthy controls	AC135	HPV45	1
Healthy controls	AF121	HPV16	4
Healthy controls	CK018	HPV56	1
Healthy controls	GG017	HPV16	125
Healthy controls	GT023	HPV58	2
Healthy controls	HK074	HPV16	2
Healthy controls	AE011	HPV16	2
Healthy controls	DZ071	HPV16	1

FIG. 20

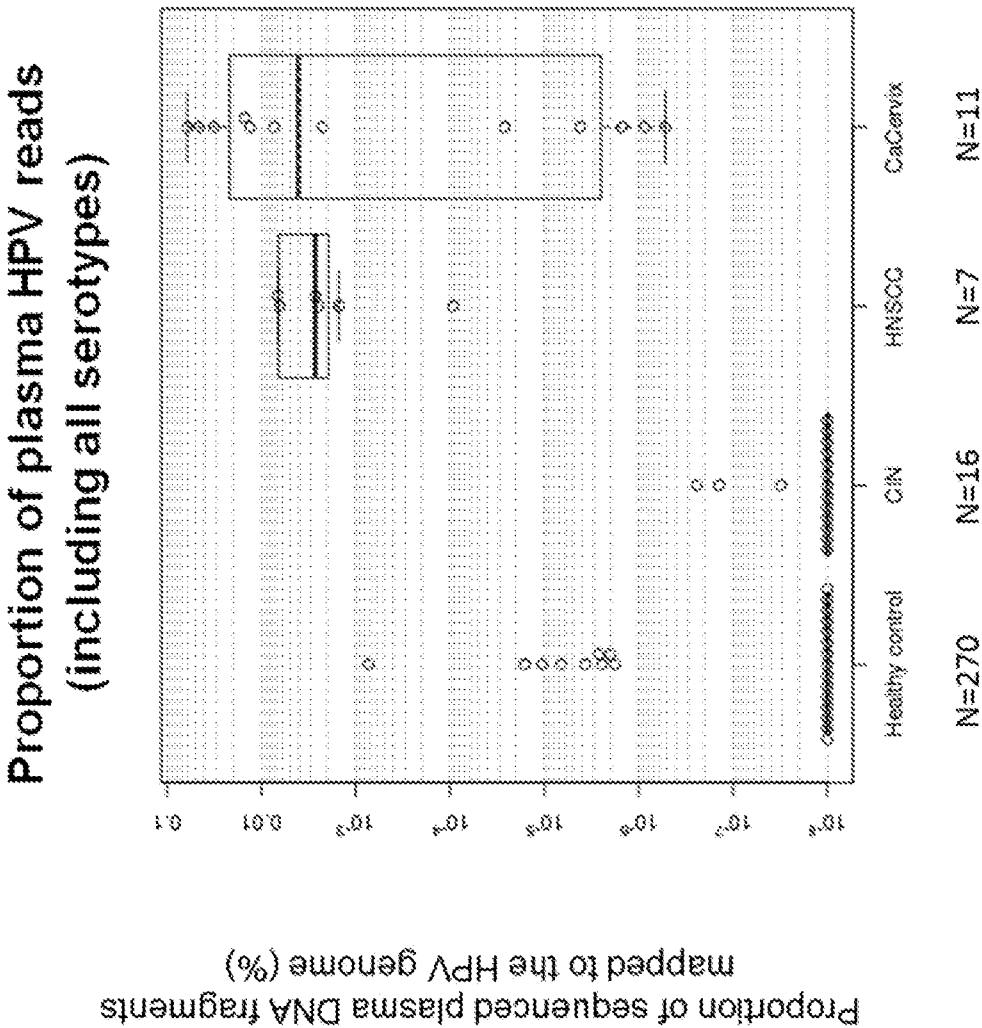
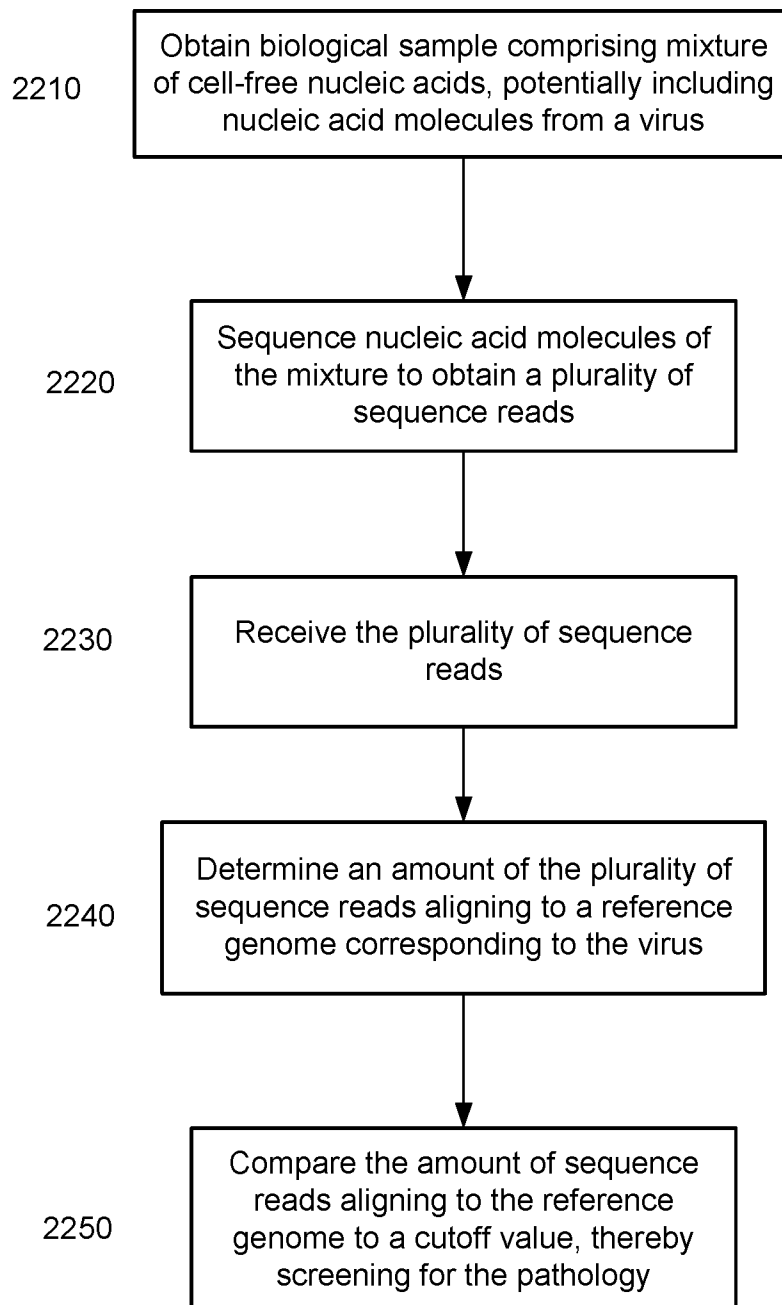


