Group Meeting

02/04/2016

IBC Background

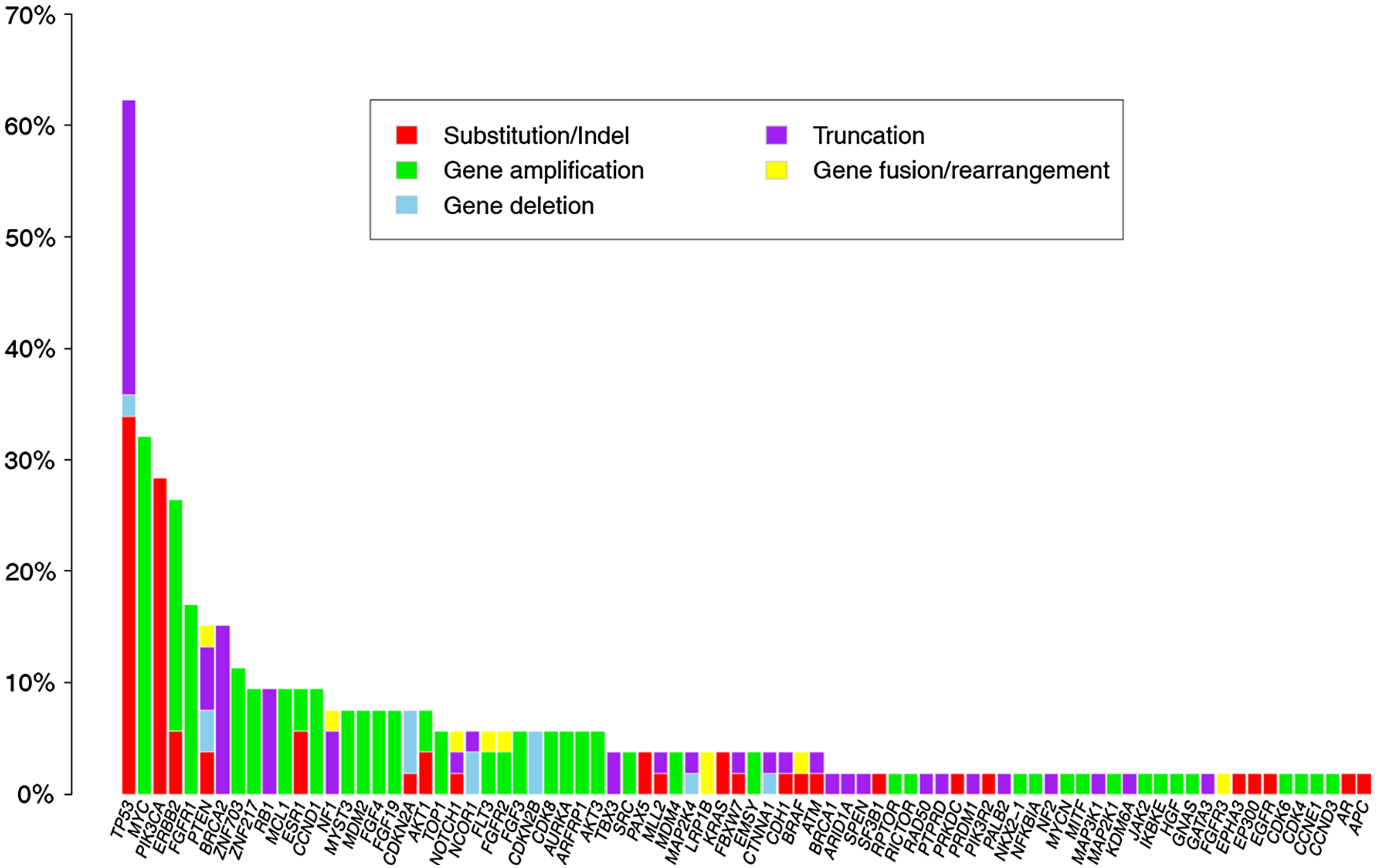
Inflammatory Breast Cancer – the most aggressive and lethal form of breast cancer

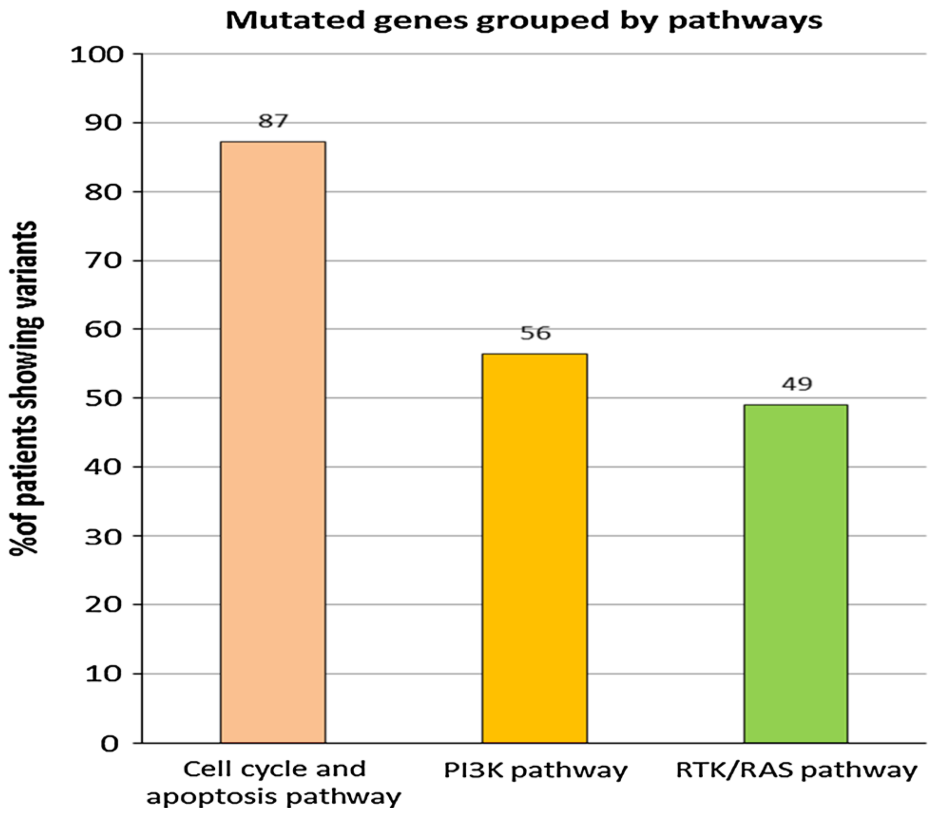
Associated with high risk of developing distant metastasis and lower survival rate

Development of skin erythema and edema due to cancer cells invading the lymphatic vasculature of the skin

No previous study for whole genome/exome characterization of IBC patients.

Hybrid-capture assay study on 55 IBC samples





Ross et. al.

Goal of current study

To identify genomic variations playing key role in progression of IBC

To differentiate between IBC and non-IBC samples on genomic level

Validation of the candidate markers in independent IBC and non-IBC samples

Clinical information for 20 IBC samples

Sample ID	**Age**	**Race**	HER2 +/-	ER +/-	PR +/-
101	59	White	Positive	Positive	positive
111	47	White	Positive	Negative	Negative
150	54	White	Negative	Positive	Positive
193	41	Black	Negative	Positive	low positive
208	56	White	Negative	Positive	Negative
220	60	Hispanic	Negative	Positive	Positive
235	42	Black	Negative	Positive	positive
266	40	Black	Negative	Positive	Positive
267	59	White	Positive	Negative	Negative
172	75	White	Negative	Negative	Low Positive
228	68	White	Negative	Negative	Negative
232	52	White	Negative	Negative	Negative
298	57	White	Negative	Negative	negative
300	39	White	Positive	Negative	Negative
305	69	White	Negative	Negative	Negative
311	49	Hispanic	Negative	Negative	negative
312	68	White	Negative	Positive	Positive
328	50	White	Positive	Negative	negative
333	64	Black	Negative	Negative	Negative
343	57	White	Negative	Low Positive	negative

IBC sequencing details

Genomic DNA from 20 snap frozen from MD Anderson Cancer Center with tumor cellularity > 60%

Standard Illumina paired-end whole genome sequencing with median coverage of 60X using the Illumina HiSeq 2500 sequencing platform for first 2 tumor-normal pair