FIG. 21

2200

**FIG. 22**

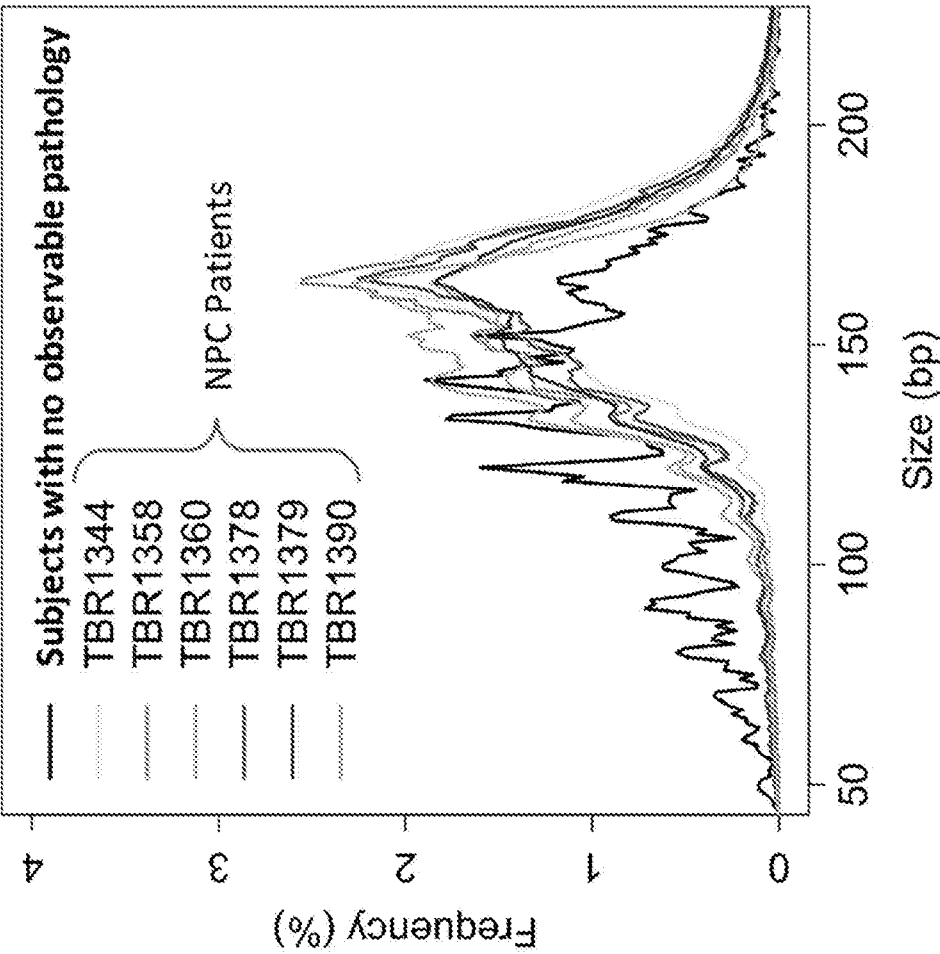


FIG. 23

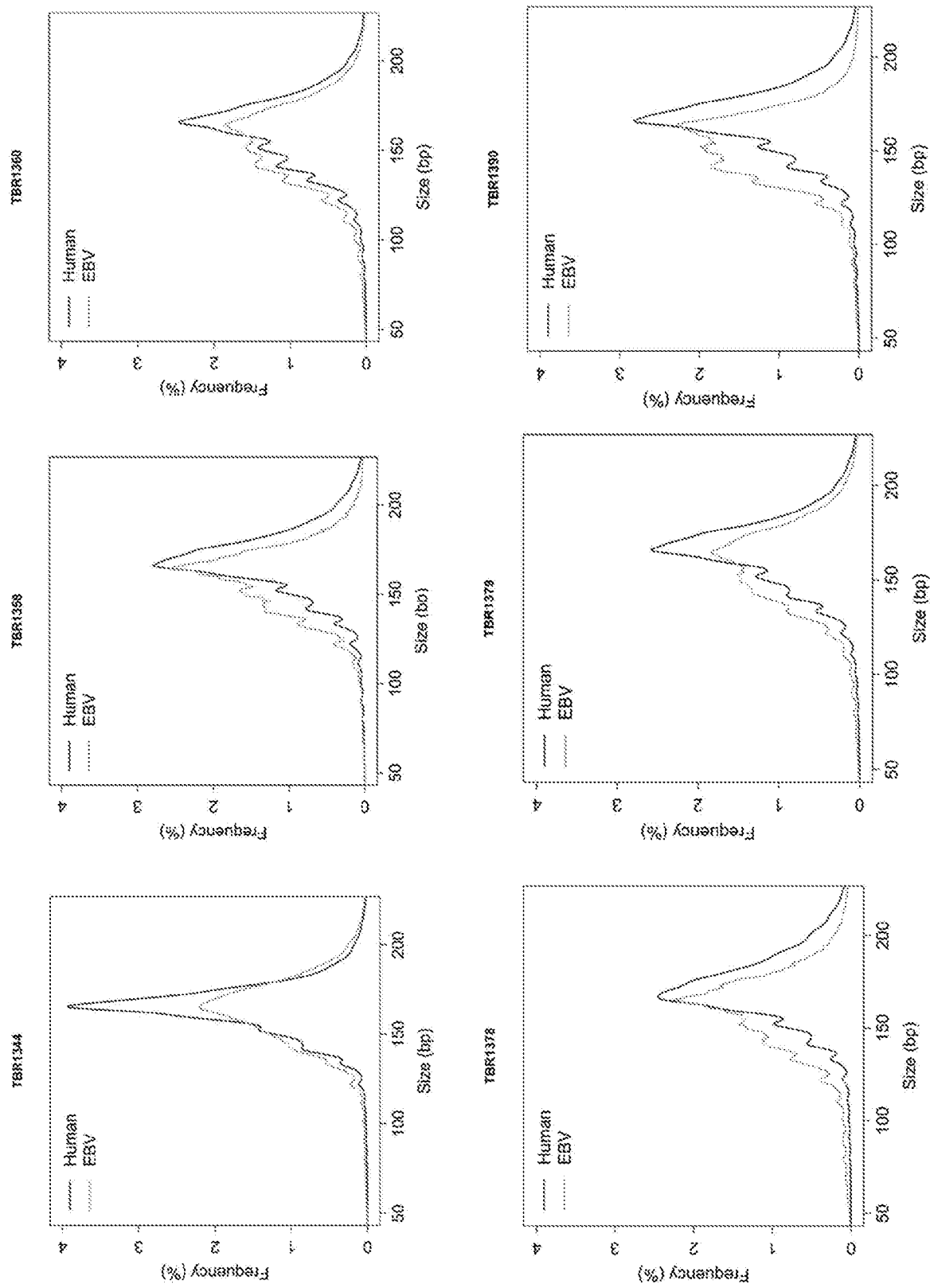


FIG. 24

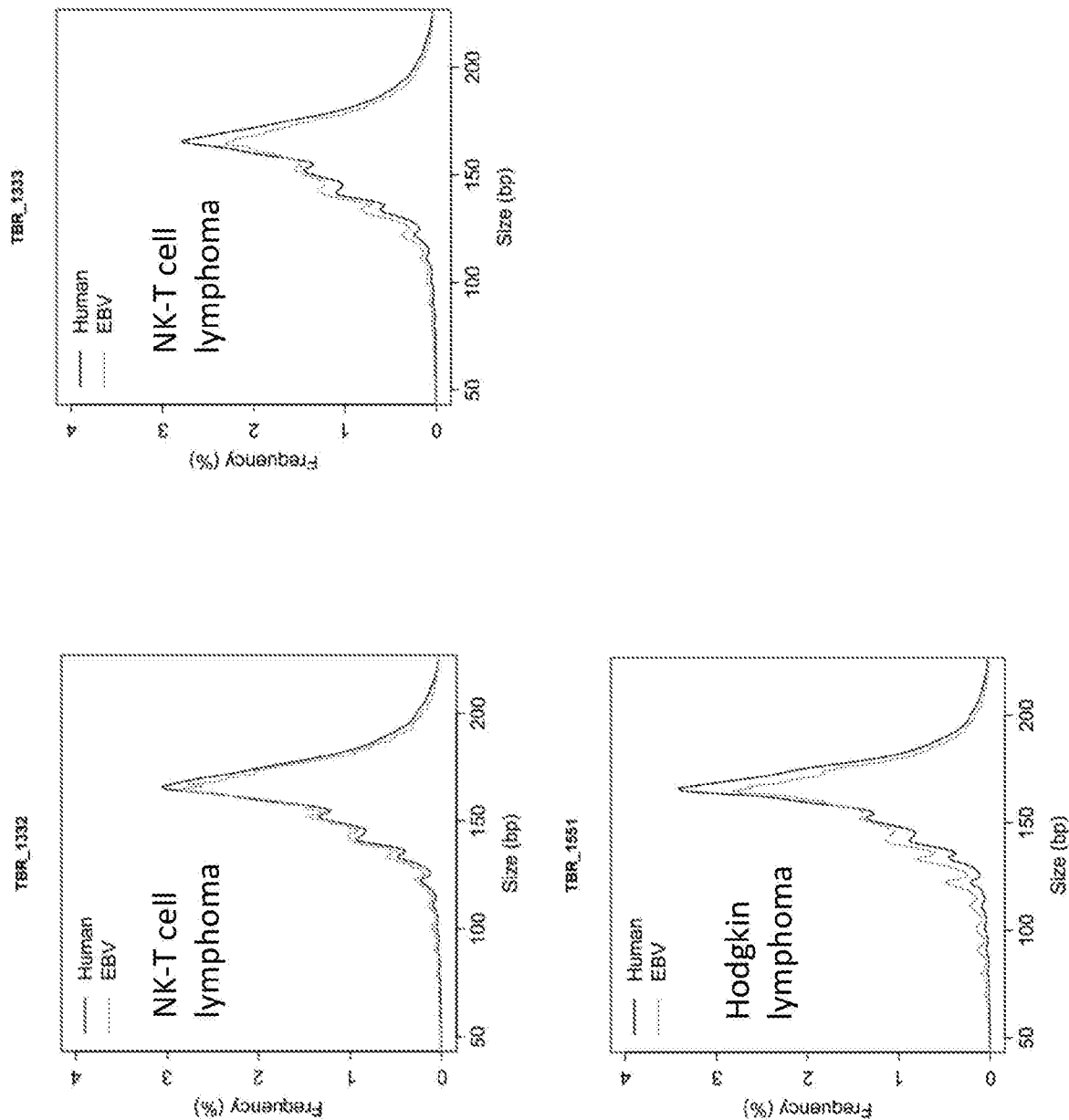


FIG. 25

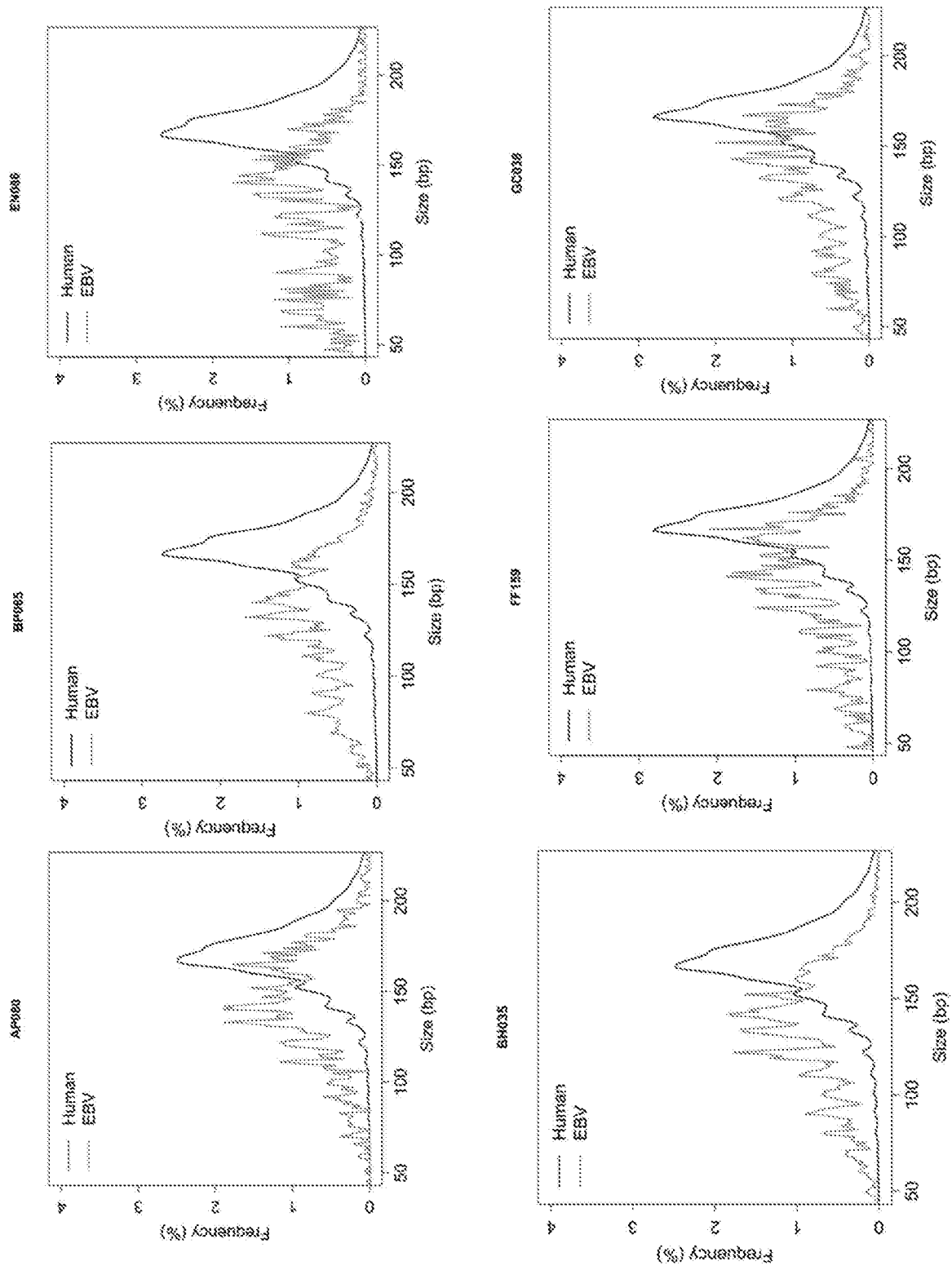


FIG. 26

Persistently
positive plasma
EBV DNA

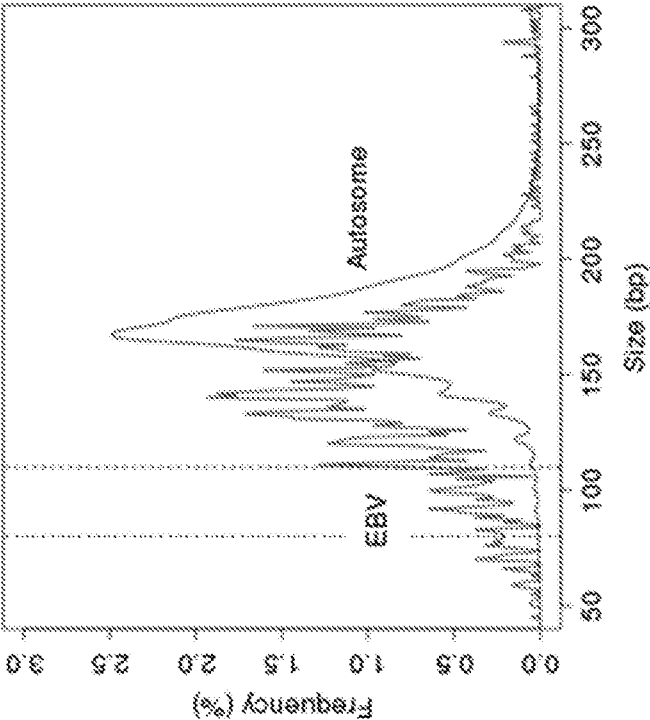


FIG. 27B

NPC

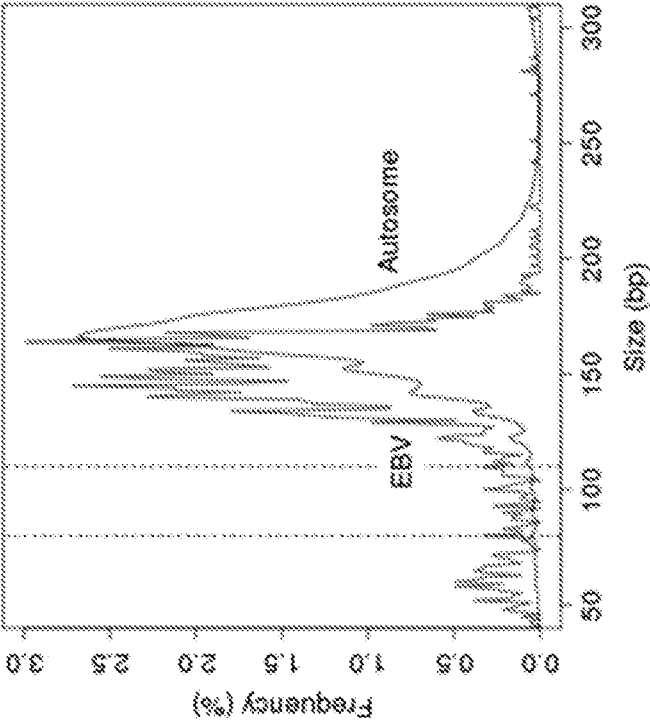


FIG. 27A

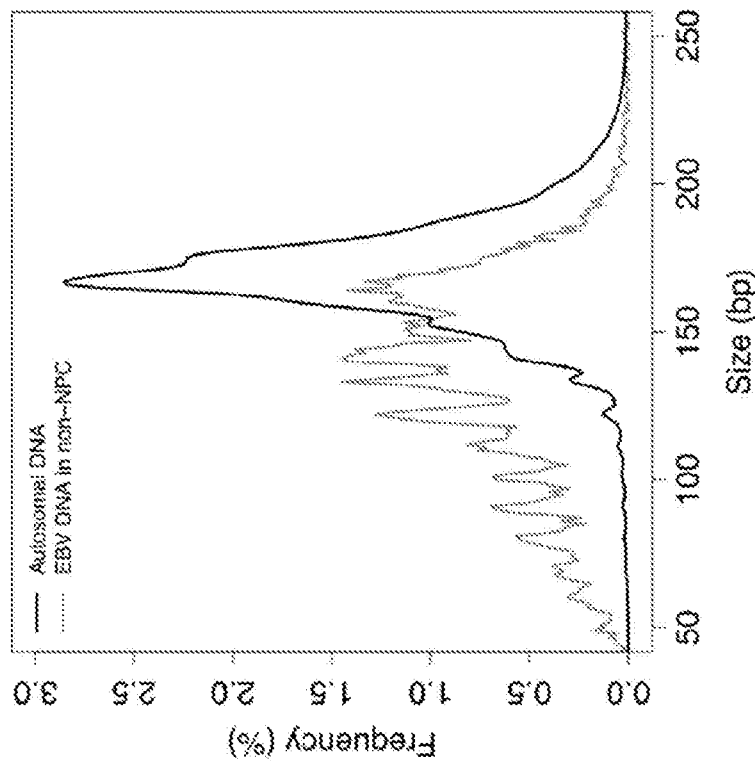


FIG. 28B

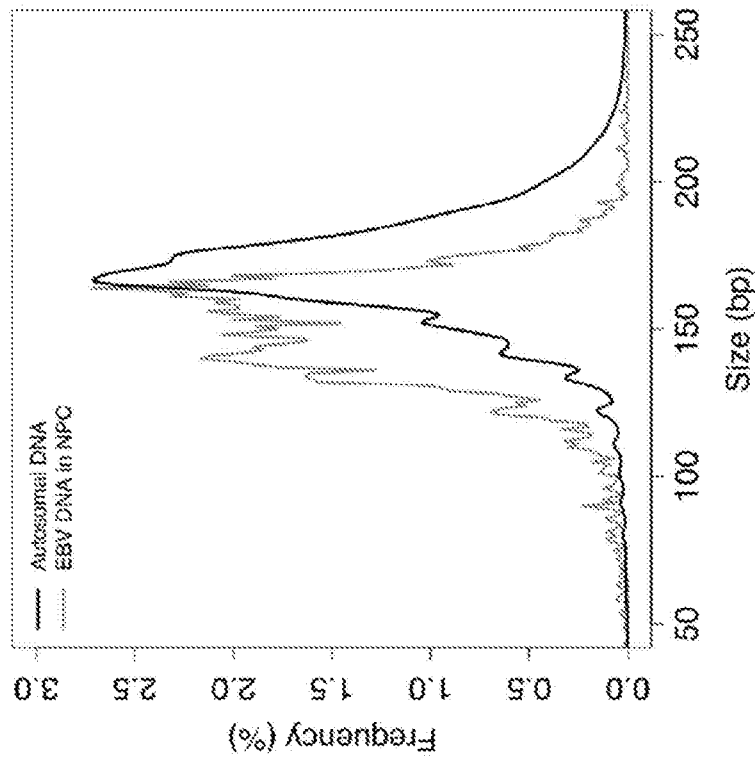
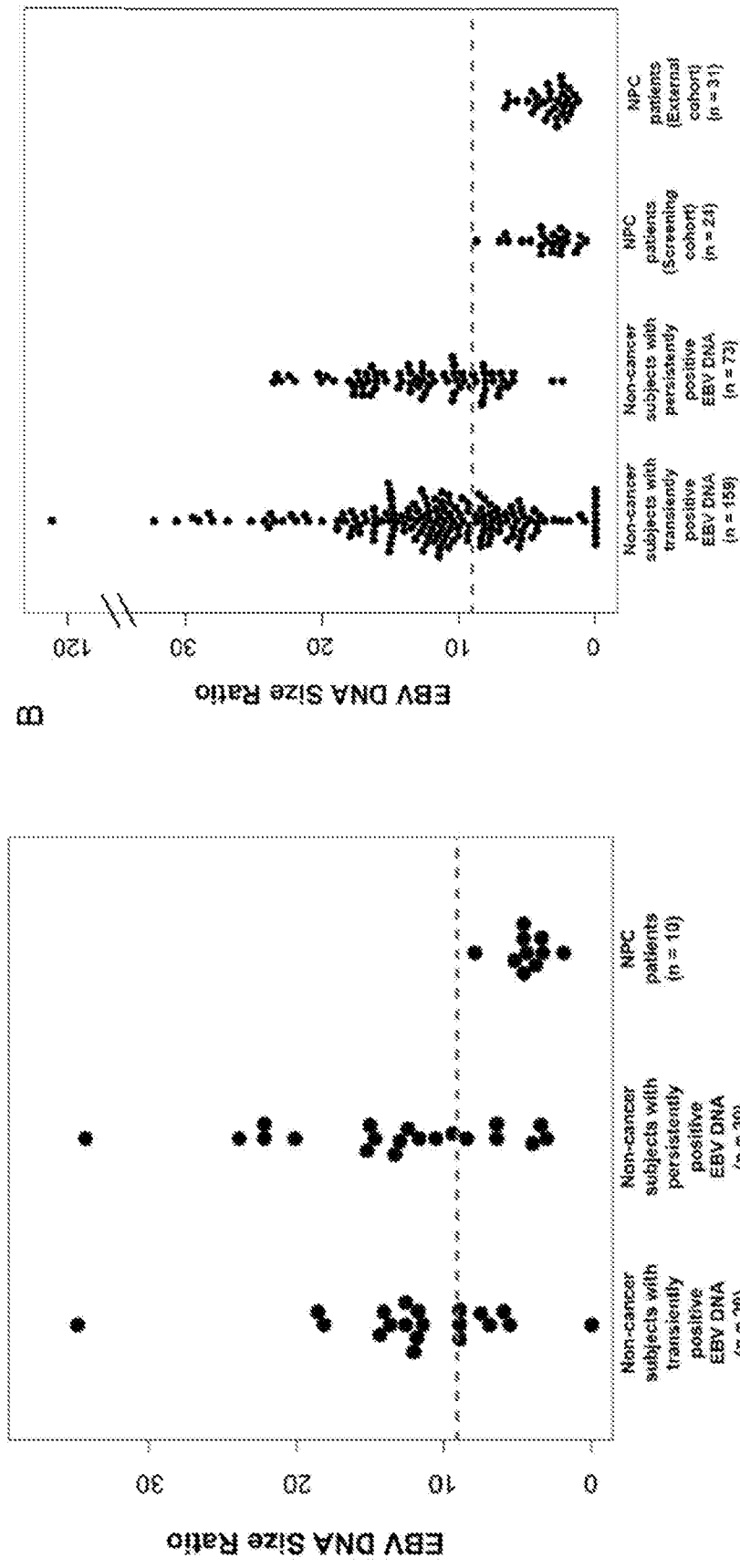


FIG. 28A



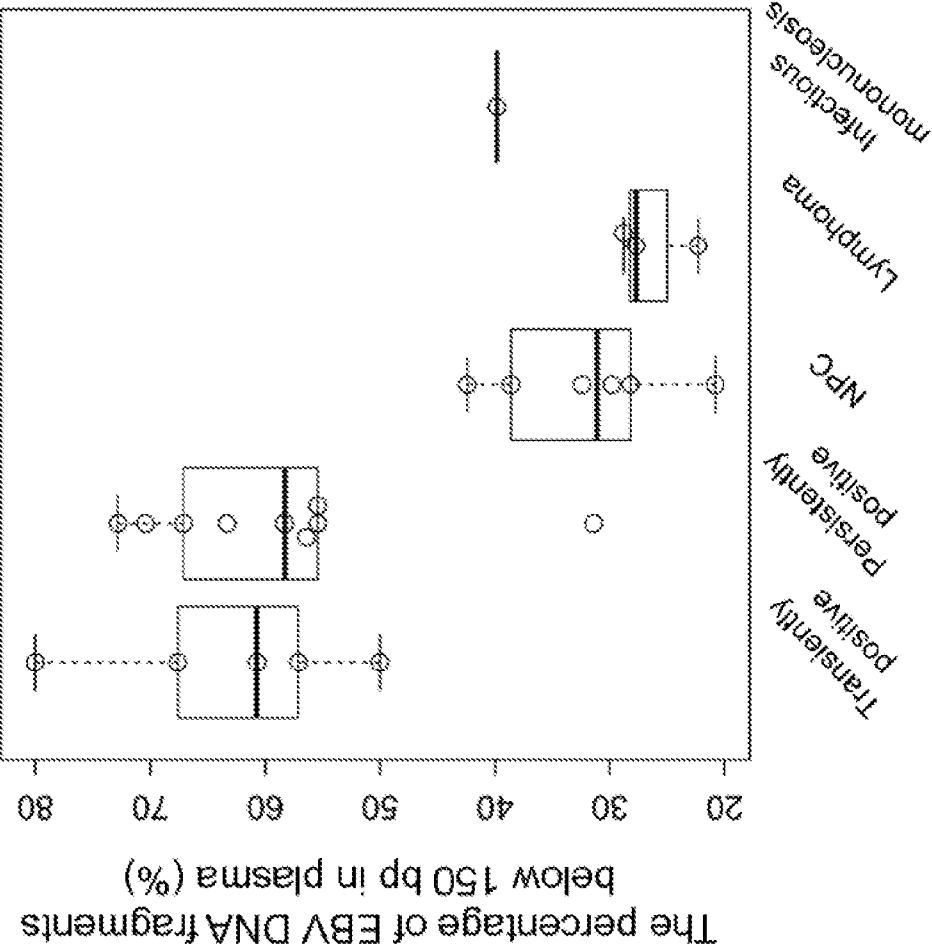


FIG. 30

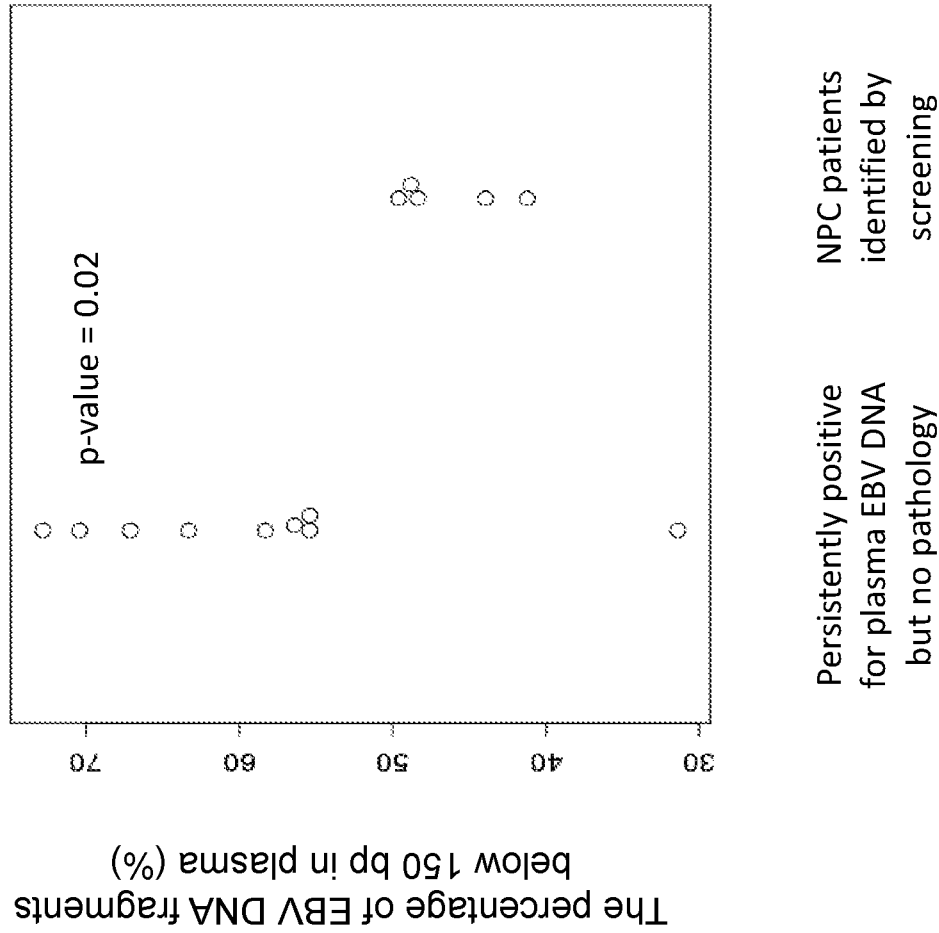


FIG. 31

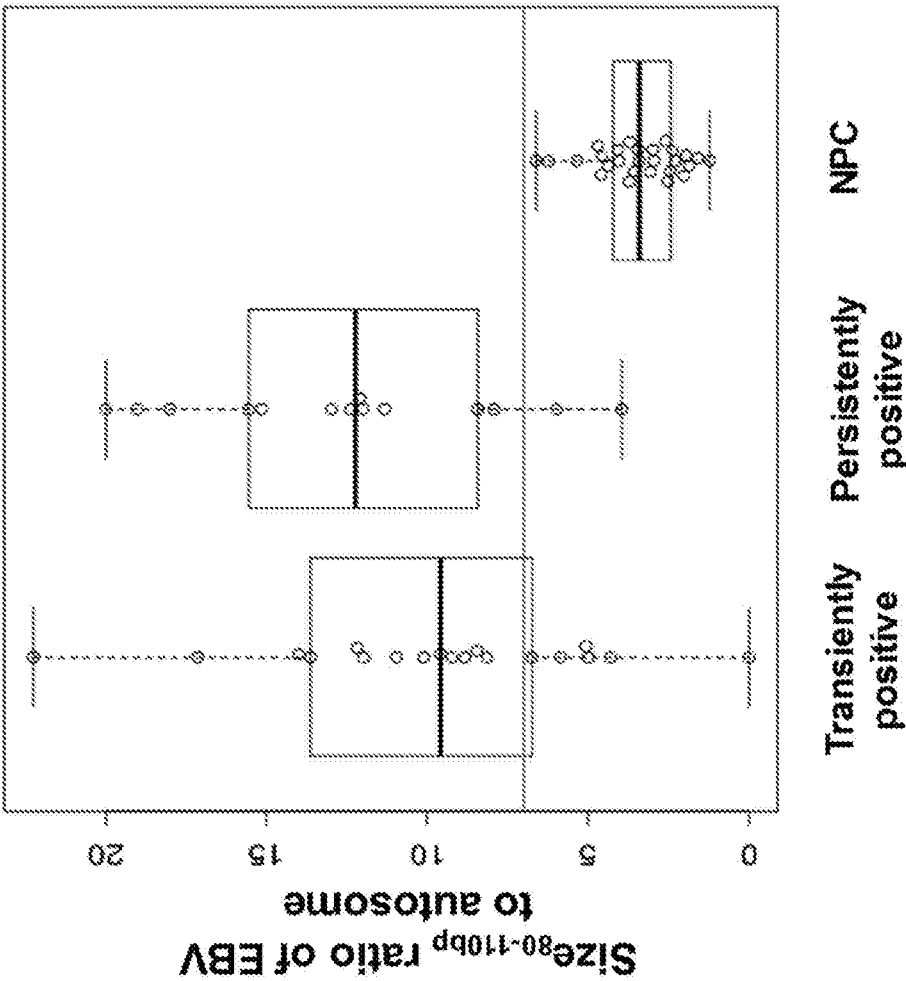


FIG. 32

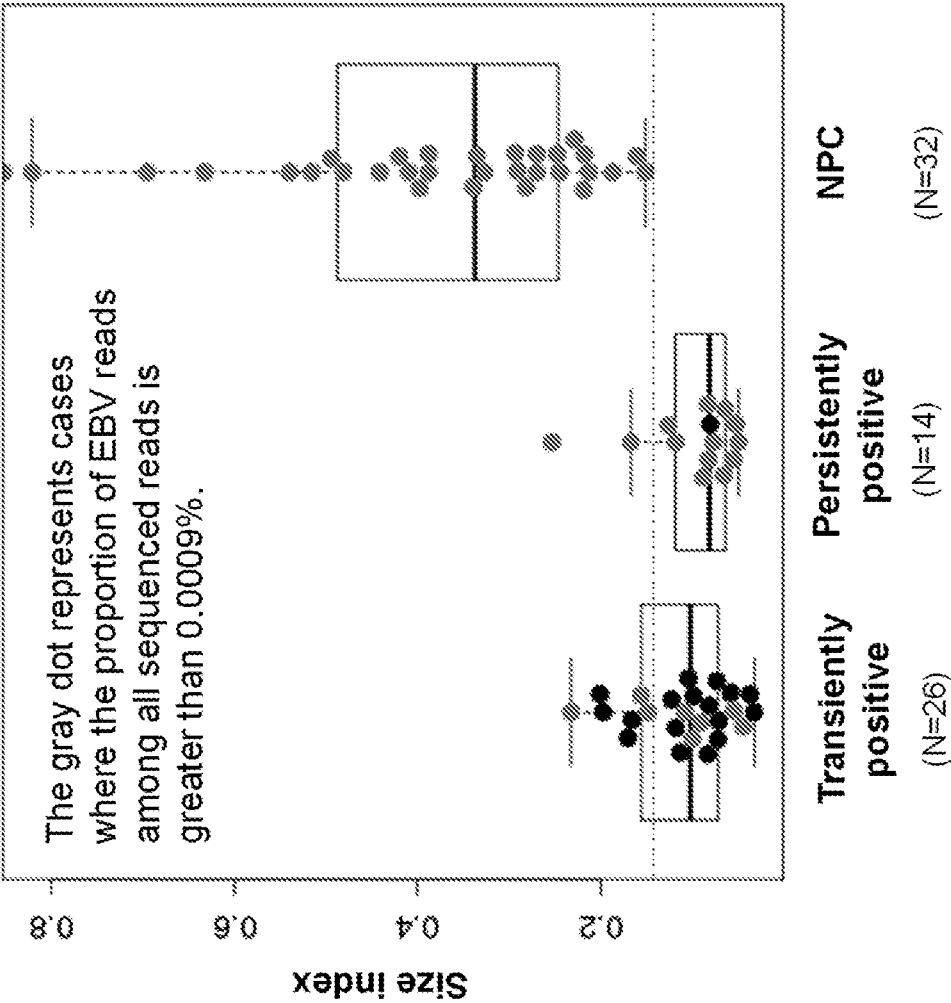


FIG. 33

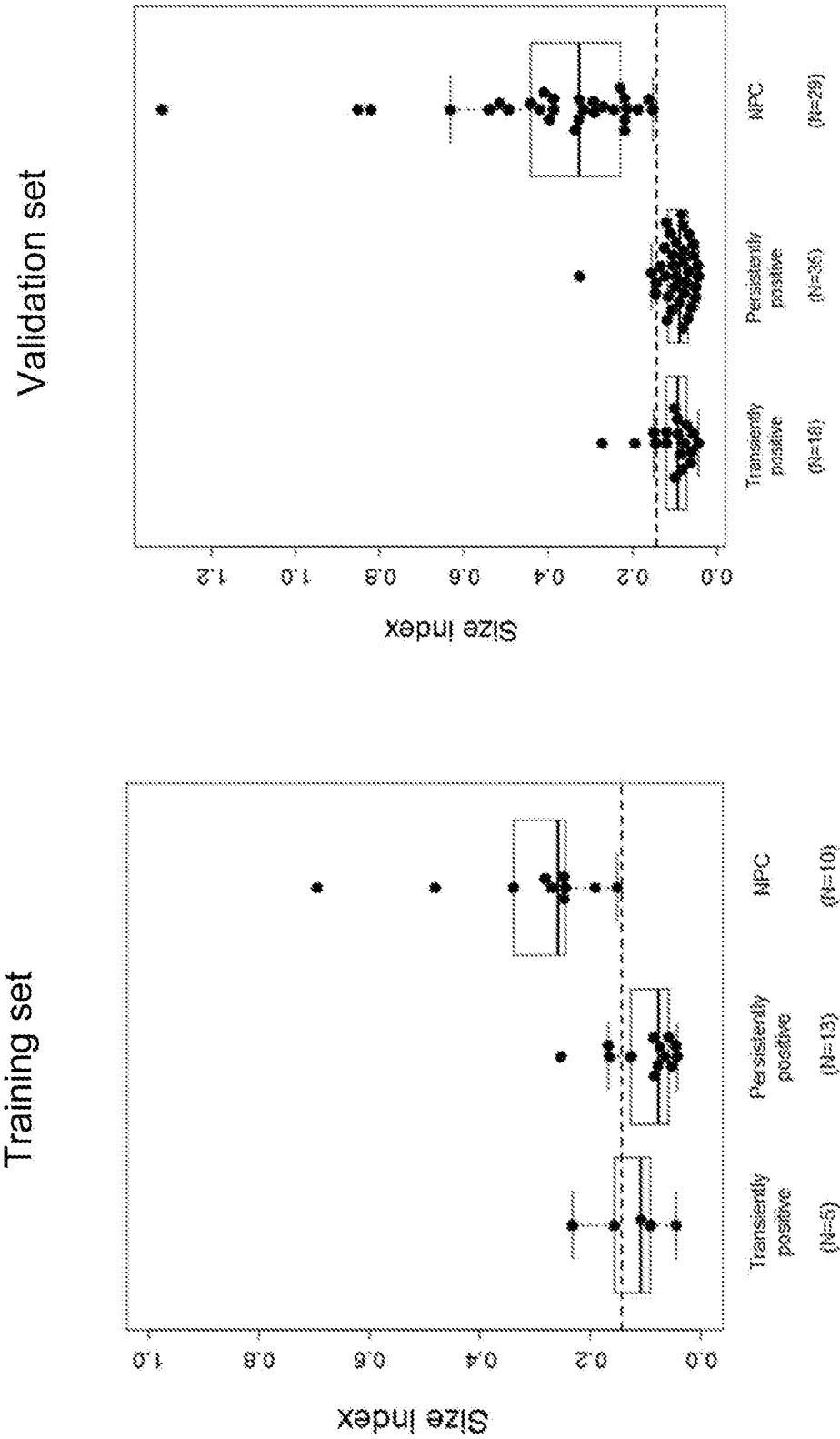


FIG. 34A

FIG. 34B

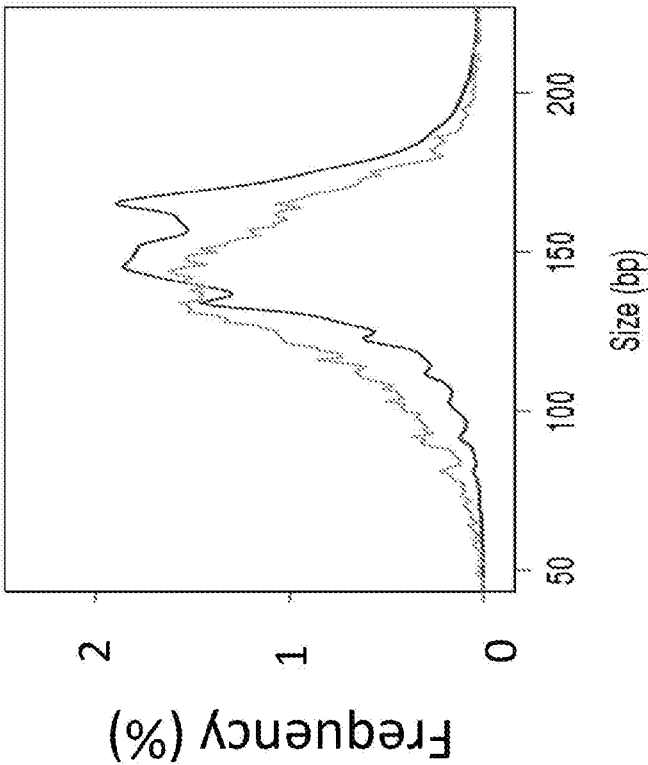


FIG. 35A

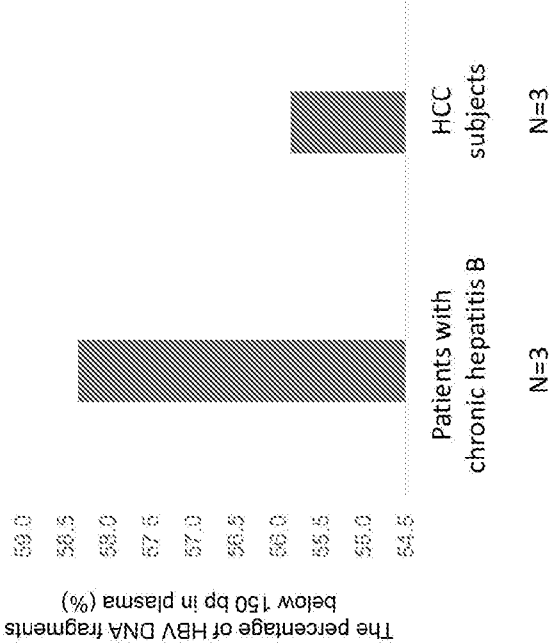


FIG. 35B

The mean proportion of HBV DNA fragments below 150bp in plasma.