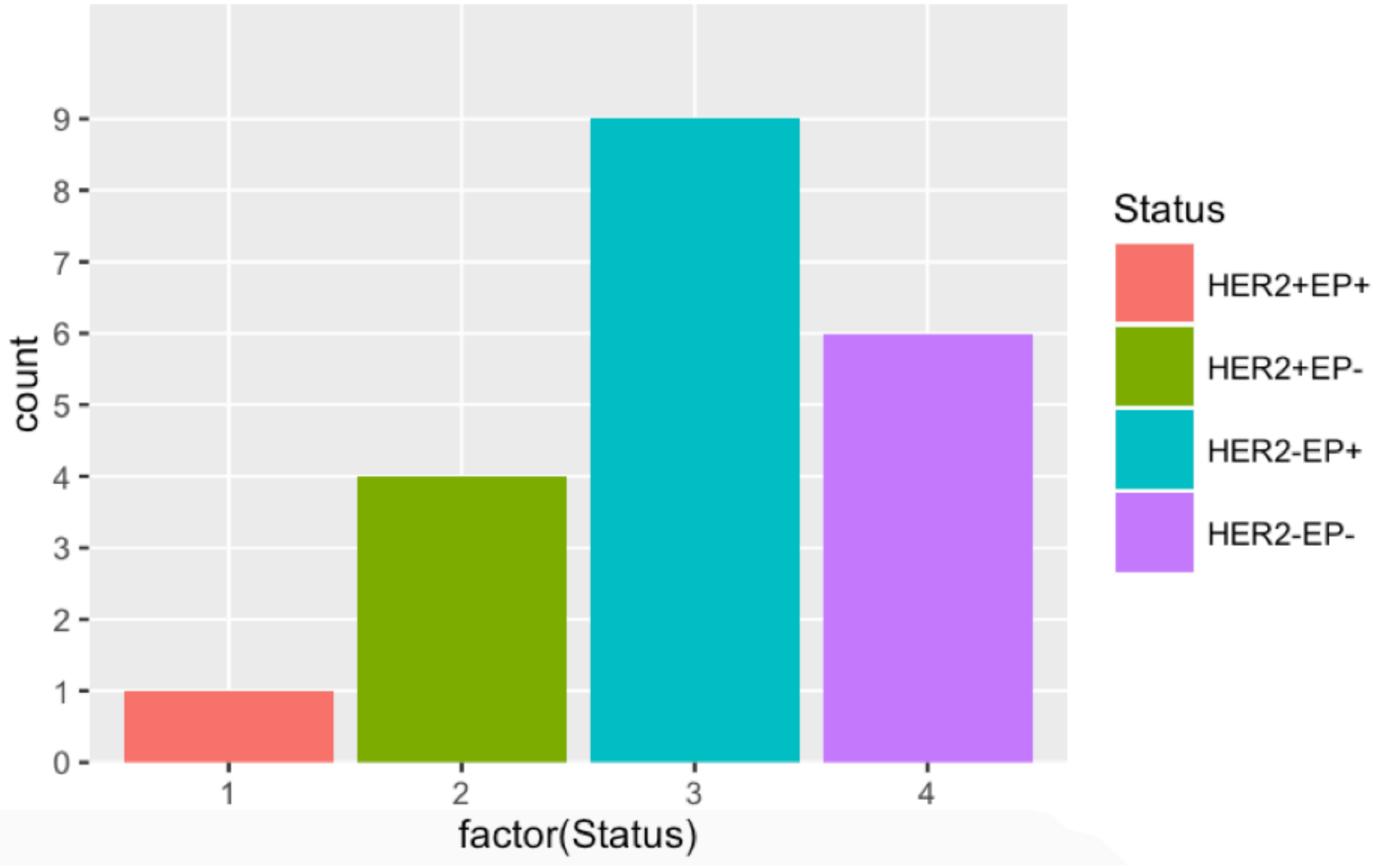
For remaining 18 samples, normal sample sequenced at 40X and tumor at 60X

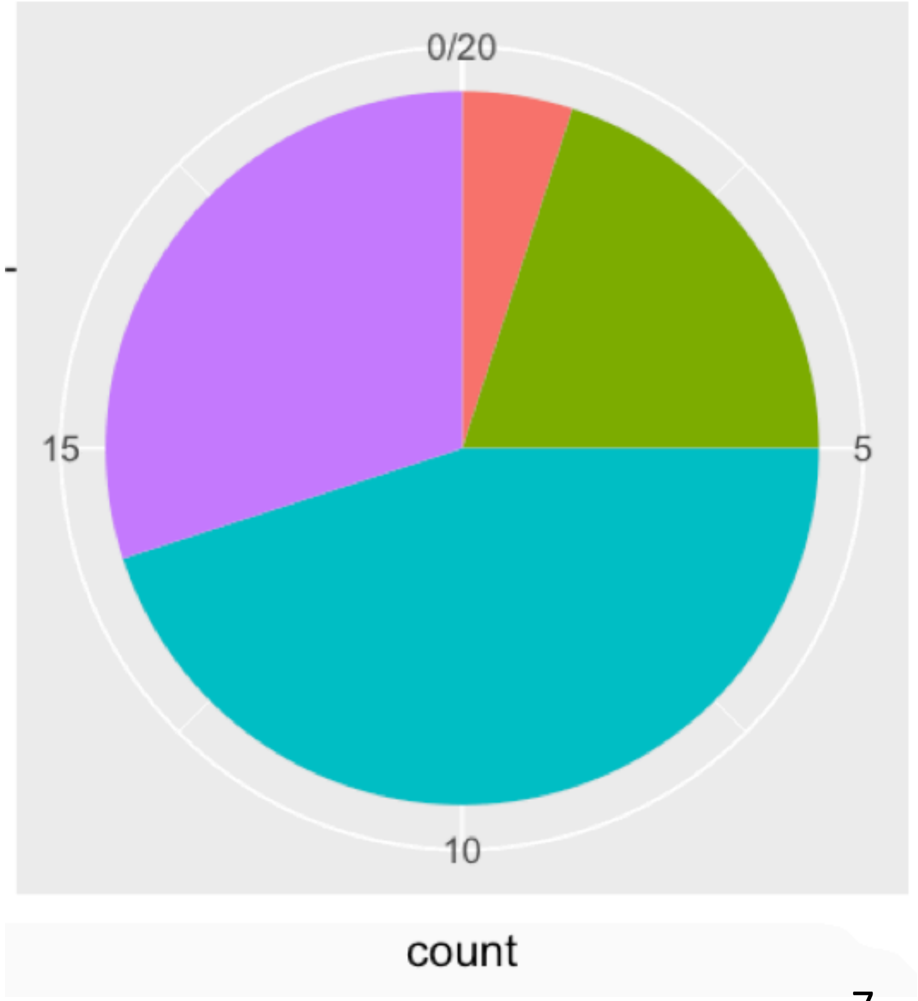
Non-IBC samples selection

- 20 IBC samples; 81 TCGA WGS samples (w/ clinical info)
- ER/PR status, HER2 status
  - HER2 + & ER/PR +*
  - HER2 + & ER/PR -
  - HER2 - & ER/PR +
  - HER2 - & ER/PR -
- Ages
- Race
- 58 TCGA samples with all info available

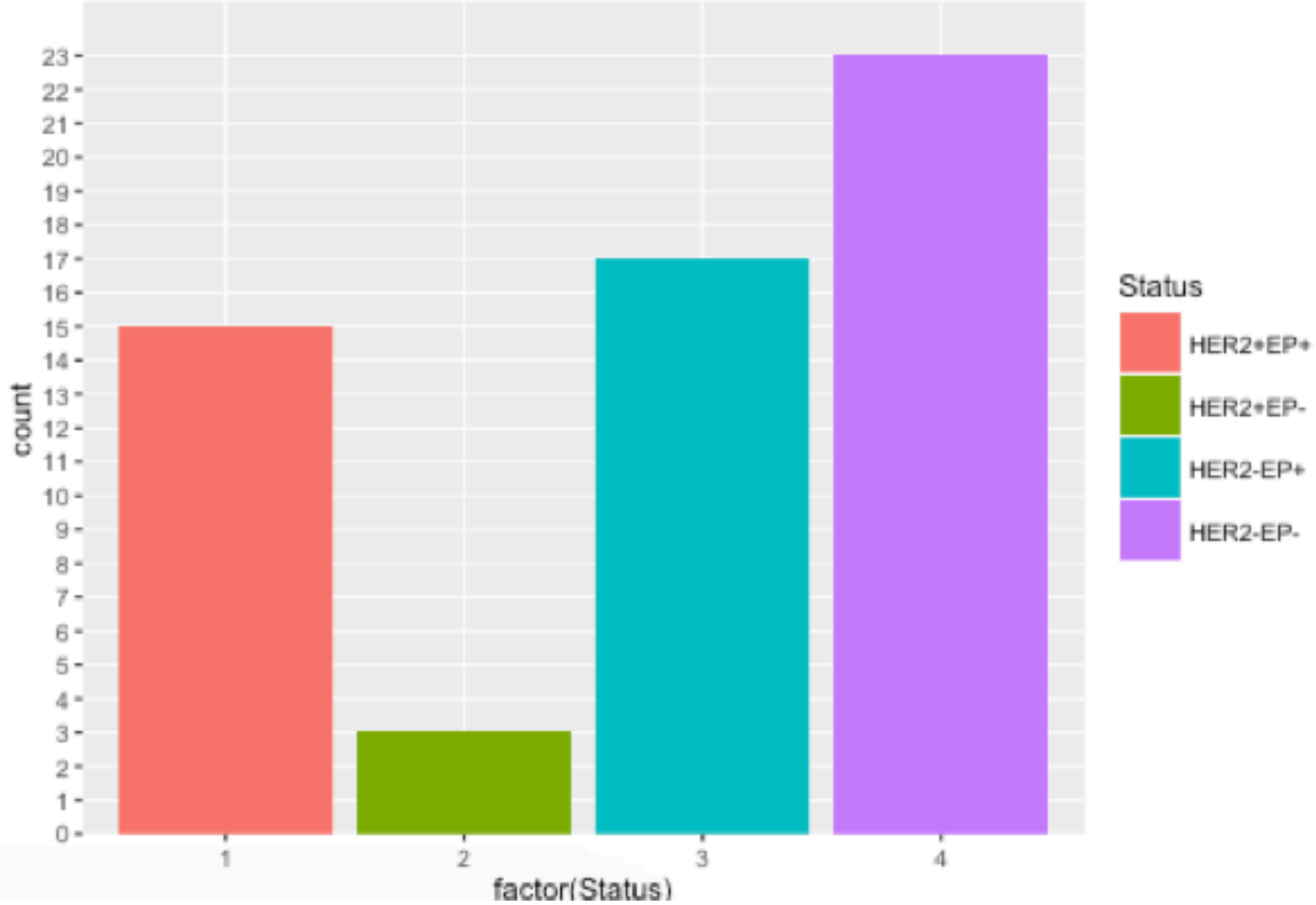
- *At least one is +; “Low-positive”: positive; “Low-negative”: negative
- “Indeterminate” or “Not Available” or “Not Evaluated” or “Equivocal”: NA

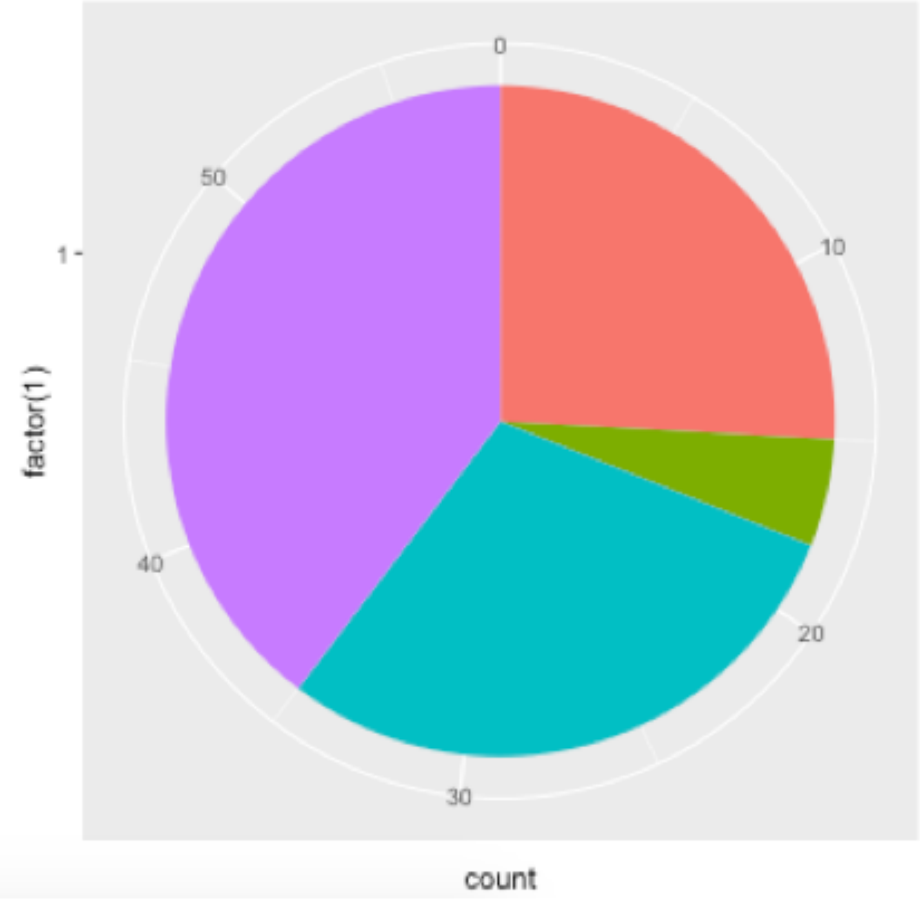
IBC Samples subtype status



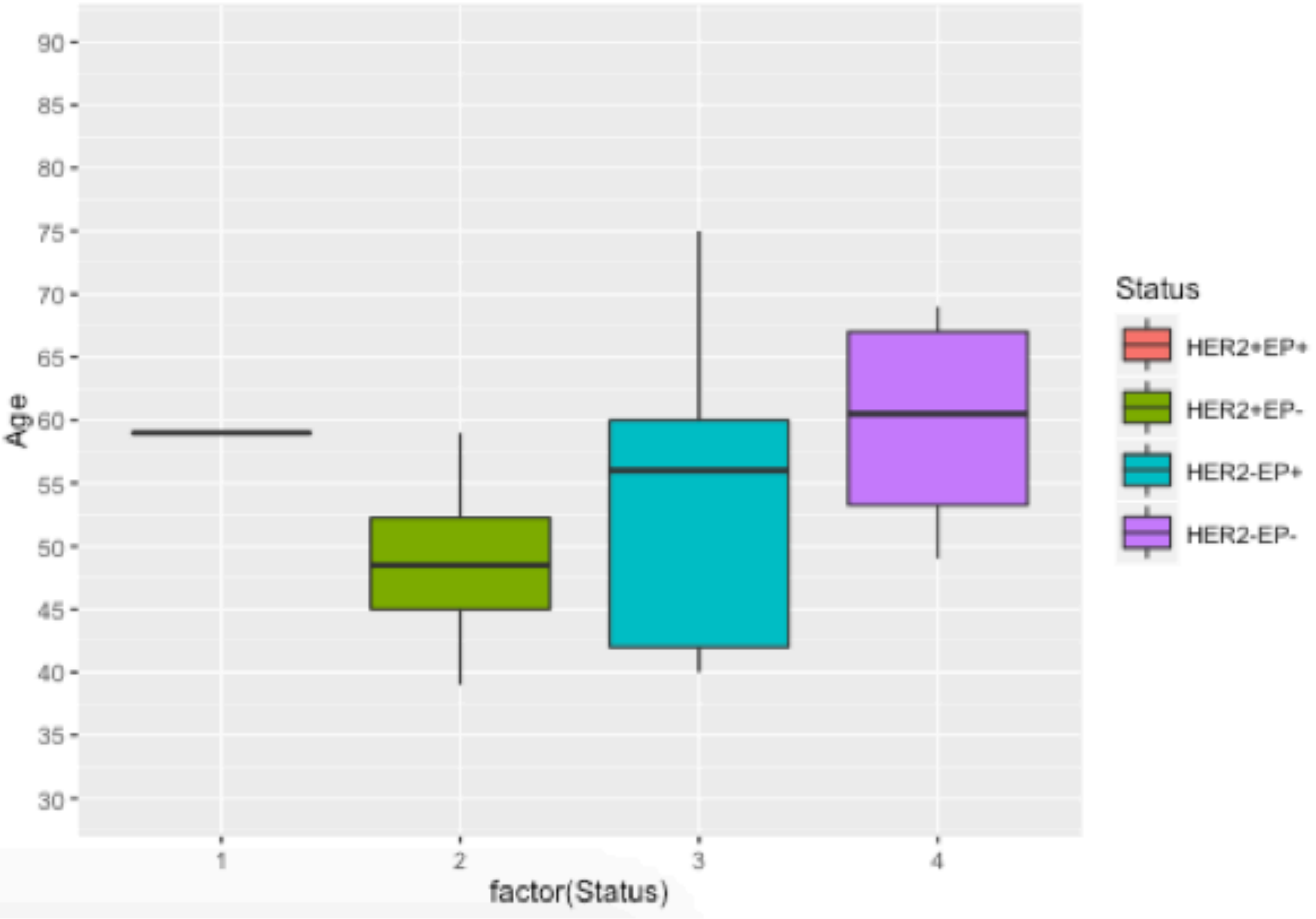


Non-IBC Samples subtype status

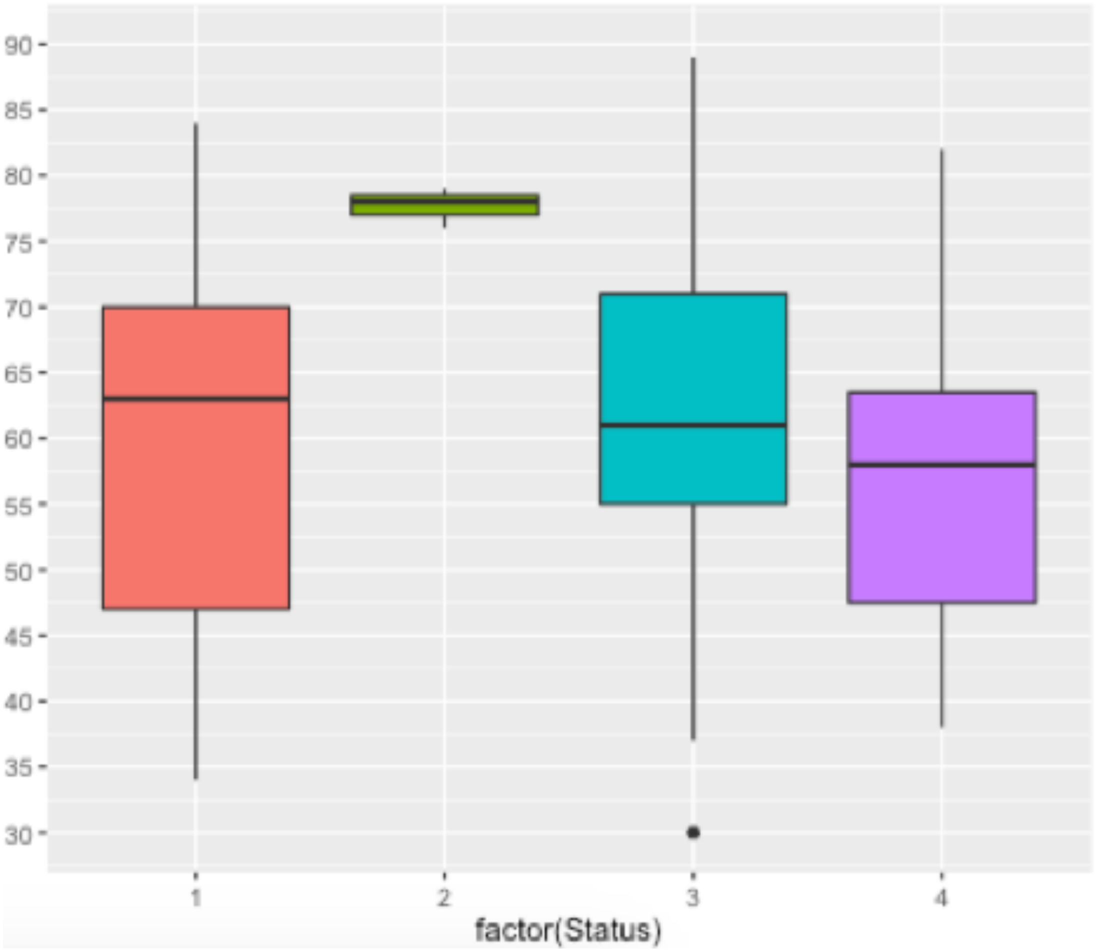




Age distribution of IBC and non-IBC patients

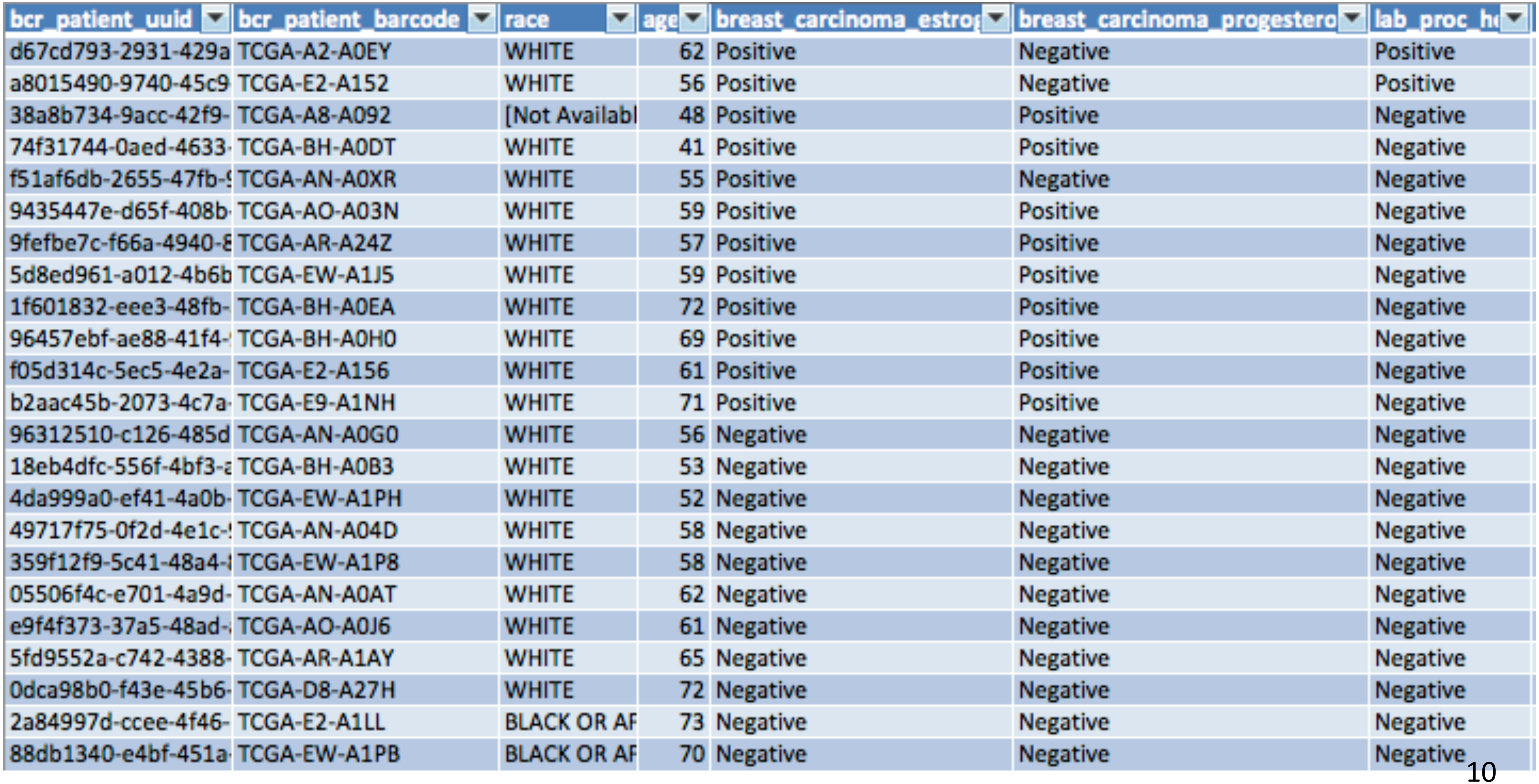


IBC



non-IBC

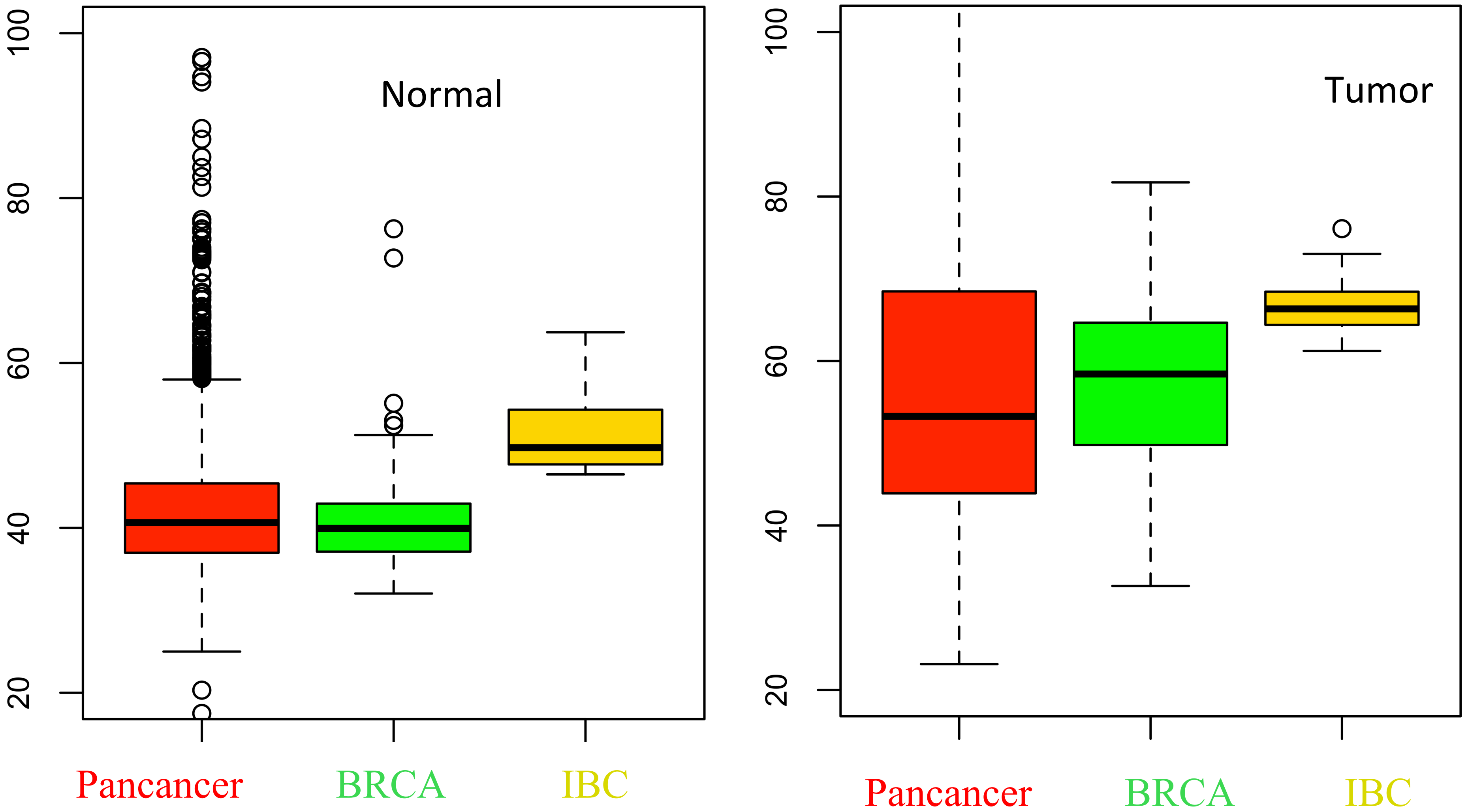
List of non-IBC Samples from TCGA



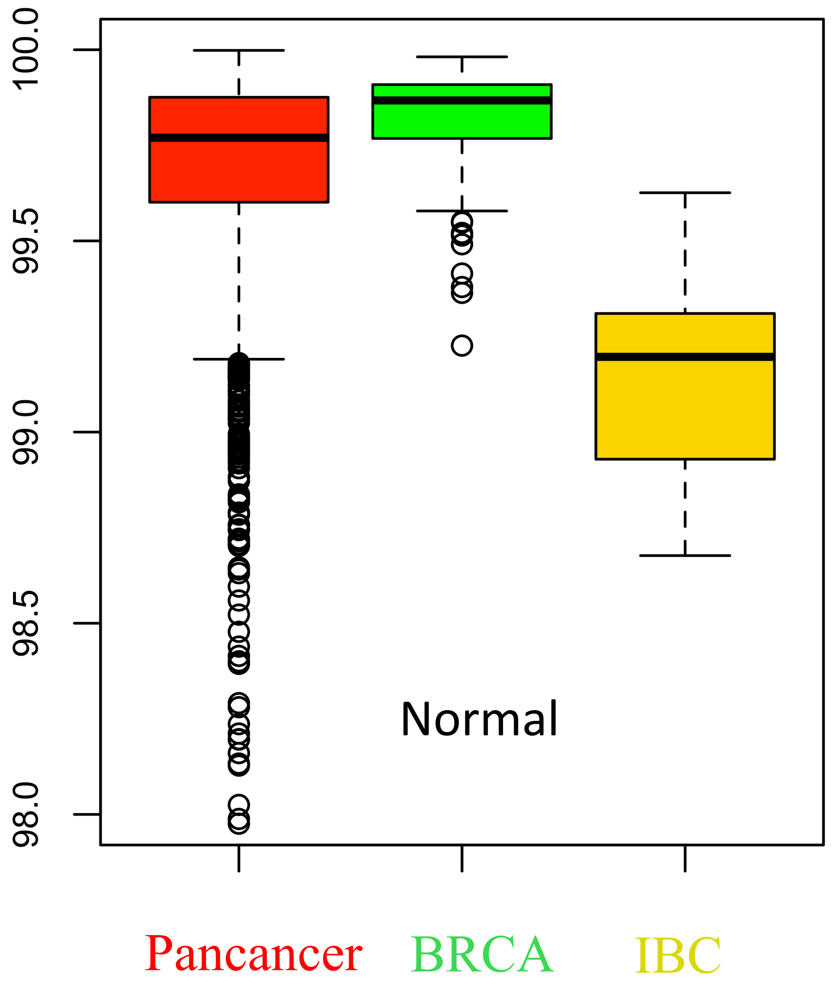
bcr_patient_uuid	bcr_patient_barcode	race	age	breast_carcinoma_estro	breast_carcinoma_progestero	lab_proc_h
d67cd793-2931-429a	TCGA-A2-A0EY	WHITE	62	Positive	Negative	Positive
a8015490-9740-45c9	TCGA-E2-A152	WHITE	56	Positive	Negative	Positive
38a8b734-9acc-42f9-	TCGA-A8-A092	[Not Availabl	48	Positive	Positive	Negative
74f31744-0aed-4633-	TCGA-BH-A0DT	WHITE	41	Positive	Positive	Negative
f51af6db-2655-47fb-	TCGA-AN-A0XR	WHITE	55	Positive	Negative	Negative
9435447e-d65f-408b-	TCGA-AO-A03N	WHITE	59	Positive	Positive	Negative
9fefbe7c-f66a-4940-	TCGA-AR-A24Z	WHITE	57	Positive	Positive	Negative
5d8ed961-a012-4b6b	TCGA-EW-A1J5	WHITE	59	Positive	Positive	Negative