Carcinoma of cervix

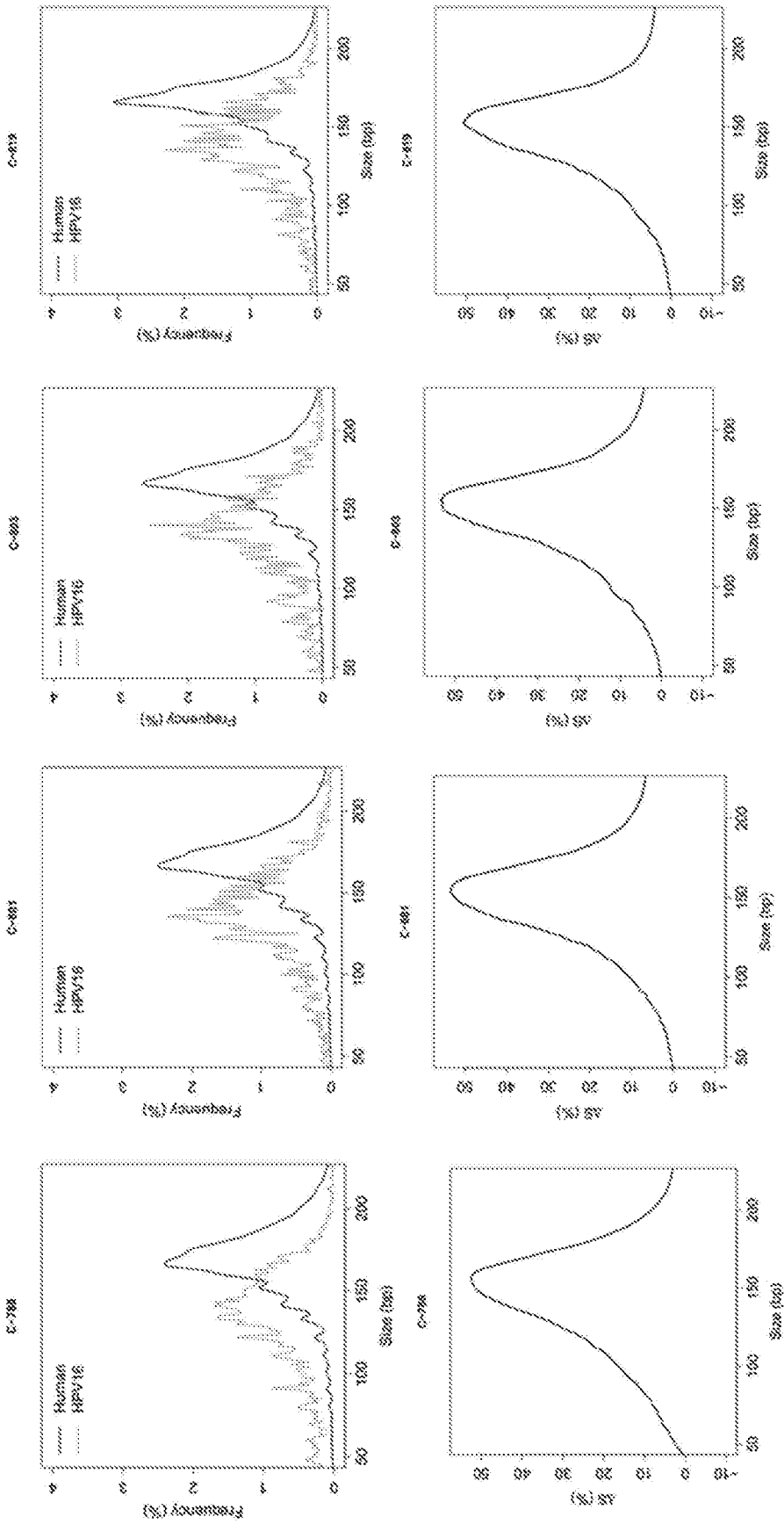


FIG. 36

Carcinoma of cervix

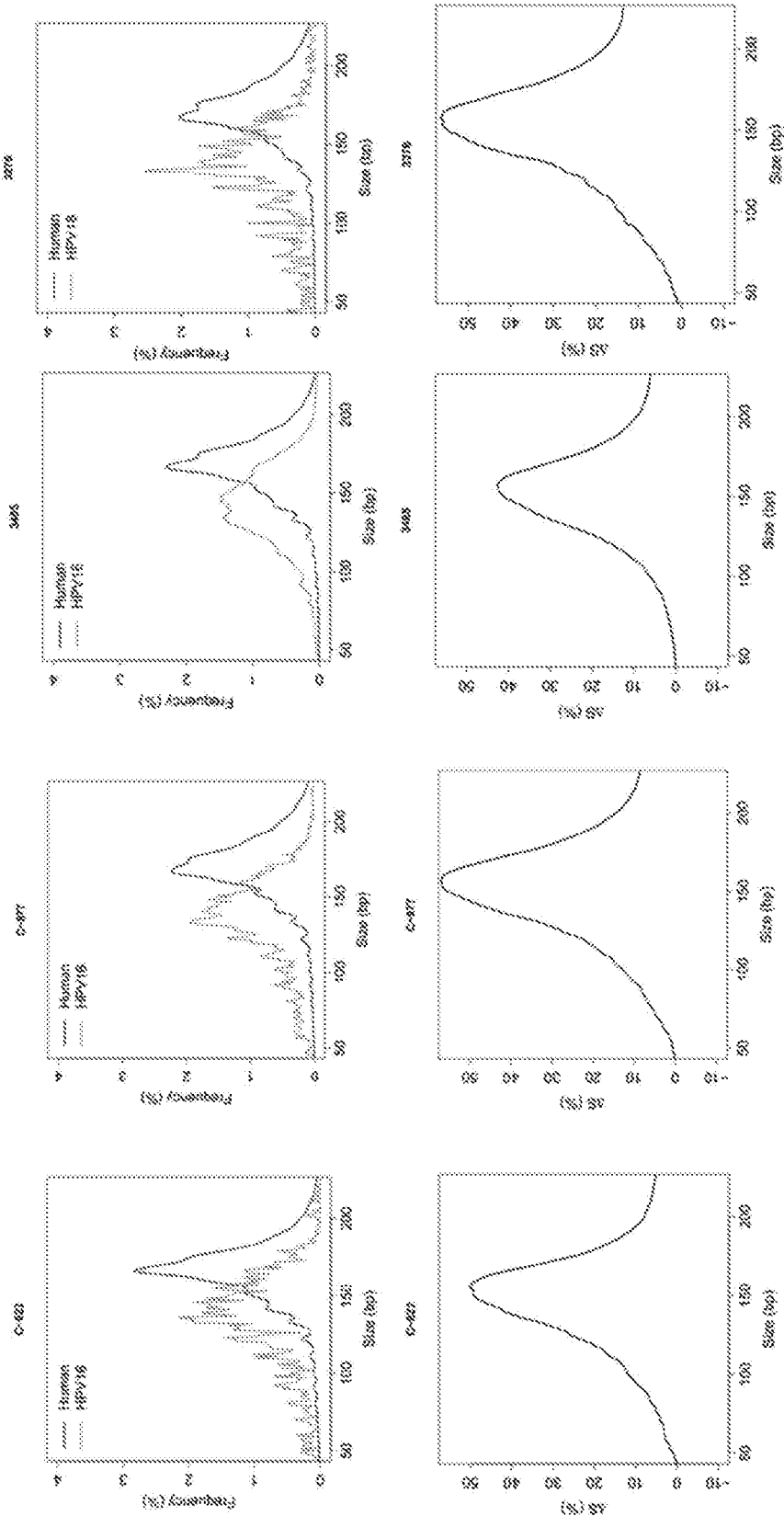


FIG. 37

HPV positive head and neck squamous cell carcinoma

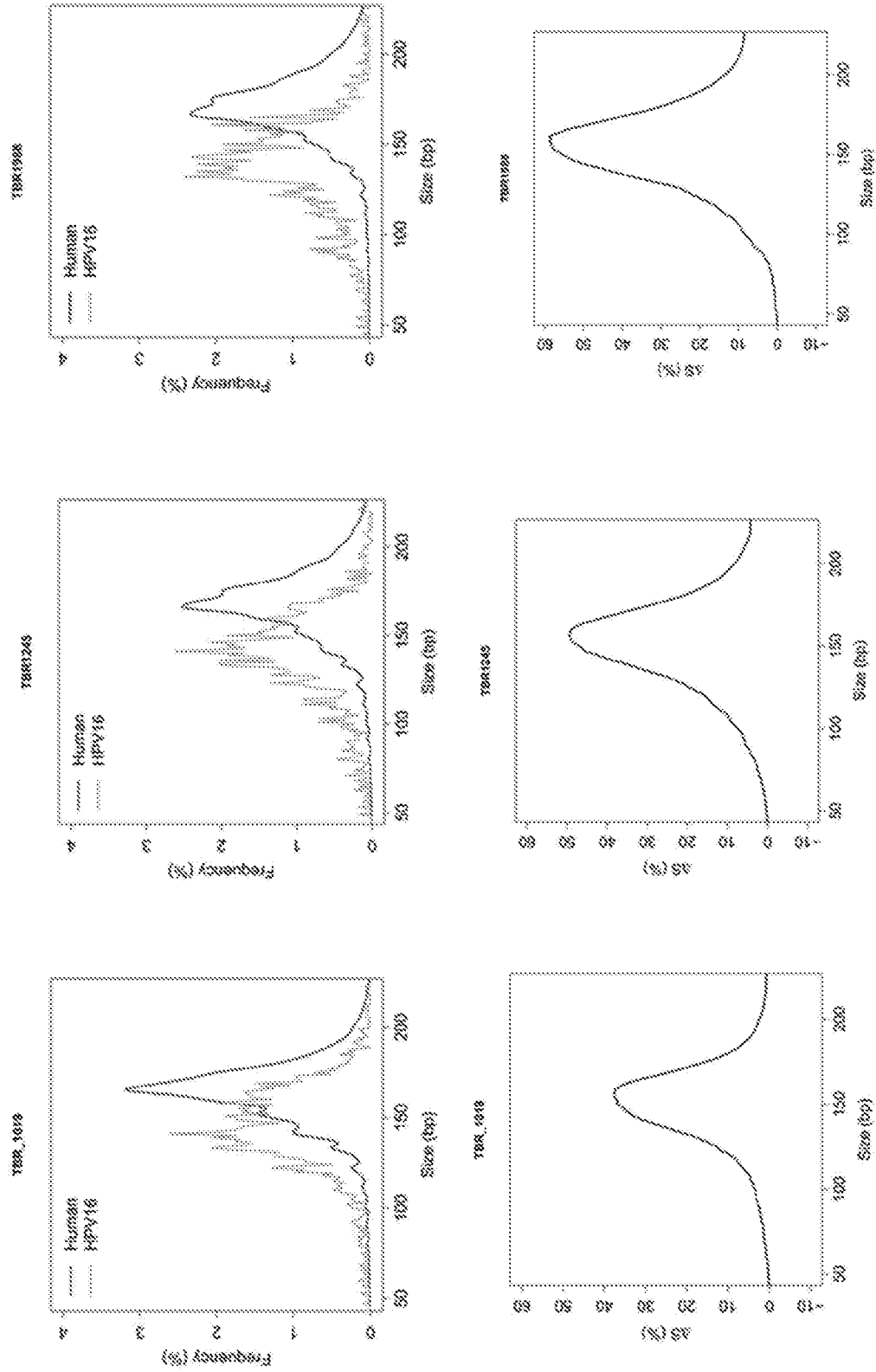


FIG. 38

HPV positive head and neck squamous cell carcinoma

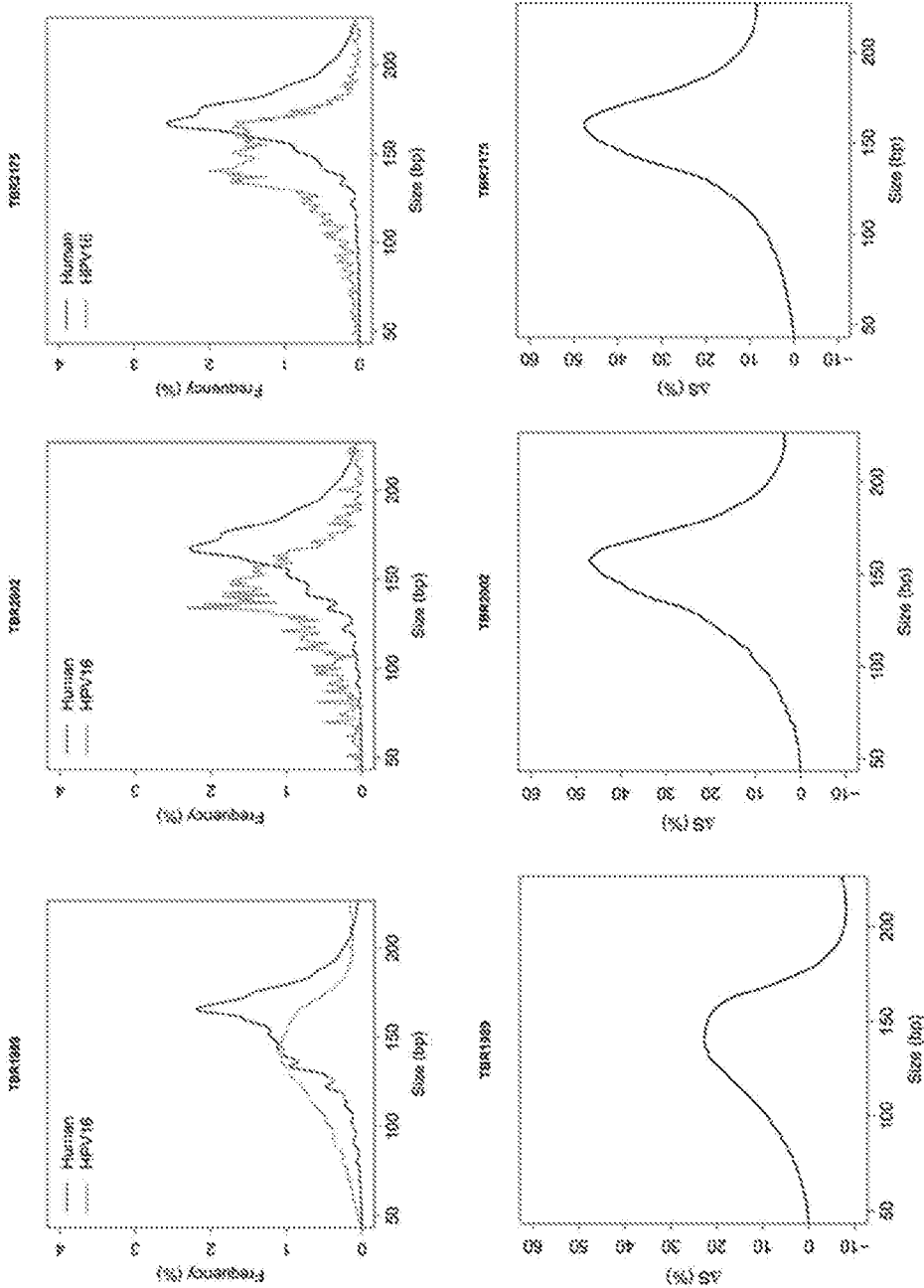
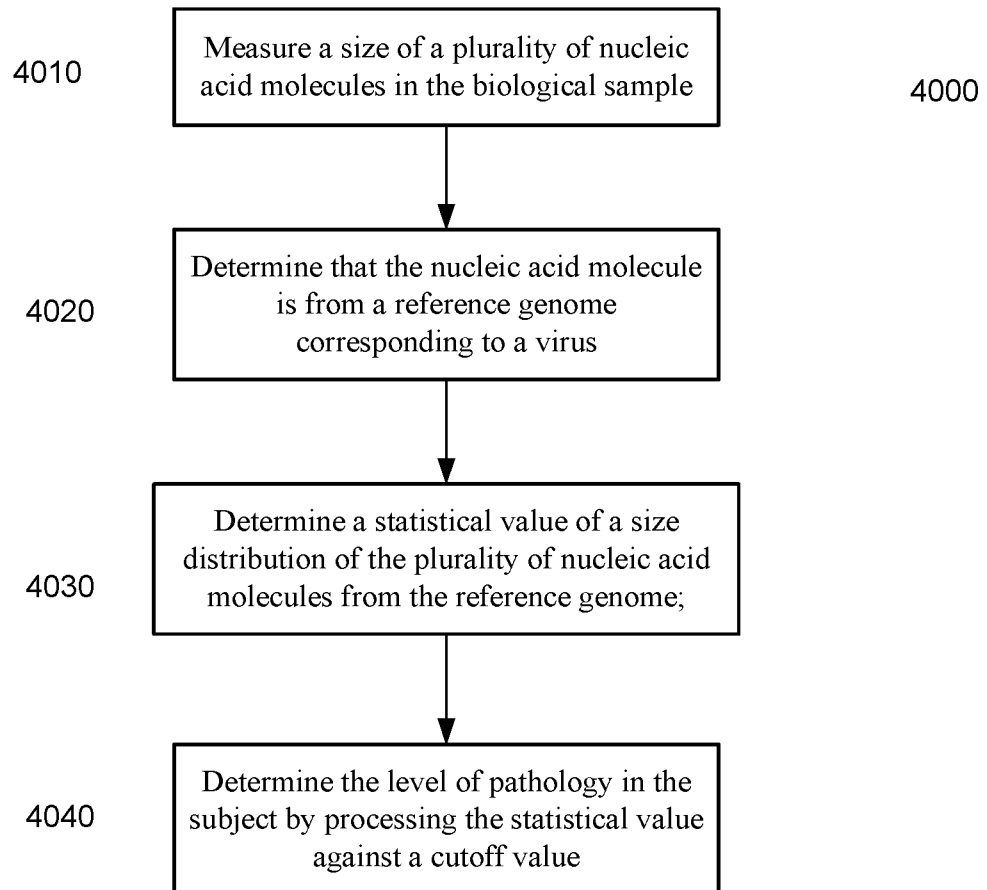
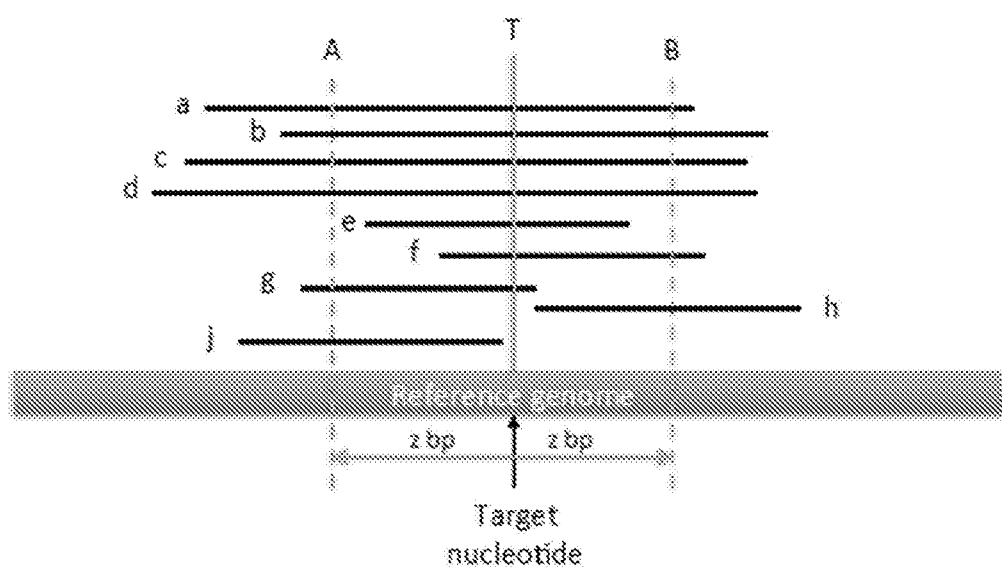


FIG. 39

**FIG. 40**



Fragments covering z nt upstream
to z nt downstream of the target nucleotide : a, b, c and d

Fragments covering the target nucleotide: a, b, c, d, e, f and g

$$P_i = \frac{4}{7}$$

FIG. 41

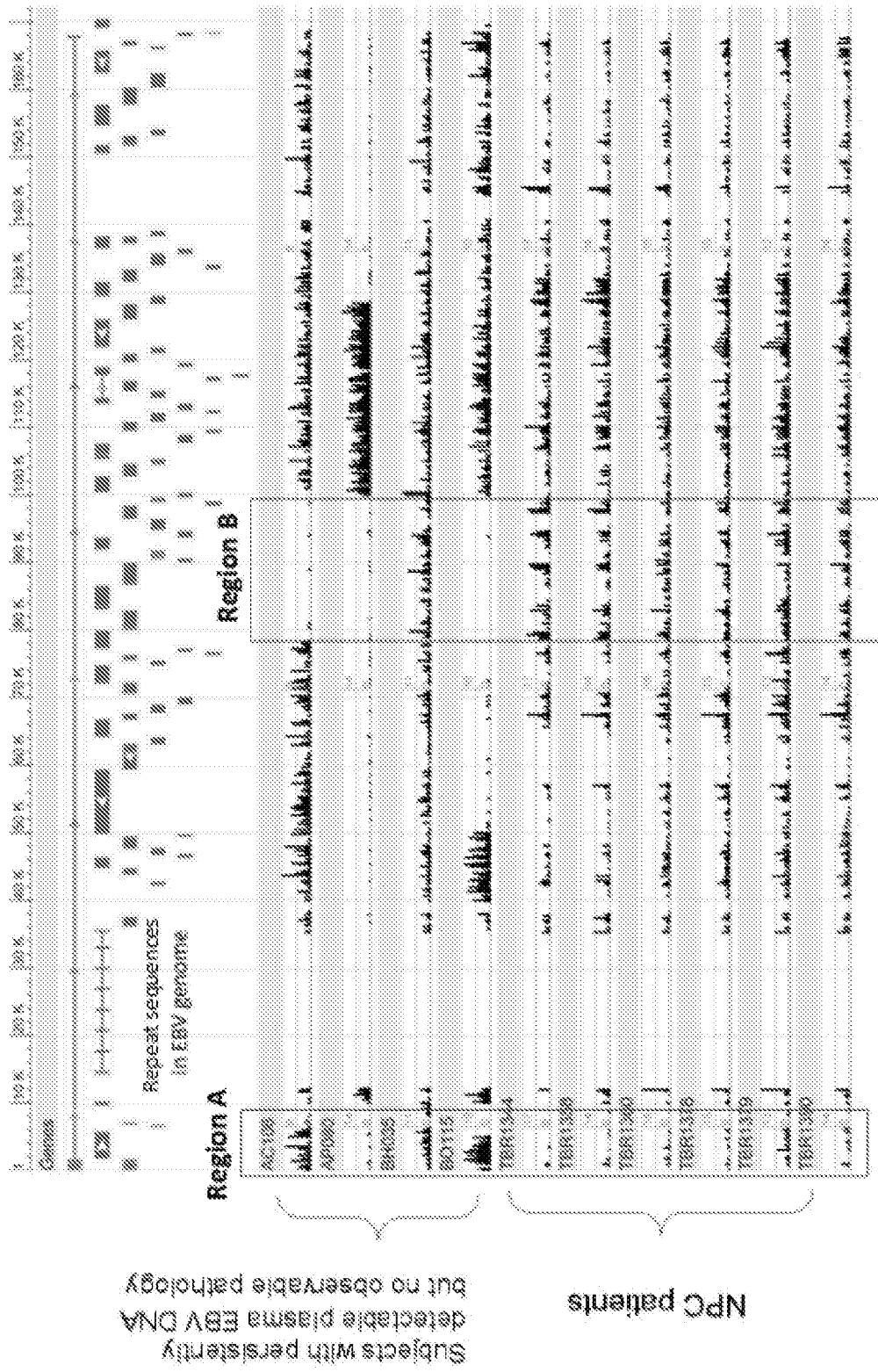


FIG. 42

400 most common ending positions
for plasma EBV DNA

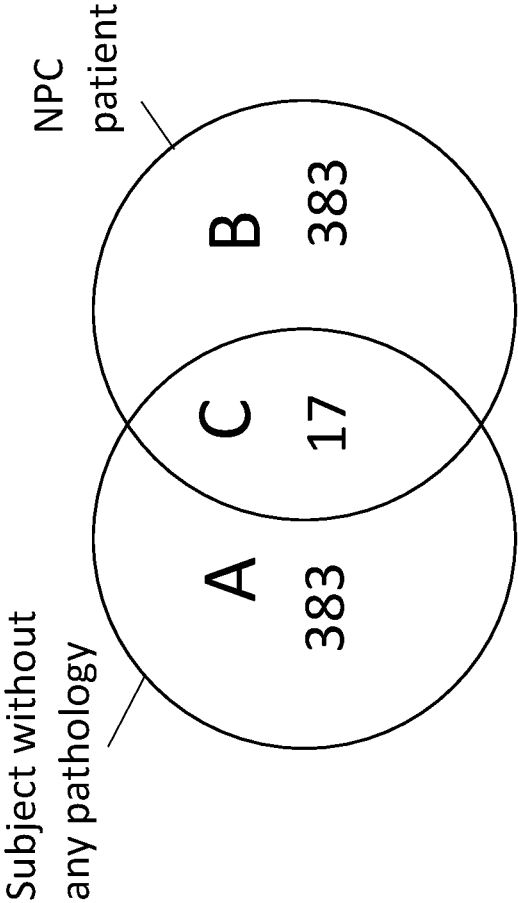


FIG. 43

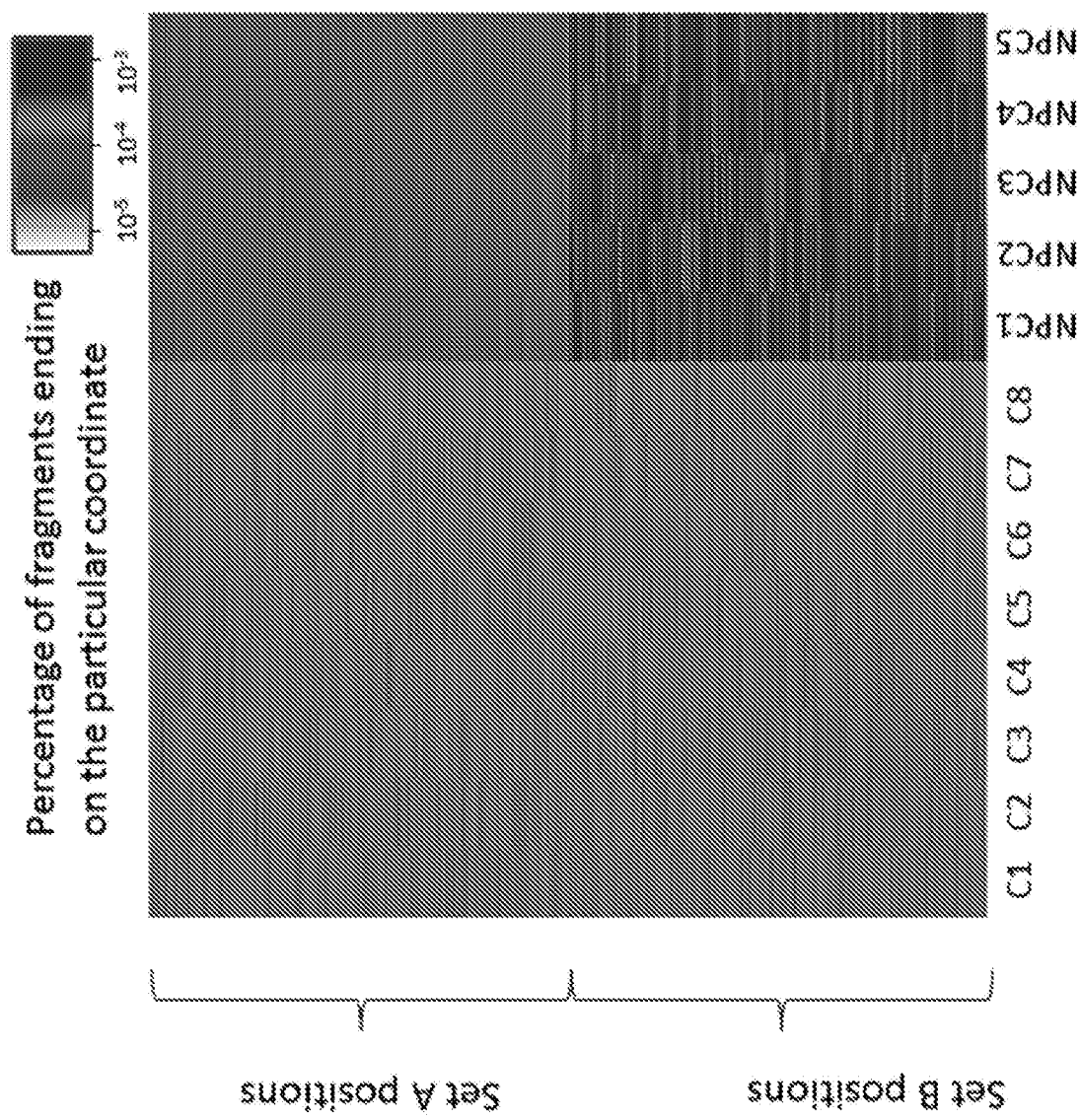


FIG. 44

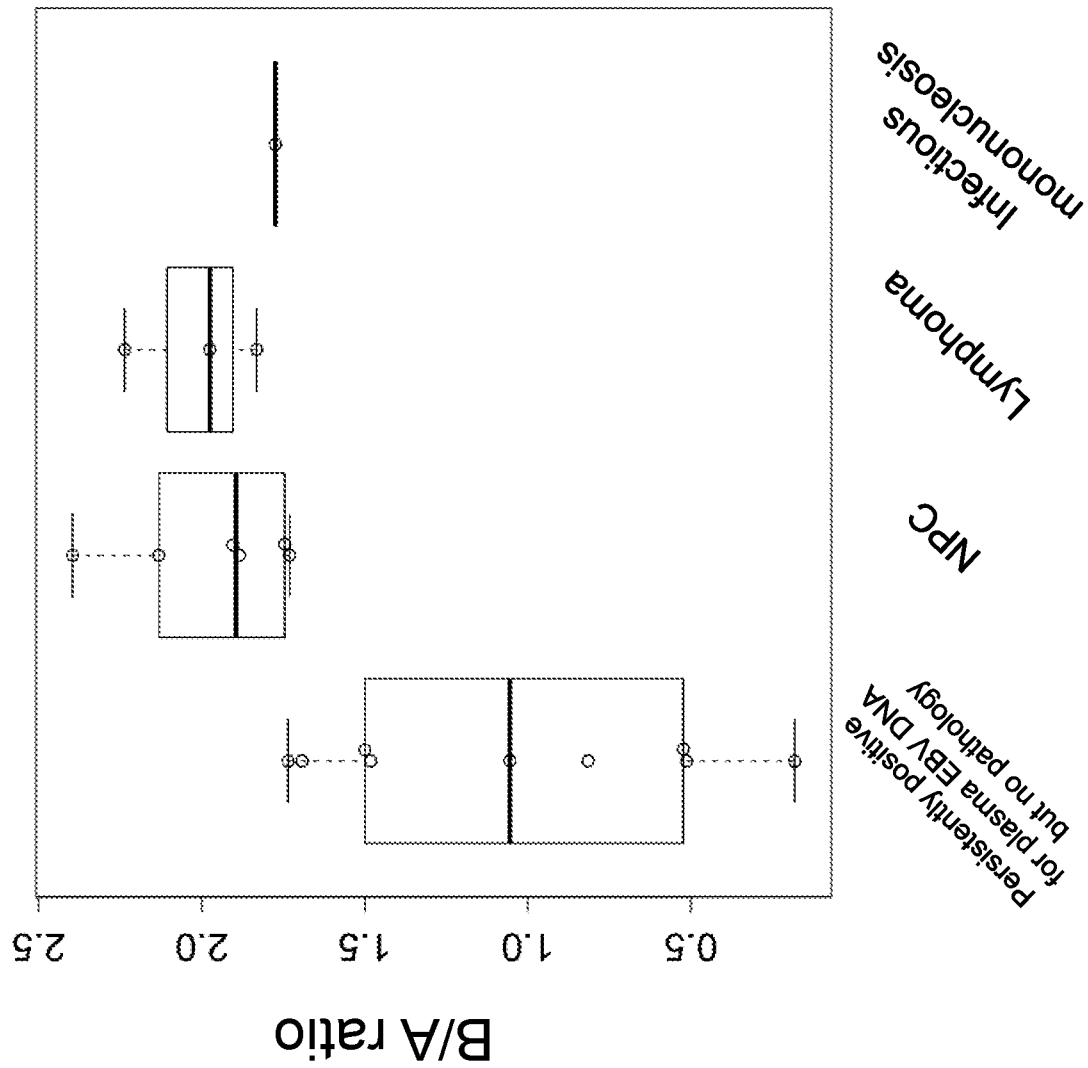


FIG. 45

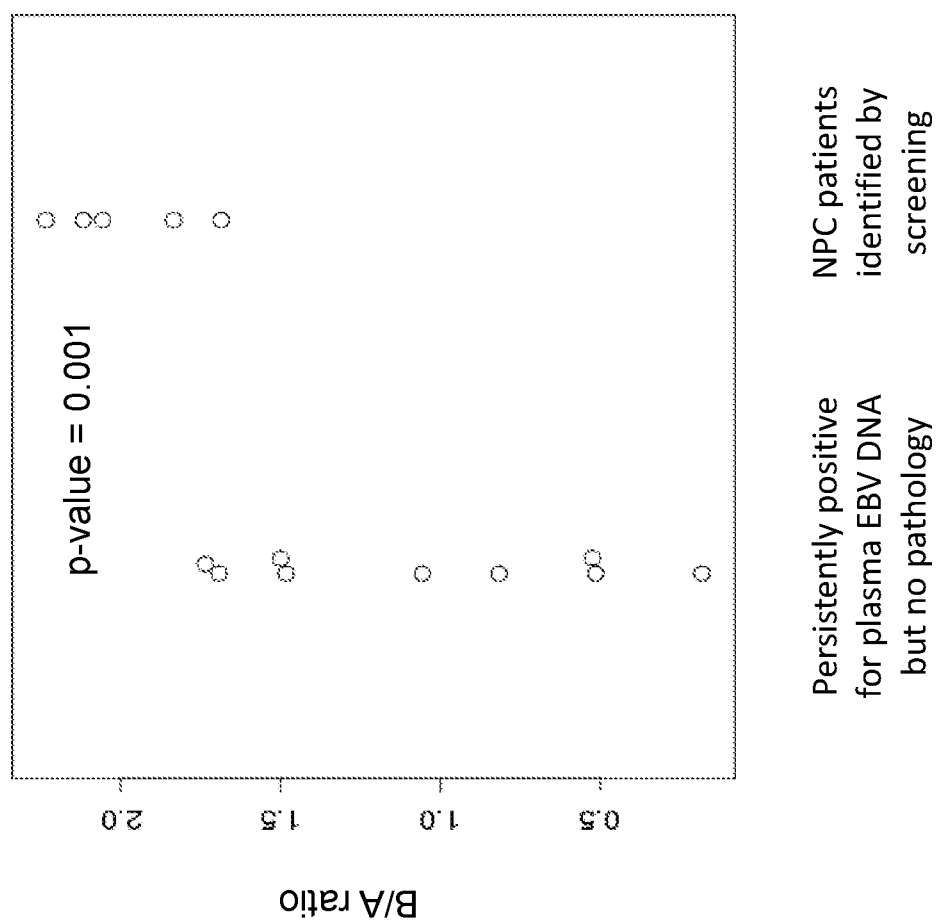


FIG. 46

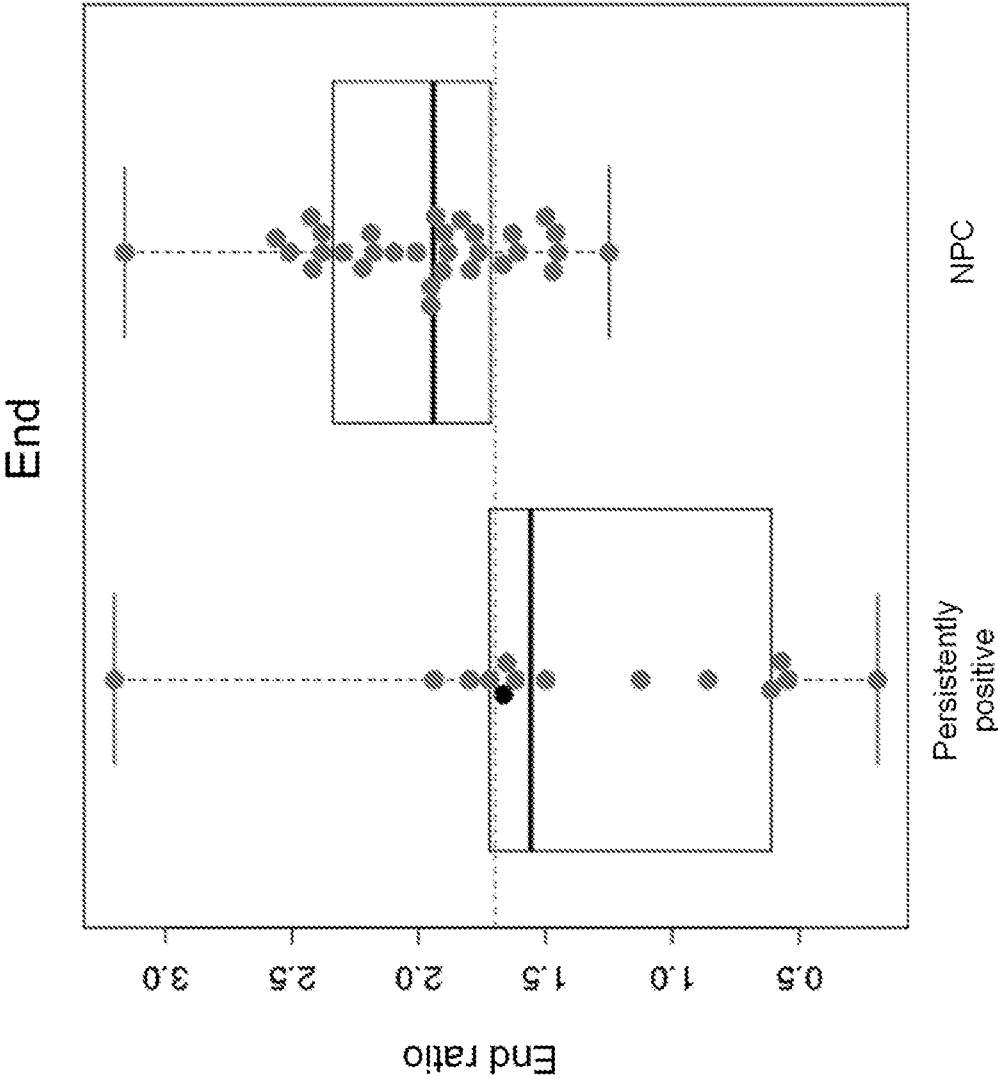