1f601832-eee3-48fb-	TCGA-BH-A0EA	WHITE	72	Positive	Positive	Negative
96457ebf-ae88-41f4-	TCGA-BH-A0H0	WHITE	69	Positive	Positive	Negative
f05d314c-5ec5-4e2a-	TCGA-E2-A156	WHITE	61	Positive	Positive	Negative
b2aac45b-2073-4c7a-	TCGA-E9-A1NH	WHITE	71	Positive	Positive	Negative
96312510-c126-485d	TCGA-AN-A0G0	WHITE	56	Negative	Negative	Negative
18eb4dfc-556f-4bf3-	TCGA-BH-A0B3	WHITE	53	Negative	Negative	Negative
4da999a0-ef41-4a0b-	TCGA-EW-A1PH	WHITE	52	Negative	Negative	Negative
49717f75-0f2d-4e1c-	TCGA-AN-A04D	WHITE	58	Negative	Negative	Negative
359f12f9-5c41-48a4-	TCGA-EW-A1P8	WHITE	58	Negative	Negative	Negative
05506f4c-e701-4a9d-	TCGA-AN-A0AT	WHITE	62	Negative	Negative	Negative
e9f4f373-37a5-48ad-	TCGA-AO-A0J6	WHITE	61	Negative	Negative	Negative
5fd9552a-c742-4388-	TCGA-AR-A1AY	WHITE	65	Negative	Negative	Negative
0dca98b0-f43e-45b6-	TCGA-D8-A27H	WHITE	72	Negative	Negative	Negative
2a84997d-ccee-4f46-	TCGA-E2-A1LL	BLACK OR AF	73	Negative	Negative	Negative
88db1340-e4bf-451a-	TCGA-EW-A1PB	BLACK OR AF	70	Negative	Negative	Negative