FIG. 47

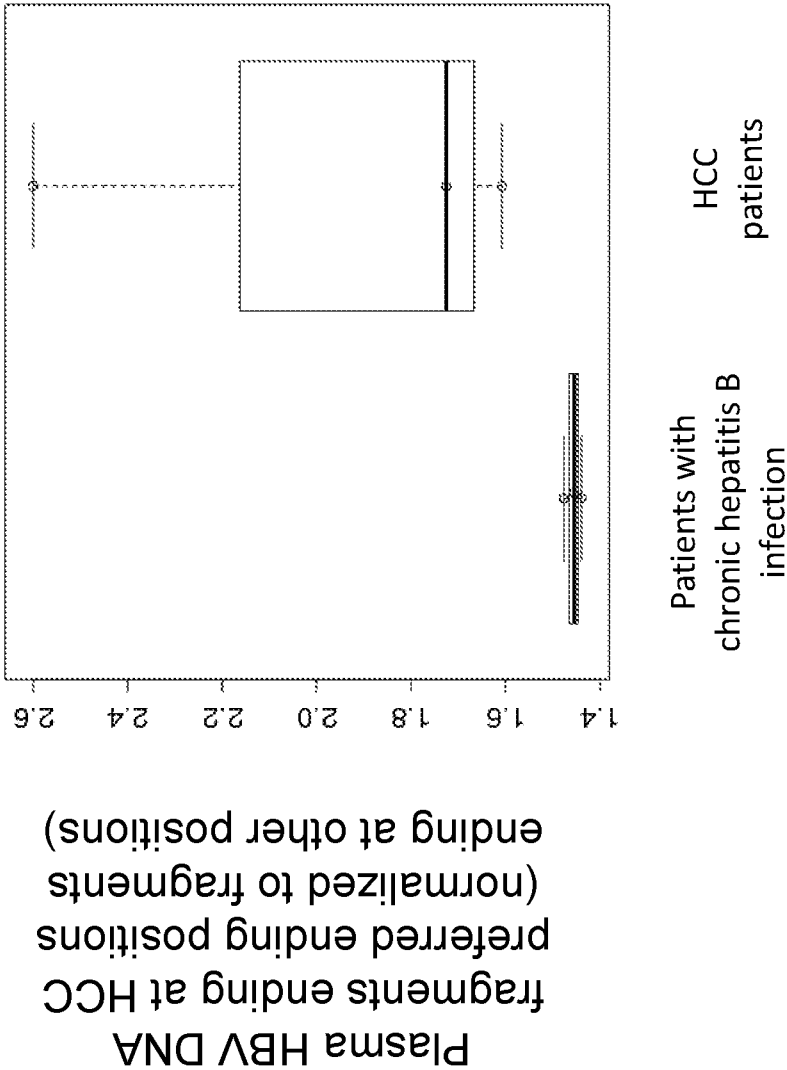


FIG. 48

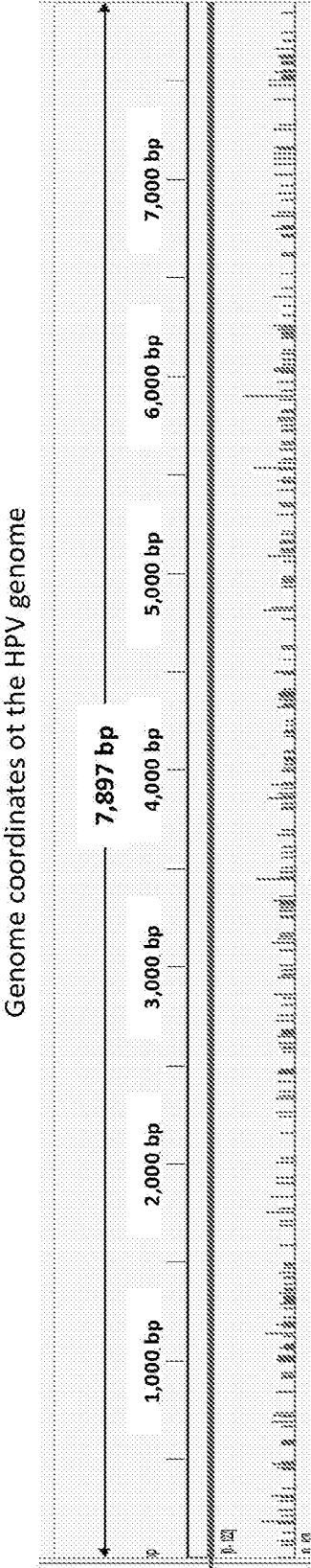


FIG. 49A

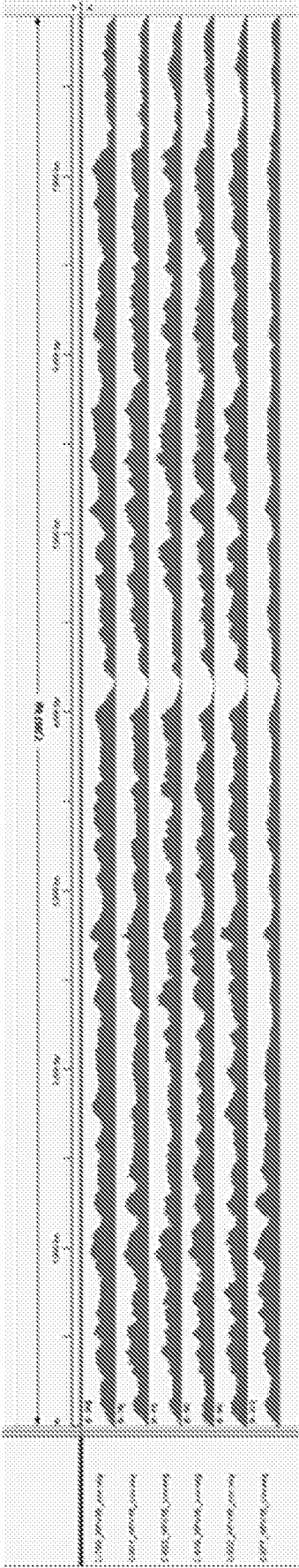


FIG. 49B

Different coverage per HPV genome between CC and HSNCC



FIG. 50

Differential abundance between C and HNSCC

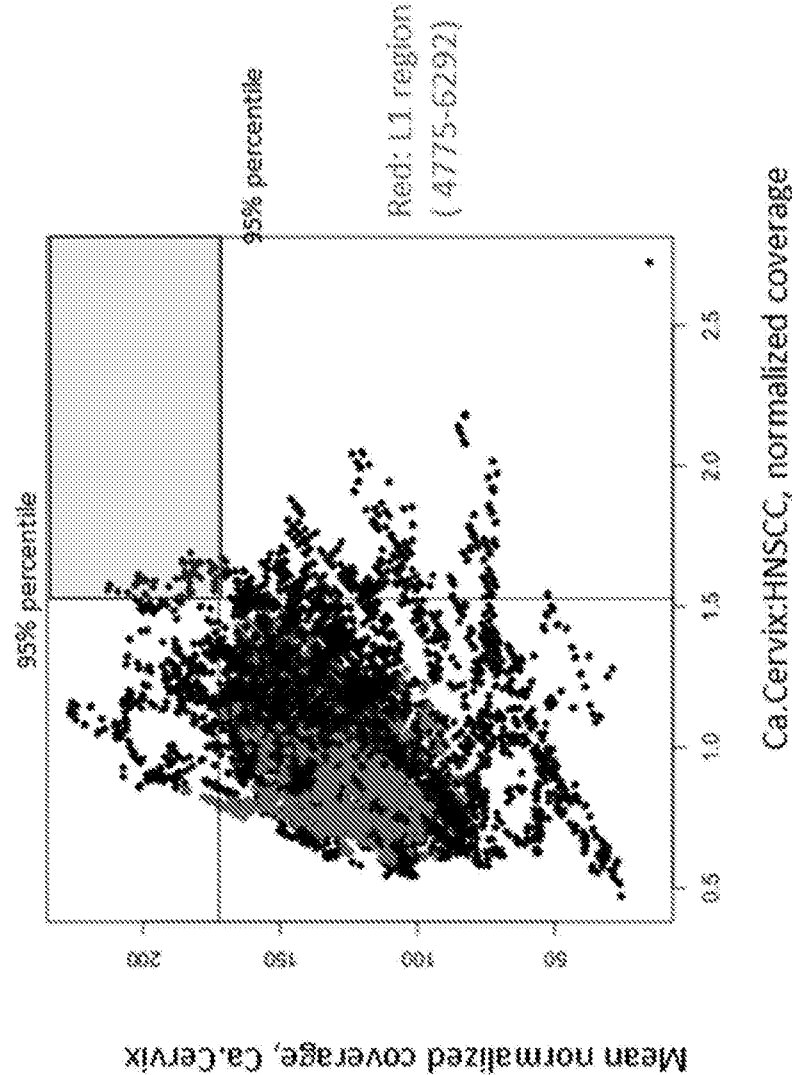


FIG. 51

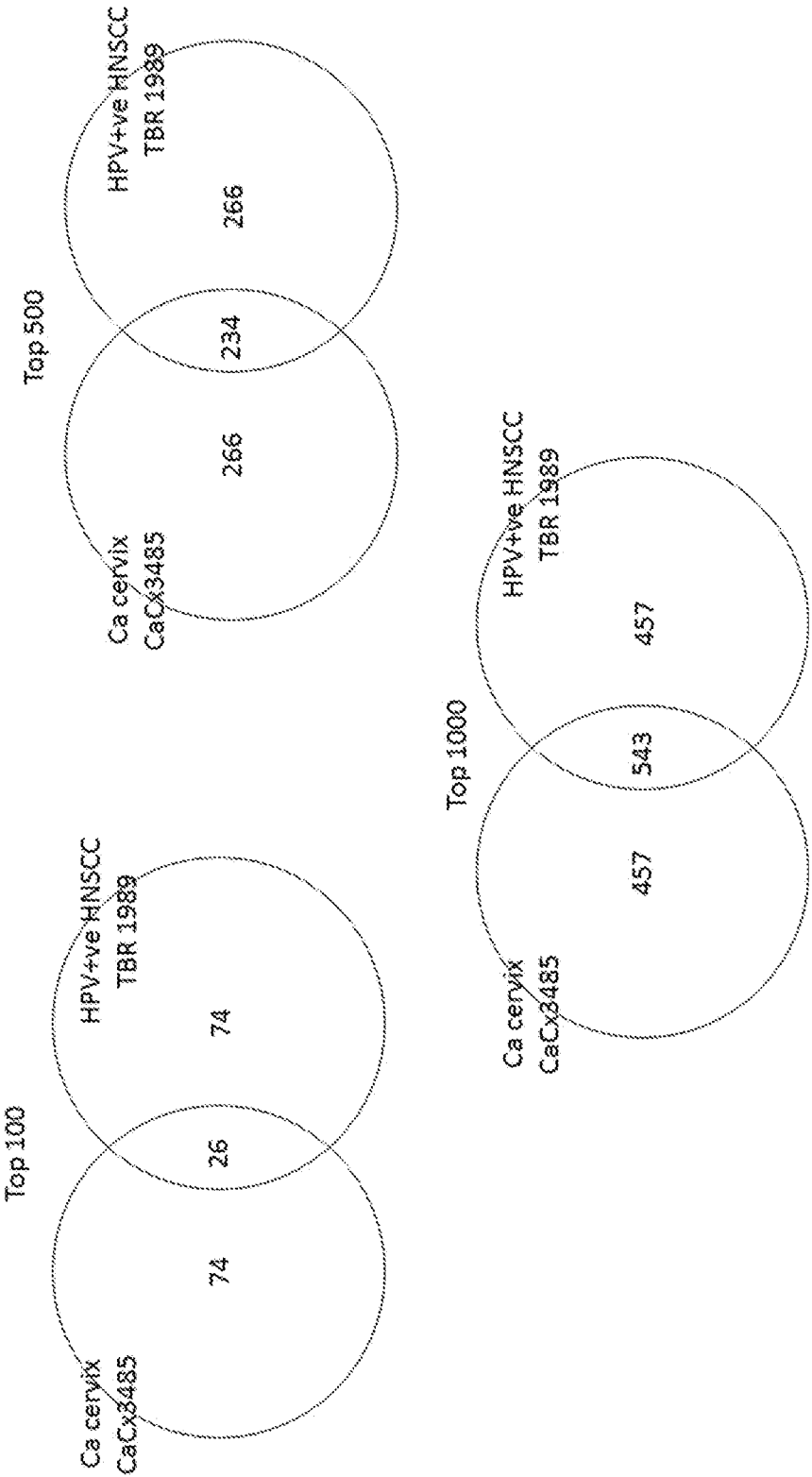
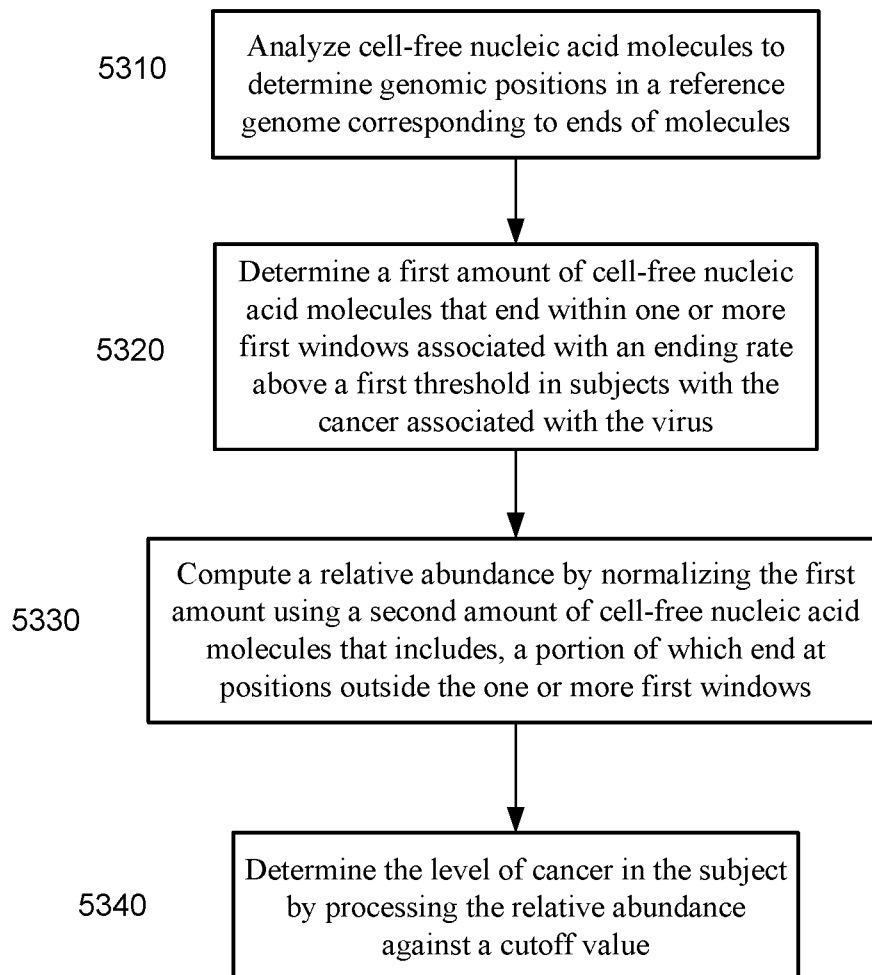


FIG. 52

5300

**FIG. 53**

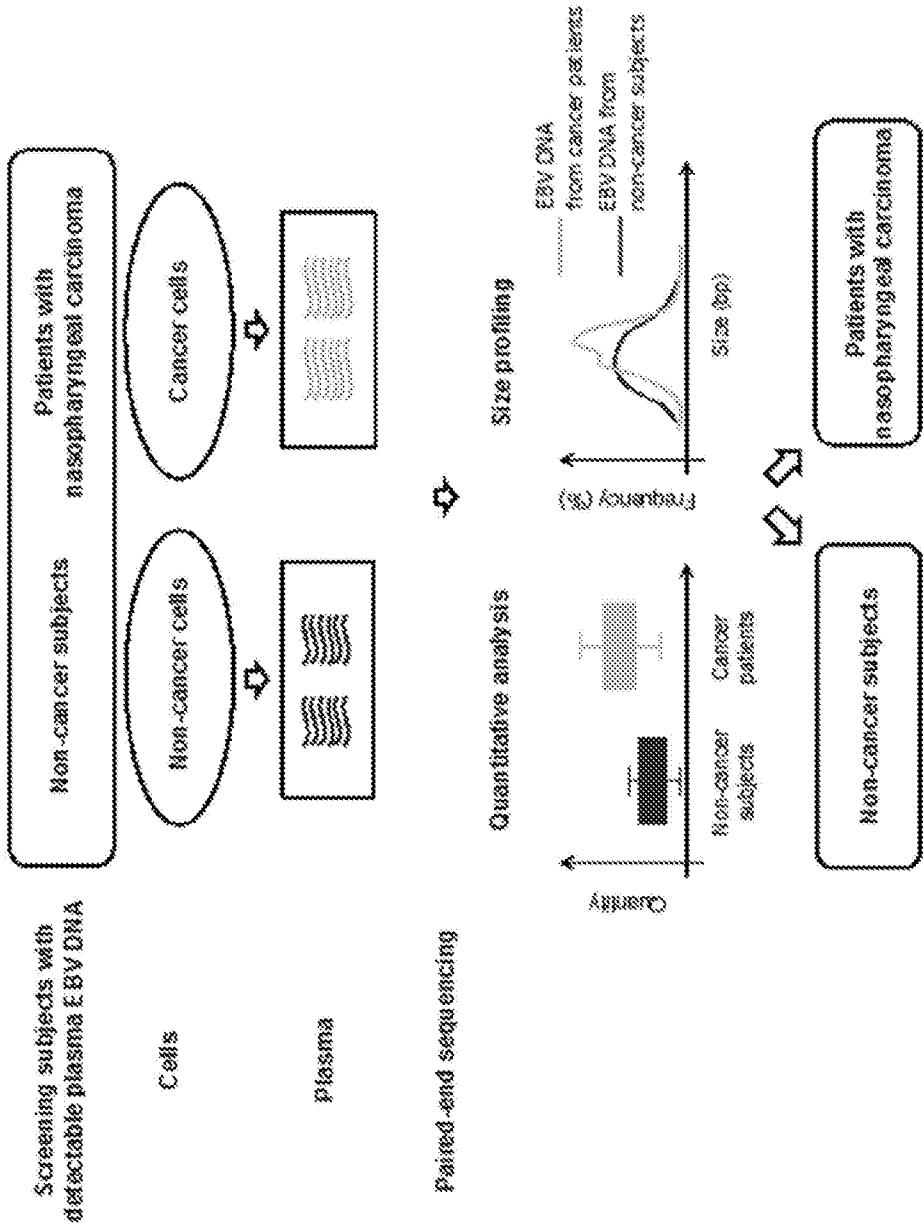


FIG. 54

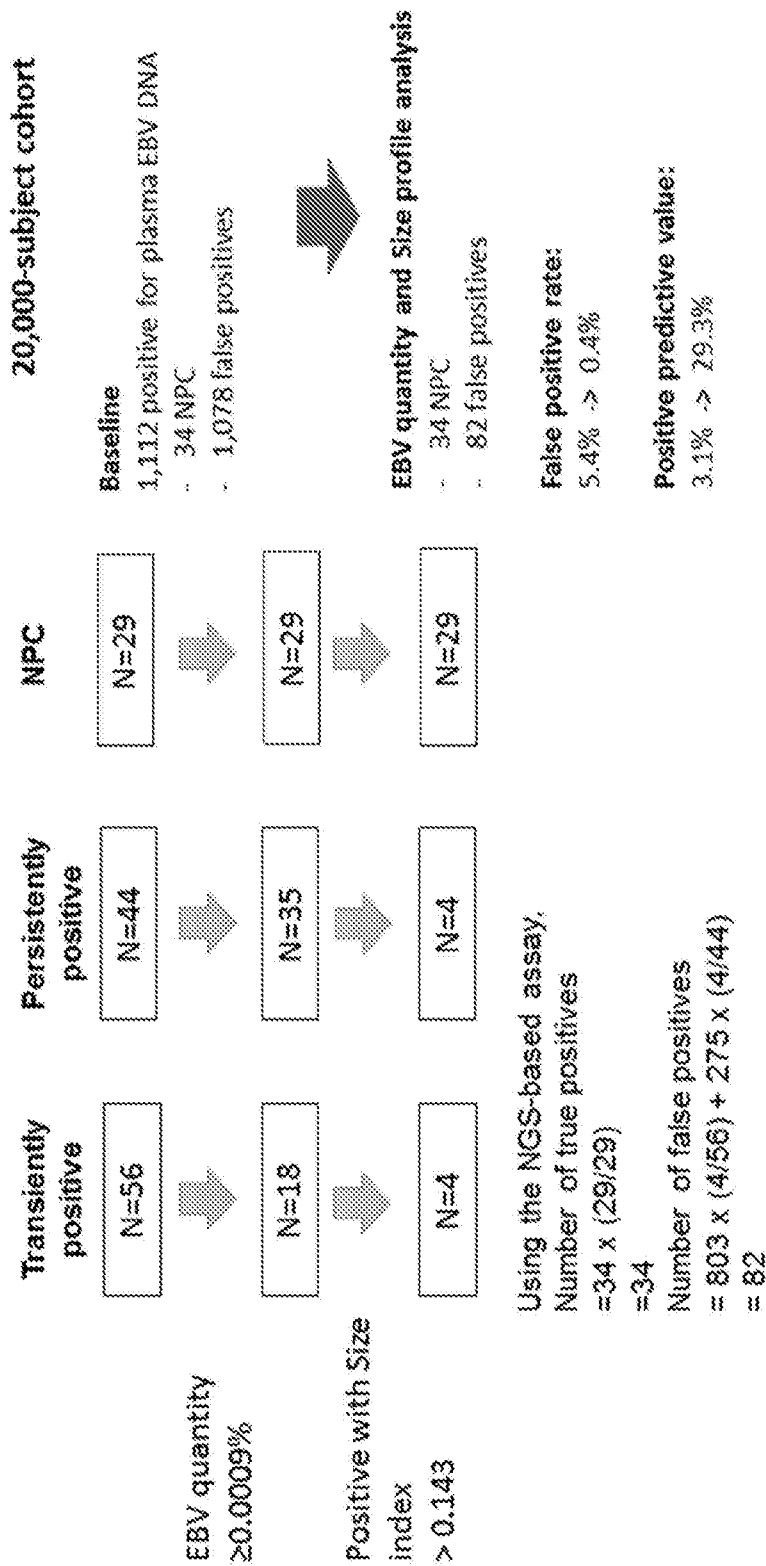


FIG. 55

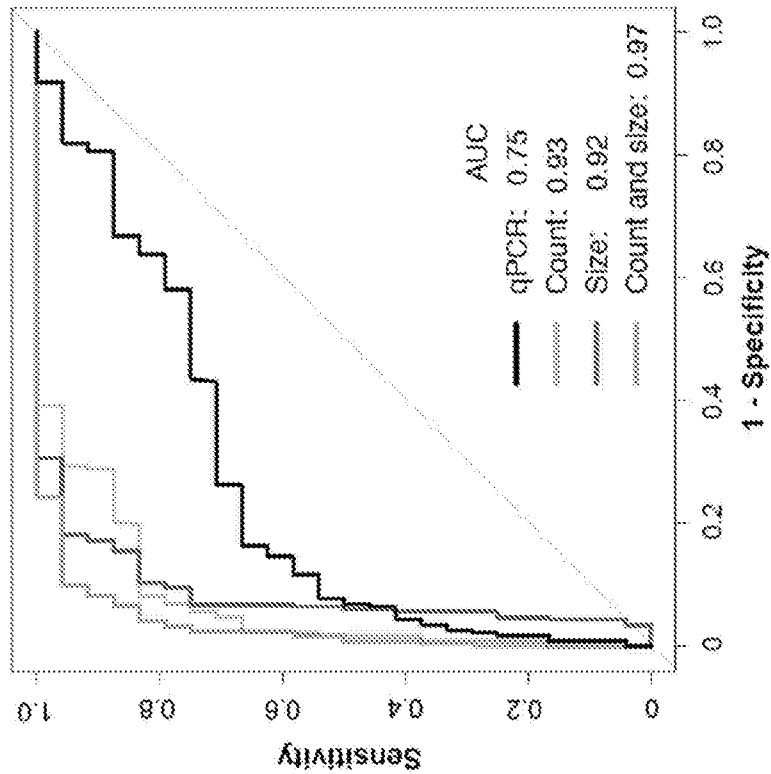


FIG. 56B

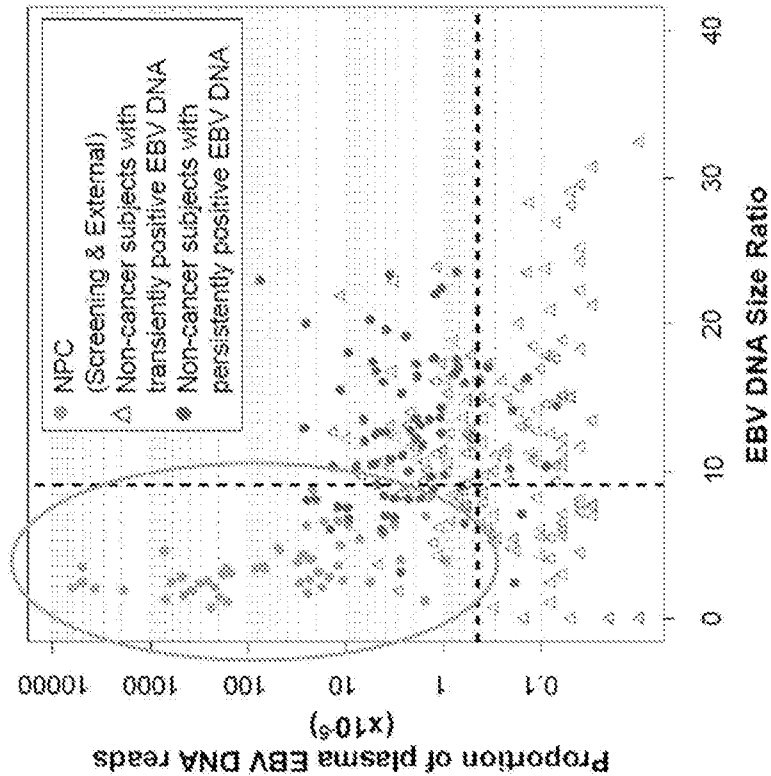


FIG. 56A

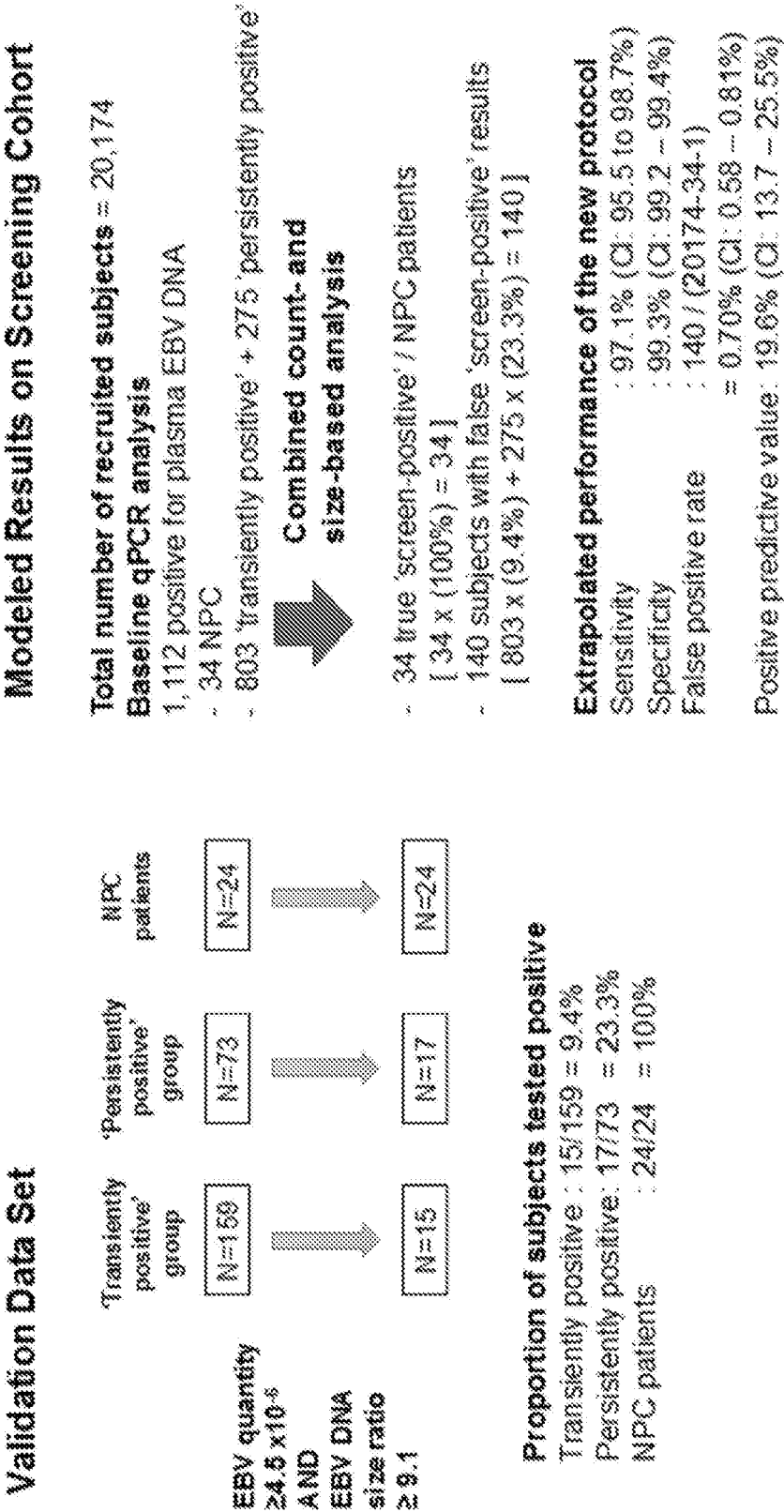


FIG. 57

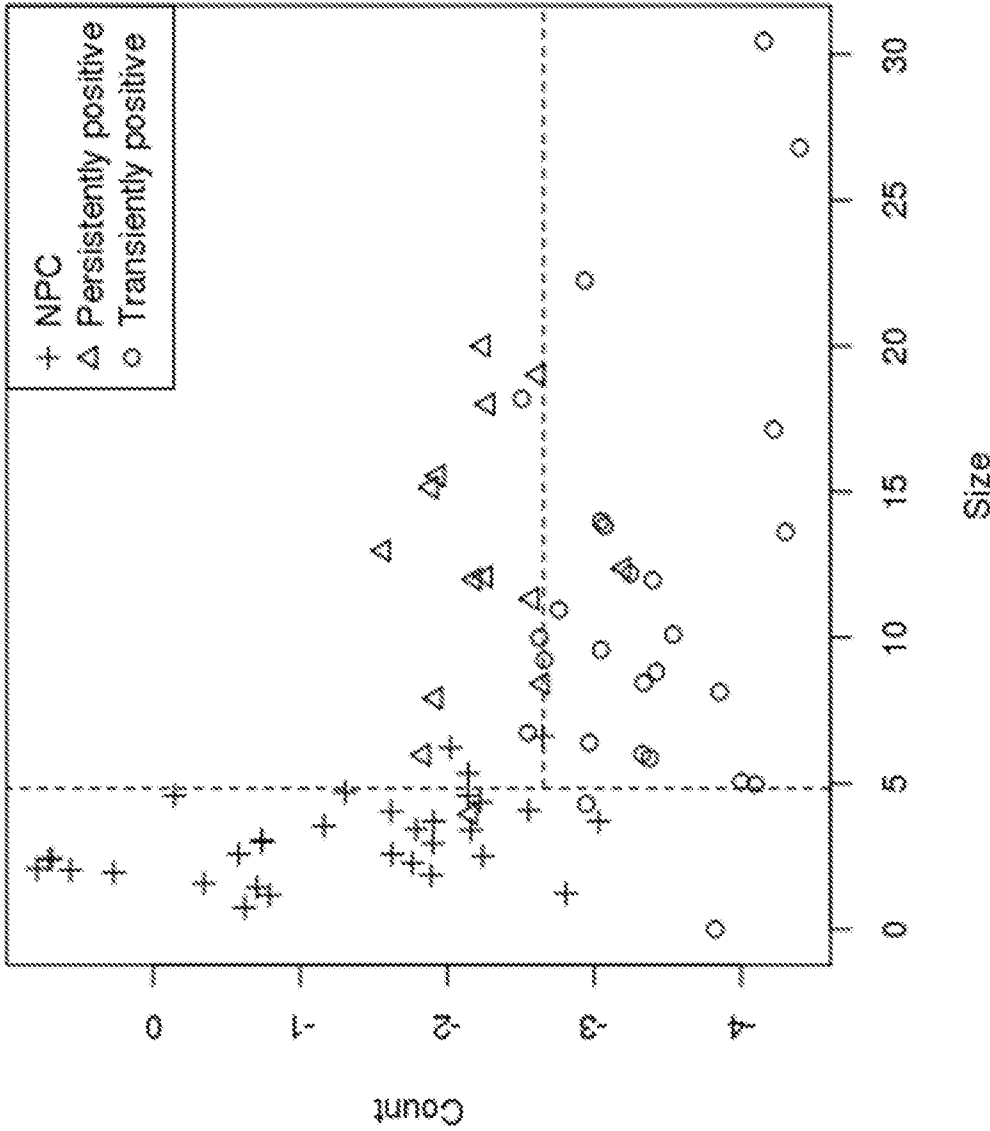