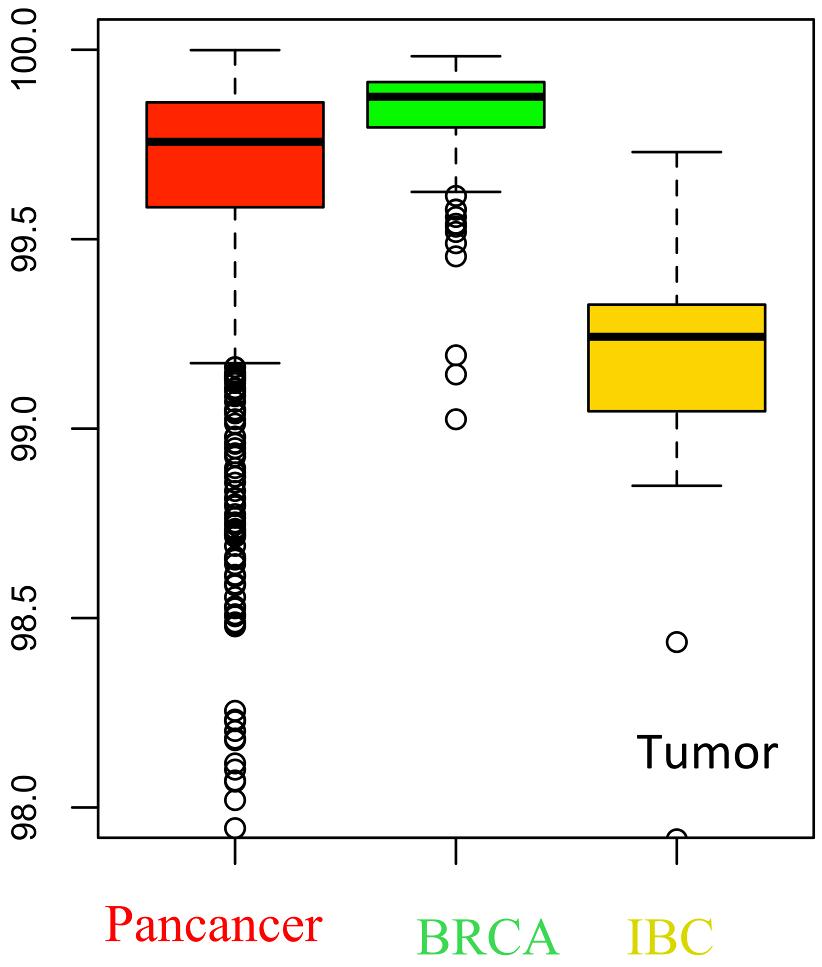
QC Analysis of 20 tumor-normal pair of IBC whole genome samples