FIG. 58

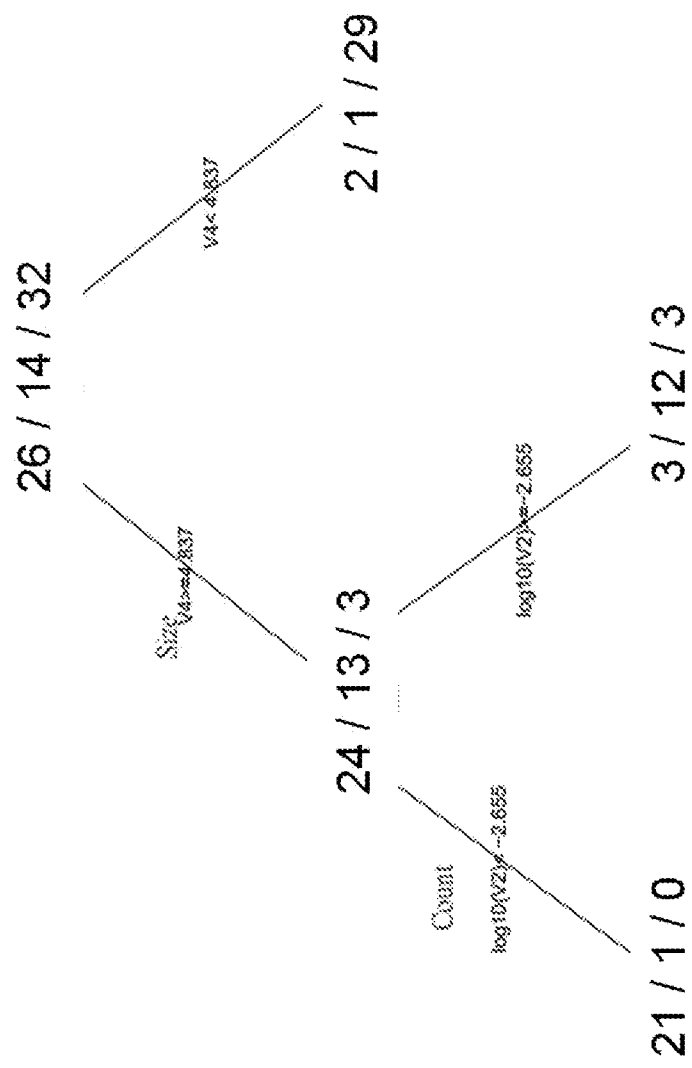
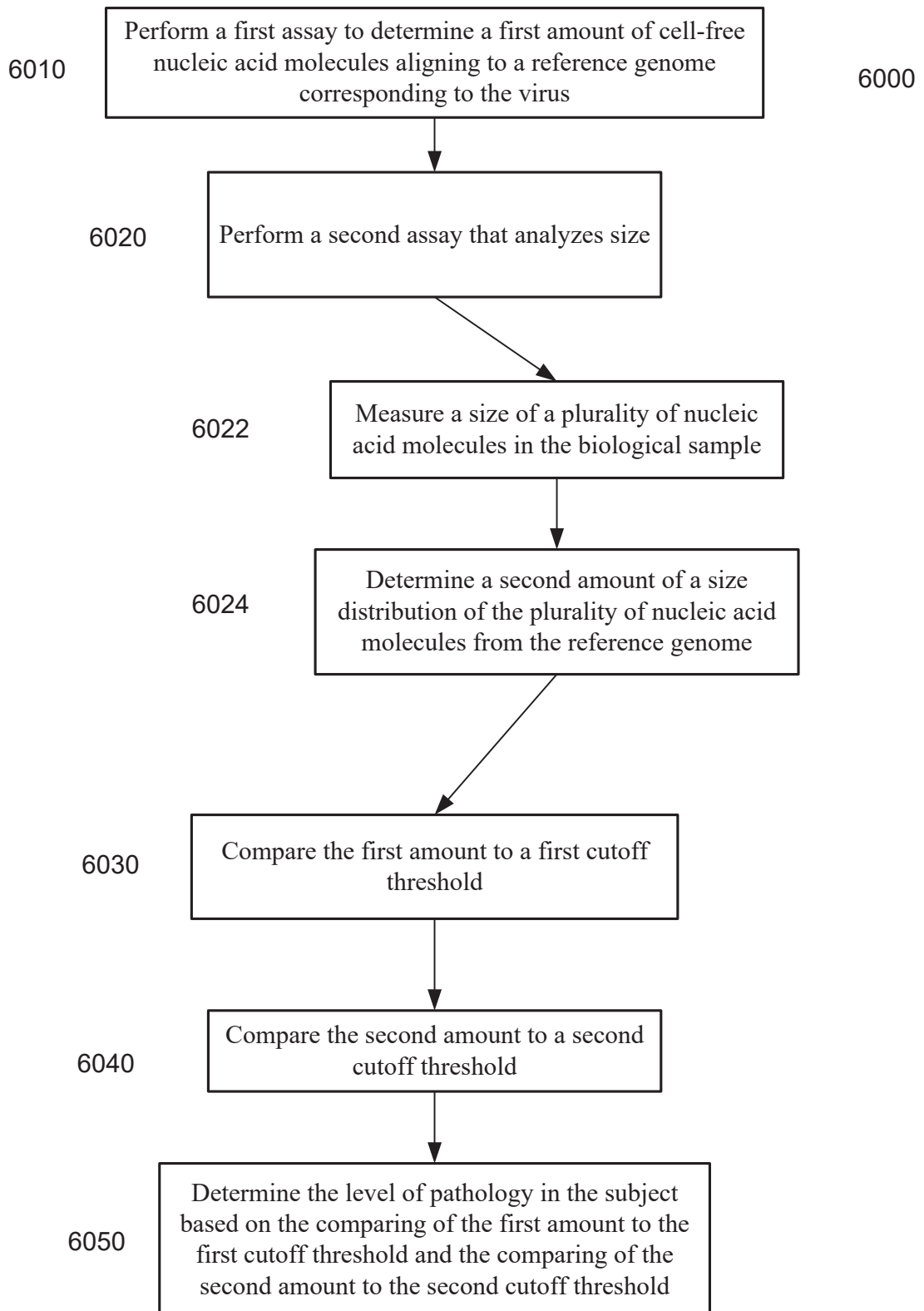
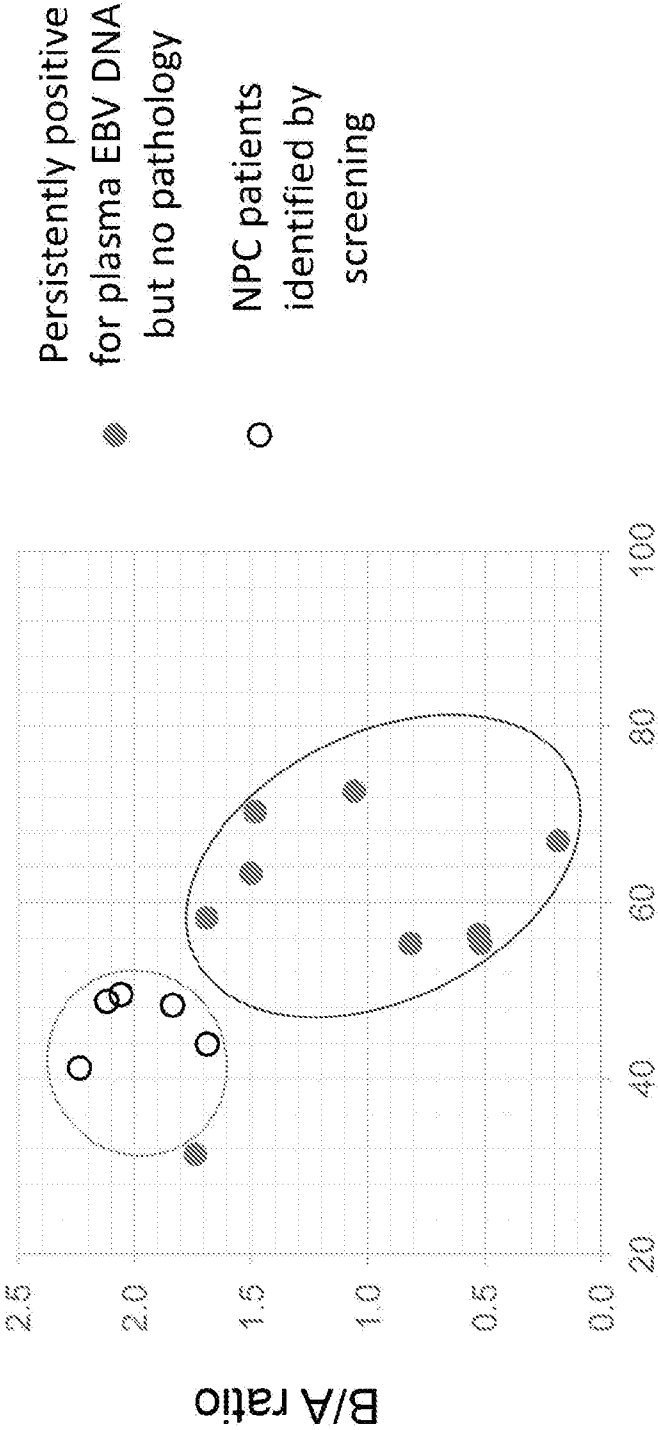


FIG. 59

**FIG. 60**



The percentage of EBV DNA fragments below 150 bp in plasma (%)

FIG. 61

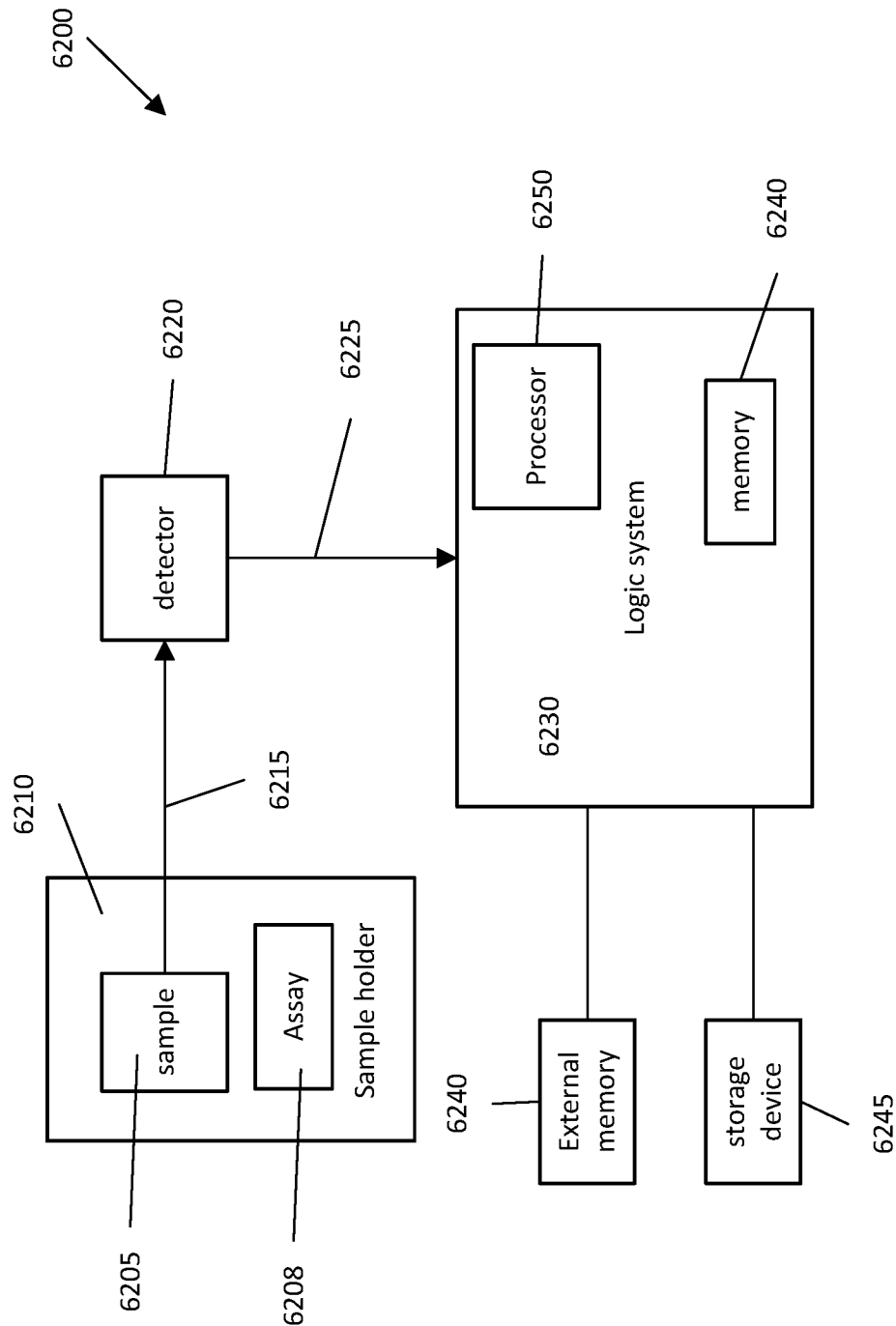


FIG. 62

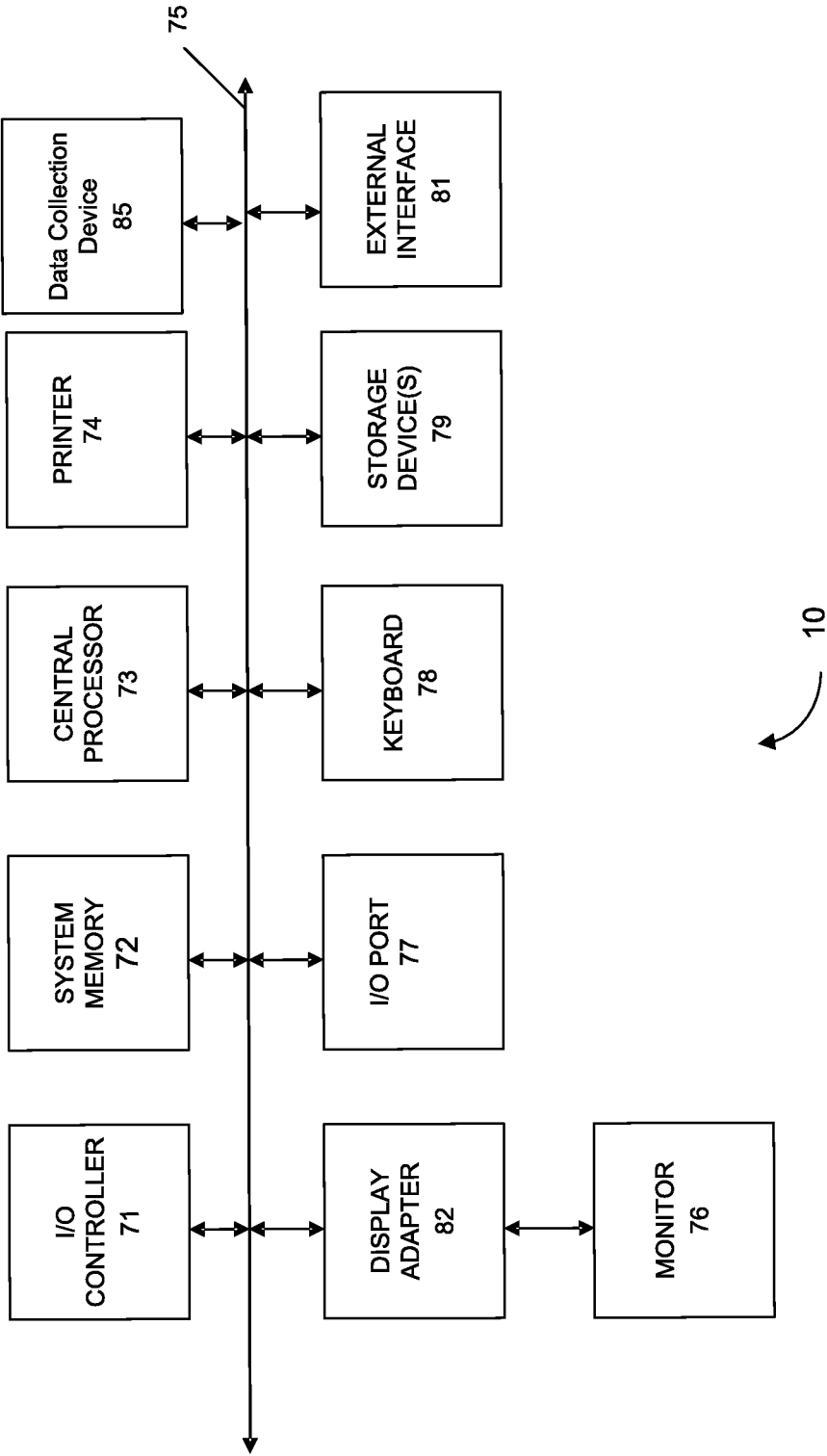


FIG. 63