Mean Depth distribution comparison

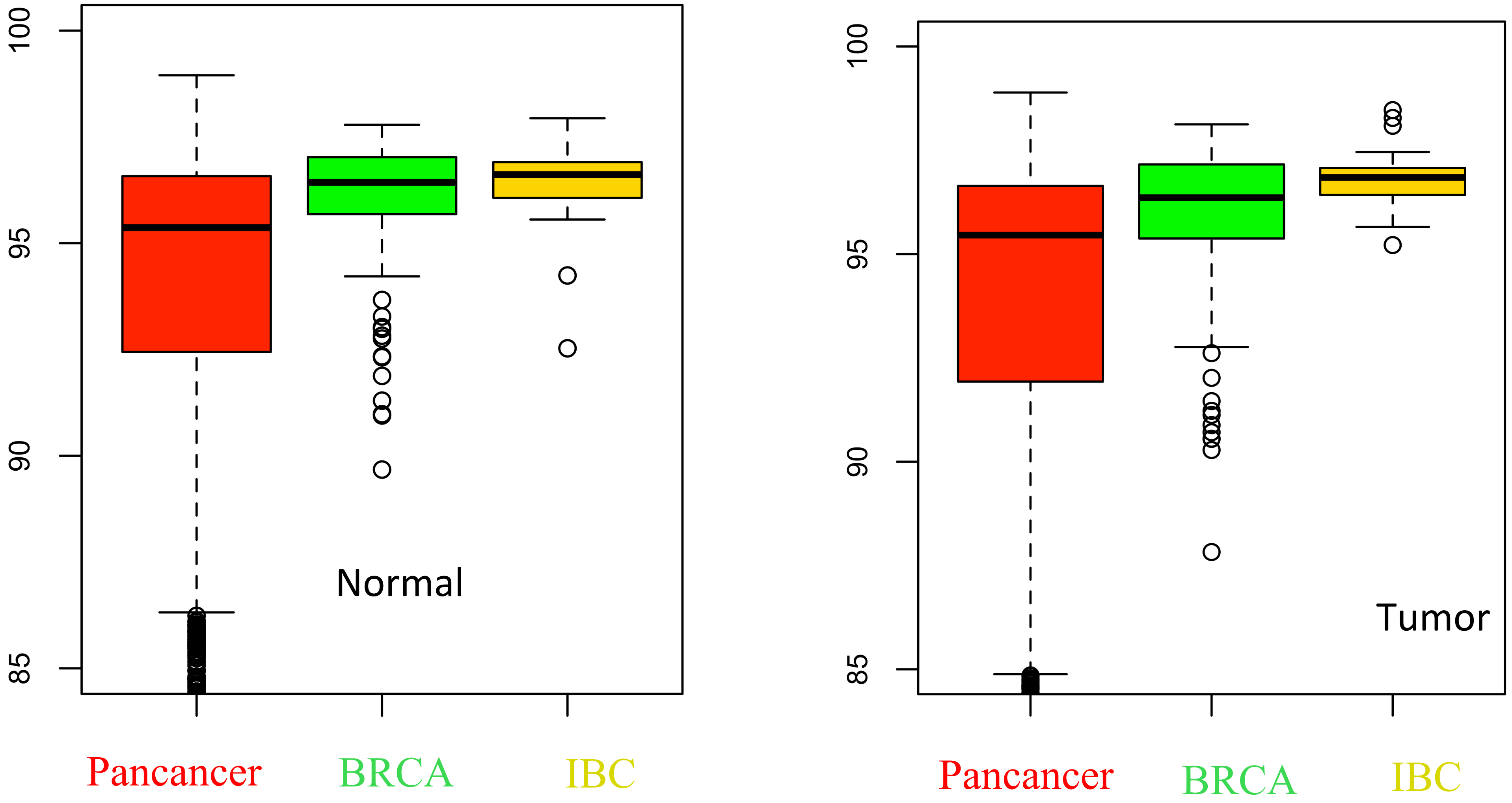


% Mapped Reads distribution comparison

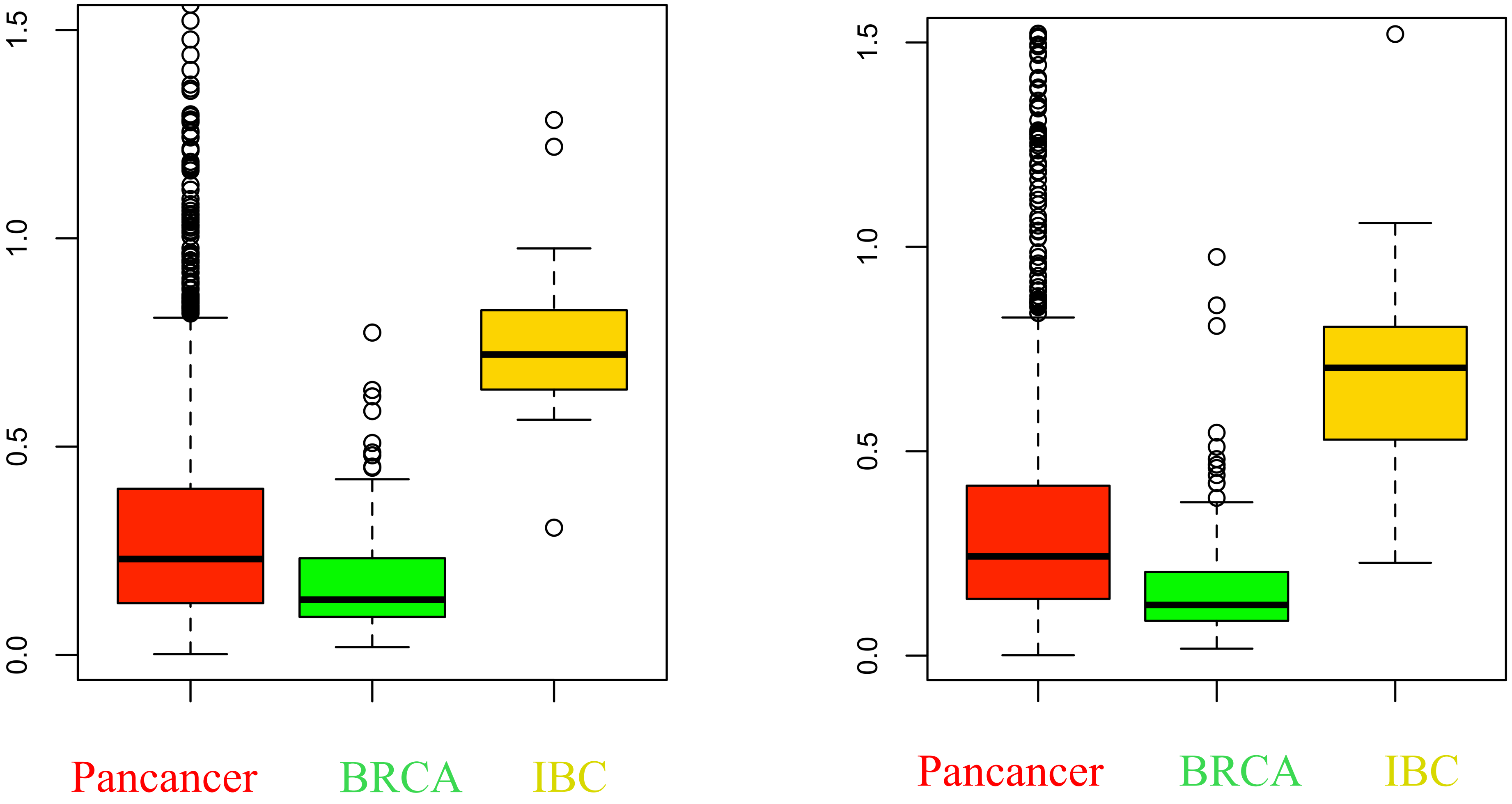


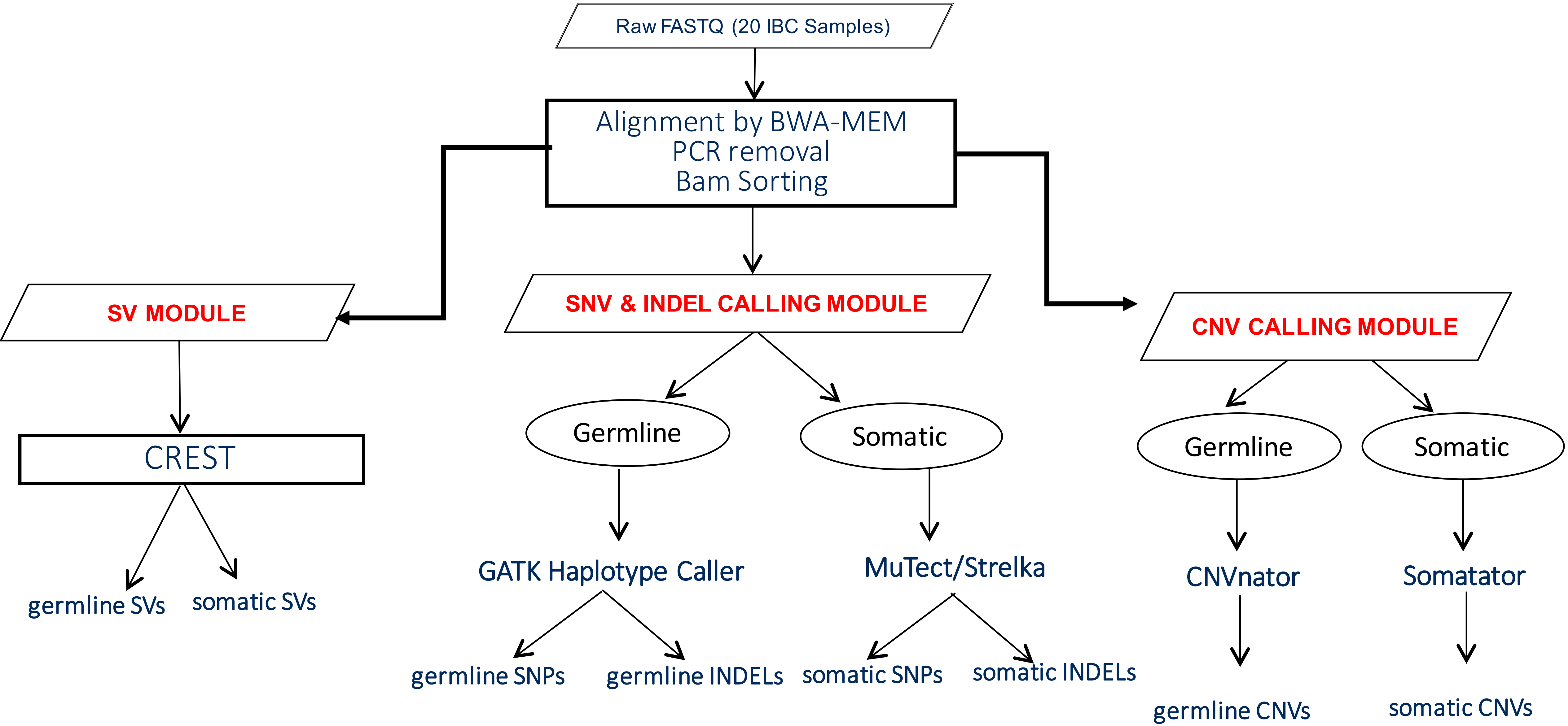


% Properly Mapped Reads distribution comparison



% unmapped Reads distribution comparison




Raw FASTQ (20 IBC Samples)

Alignment by BWA-MEM
PCR removal
Bam Sorting

SV MODULE

CREST

germline SVs

somatic SVs

SNV & INDEL CALLING MODULE

Germline

GATK Haplotype Caller

germline SNPs

germline INDELs

Somatic

MuTect/Strelka

somatic SNPs

somatic INDELs

CNV CALLING MODULE

Germline

CNVnator

germline CNVs

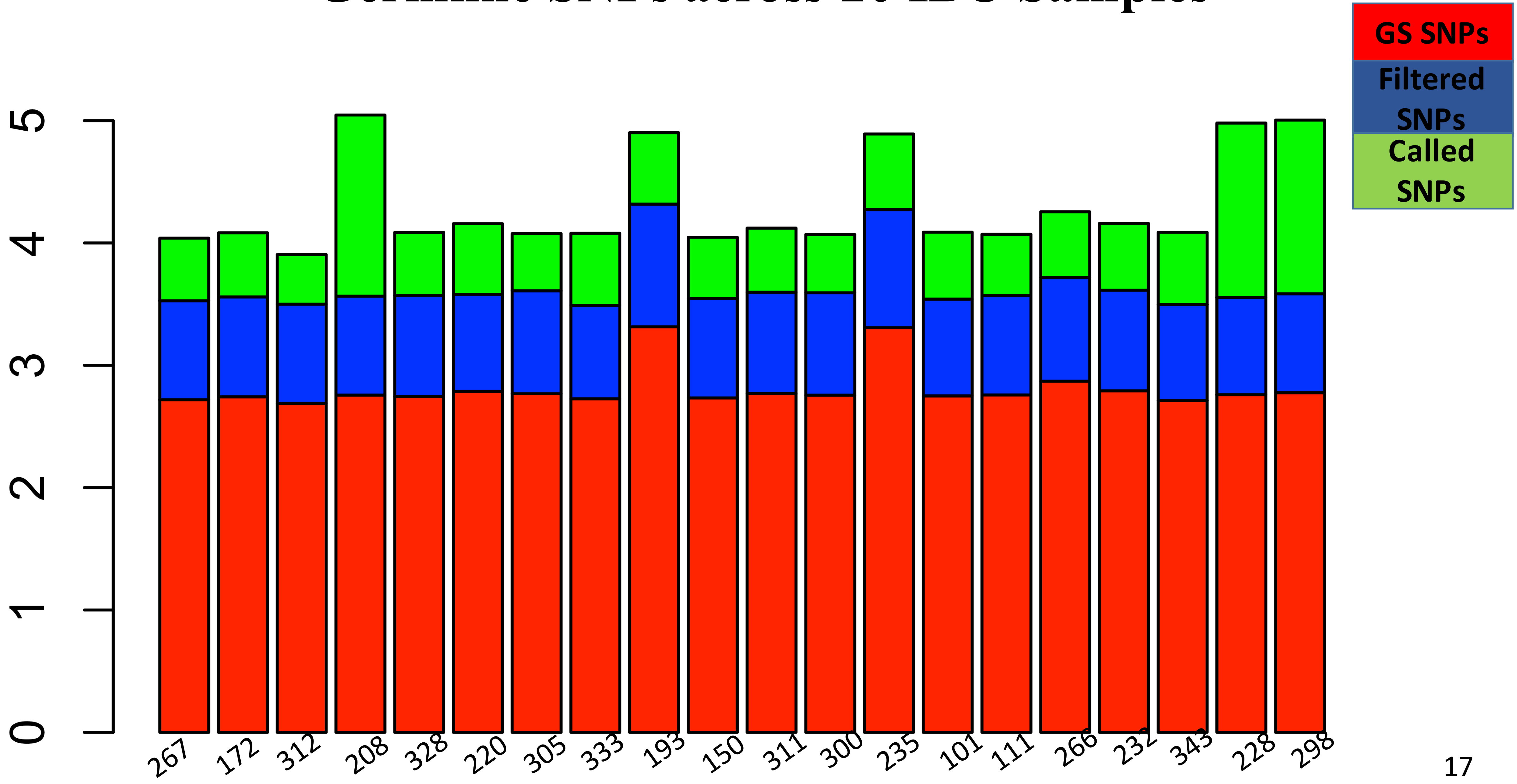
Somatic

Somatator

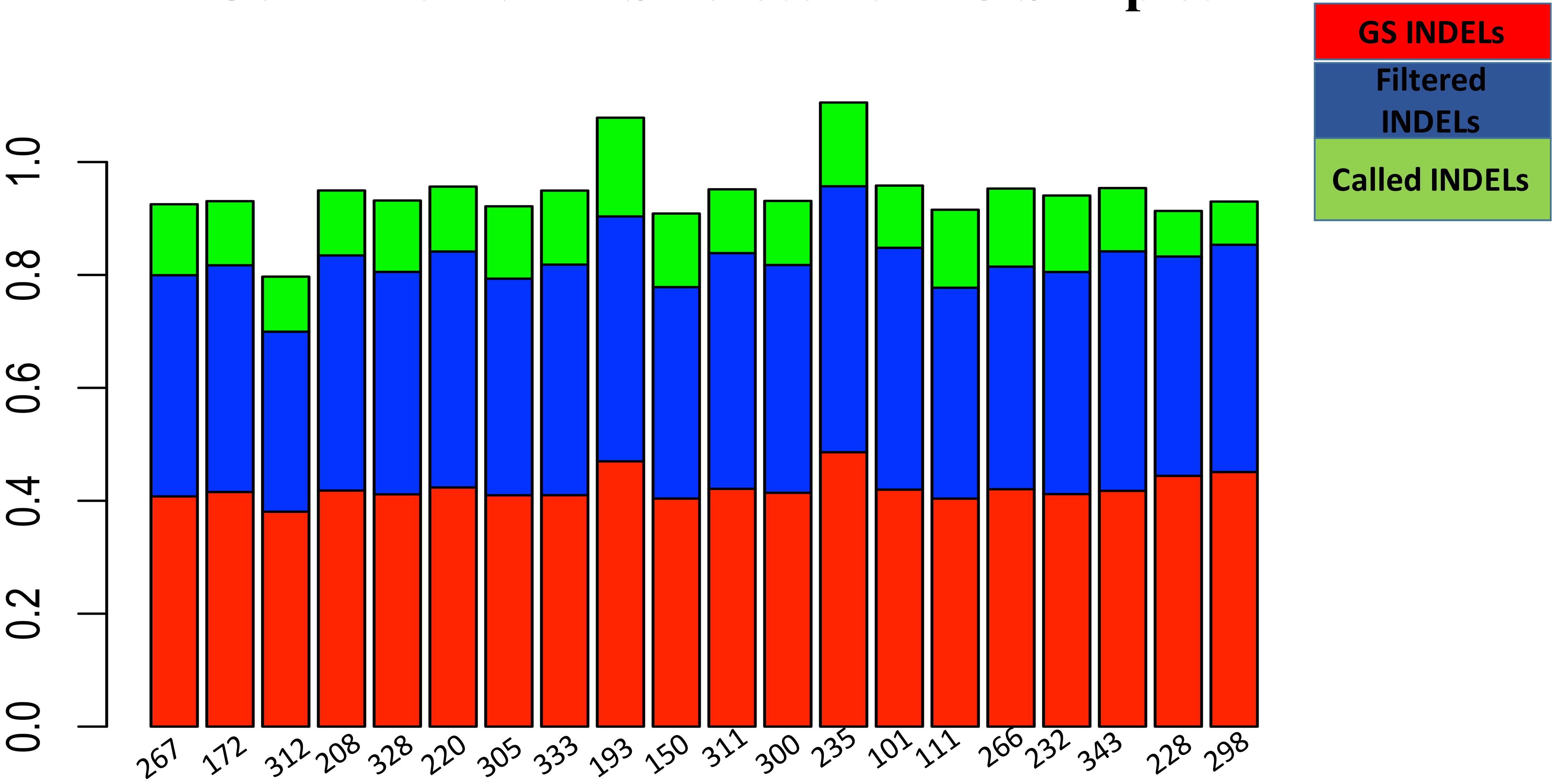
somatic CNVs

Pipeline to generate catalogue of genomic variants

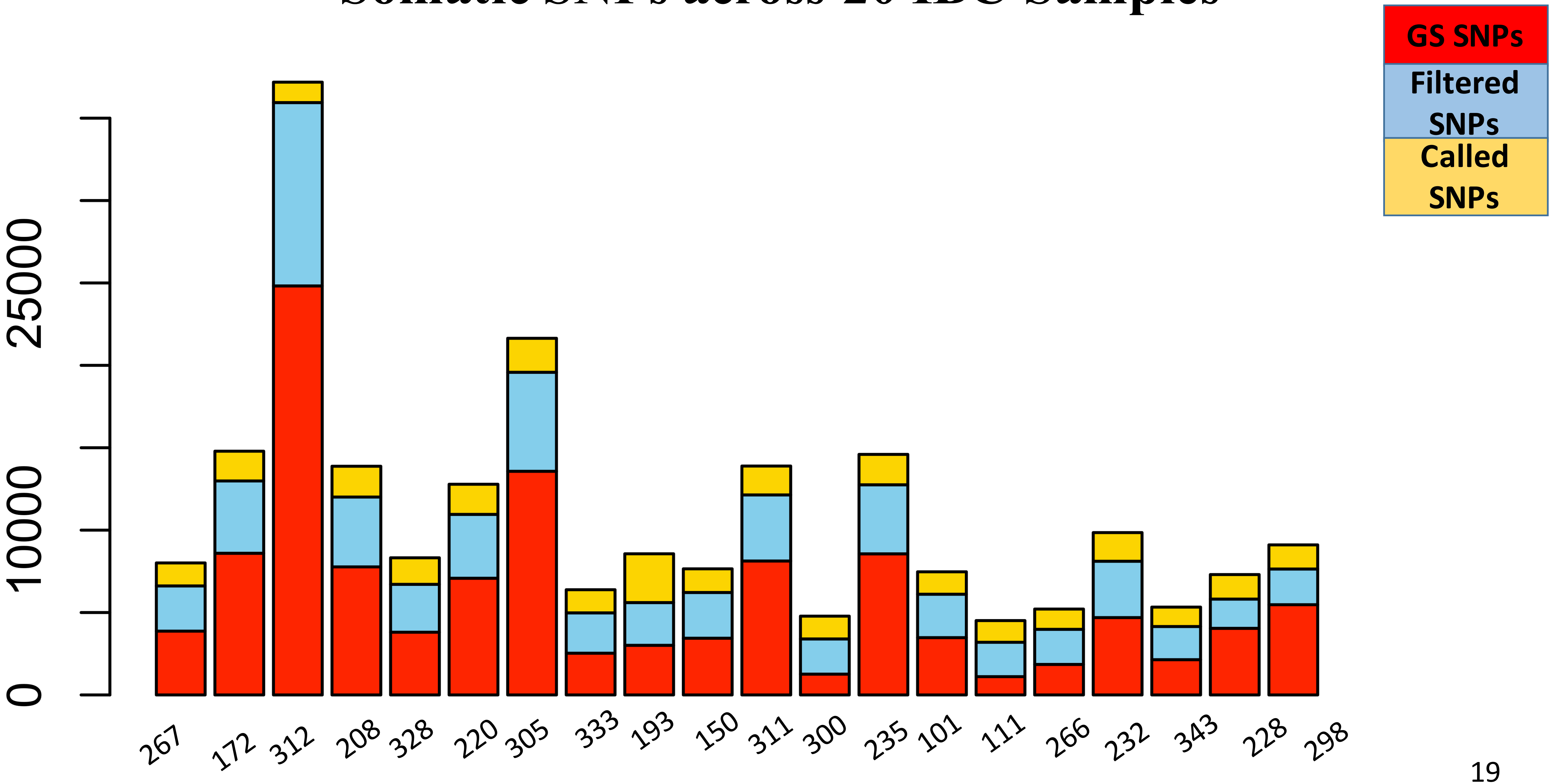
Germline SNPs across 20 IBC Samples



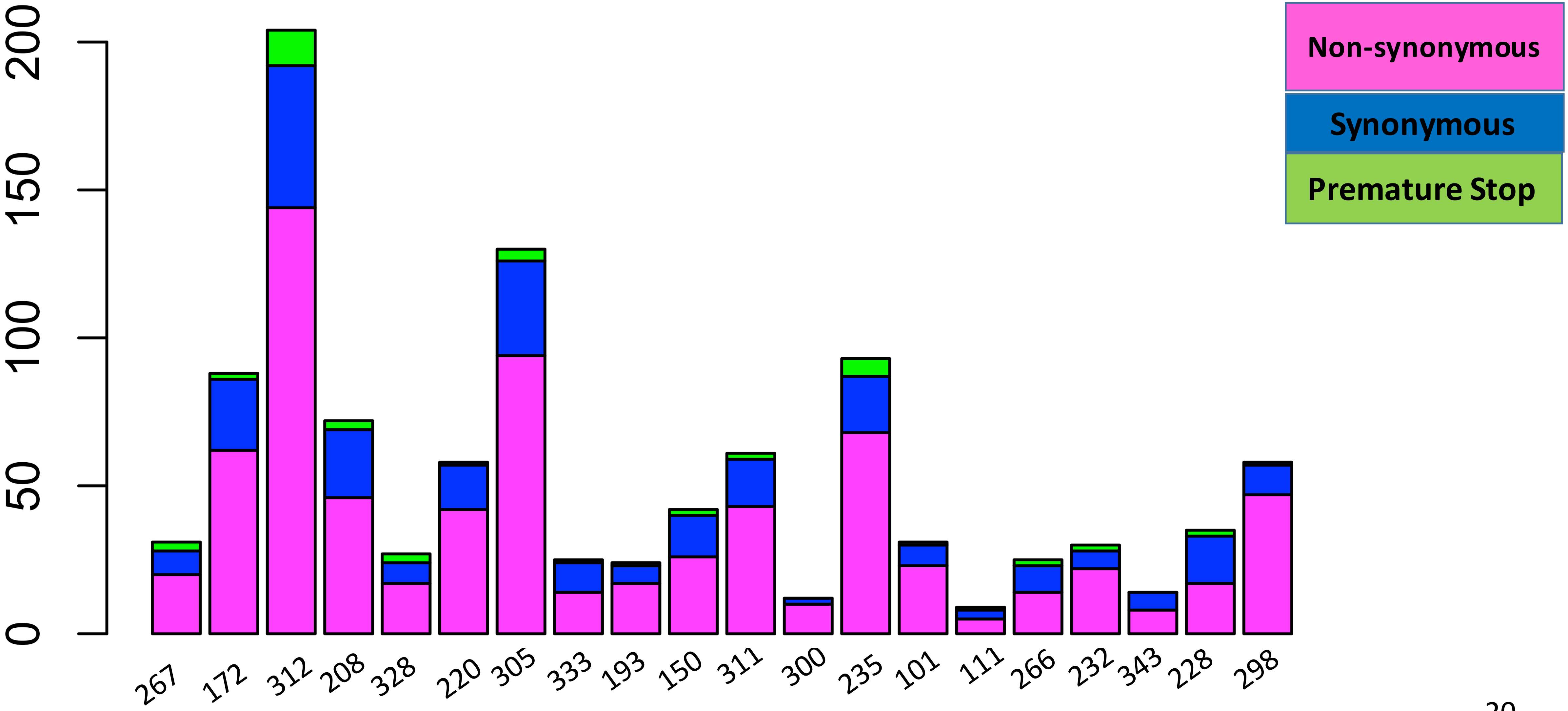
Germline INDELS across 20 IBC Samples



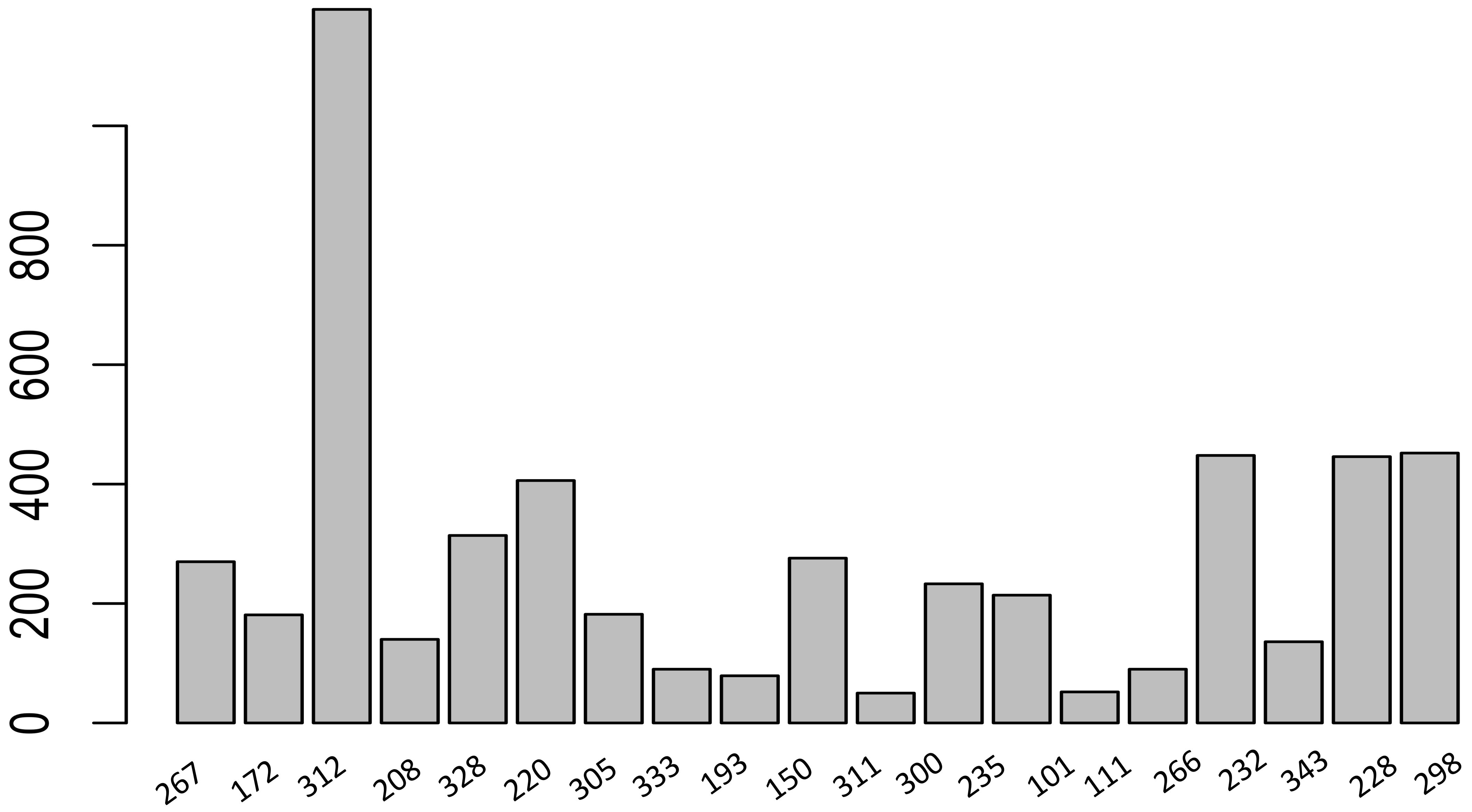
Somatic SNPs across 20 IBC Samples



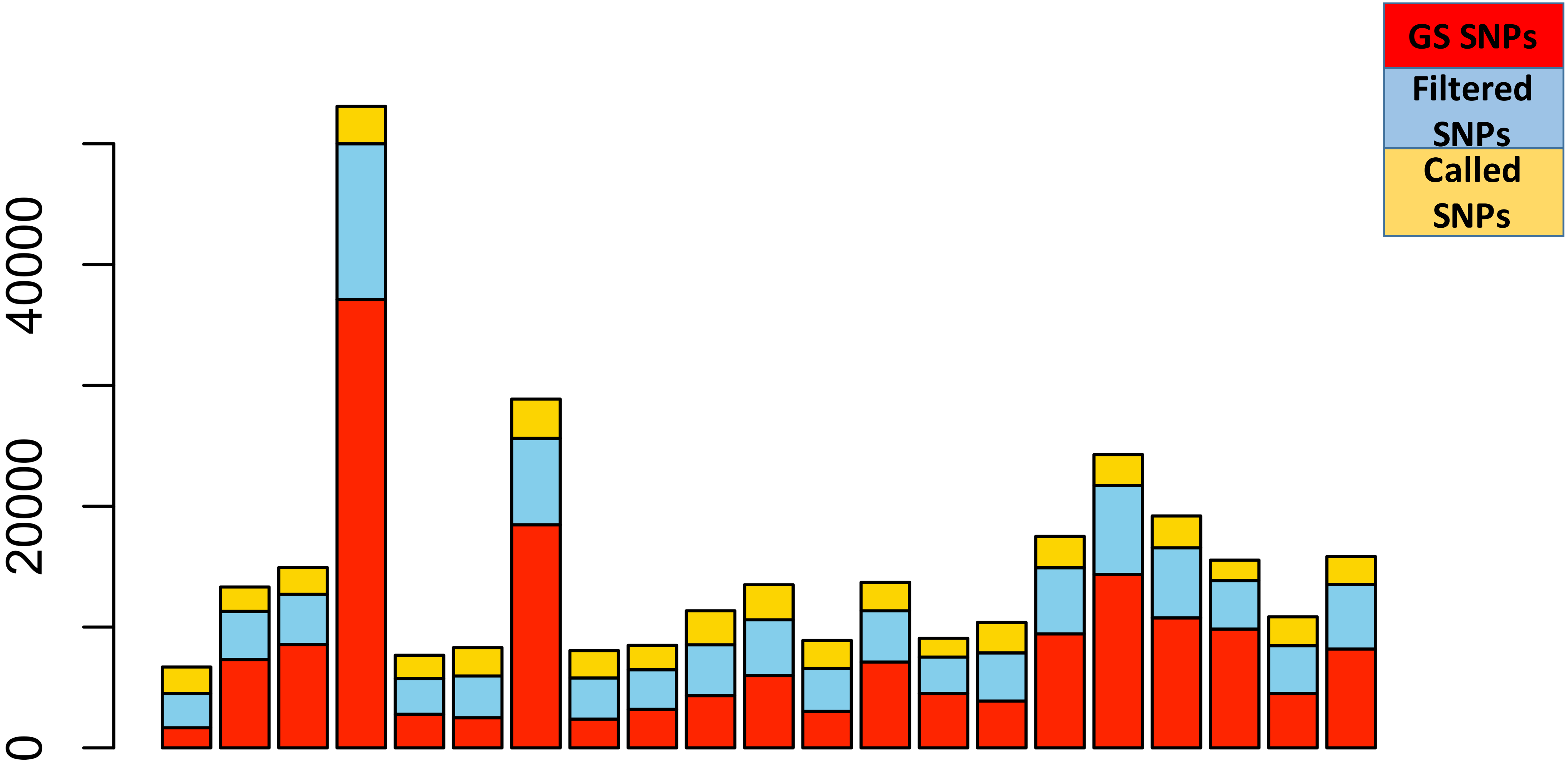
Somatic Coding SNPs across 20 IBC Samples



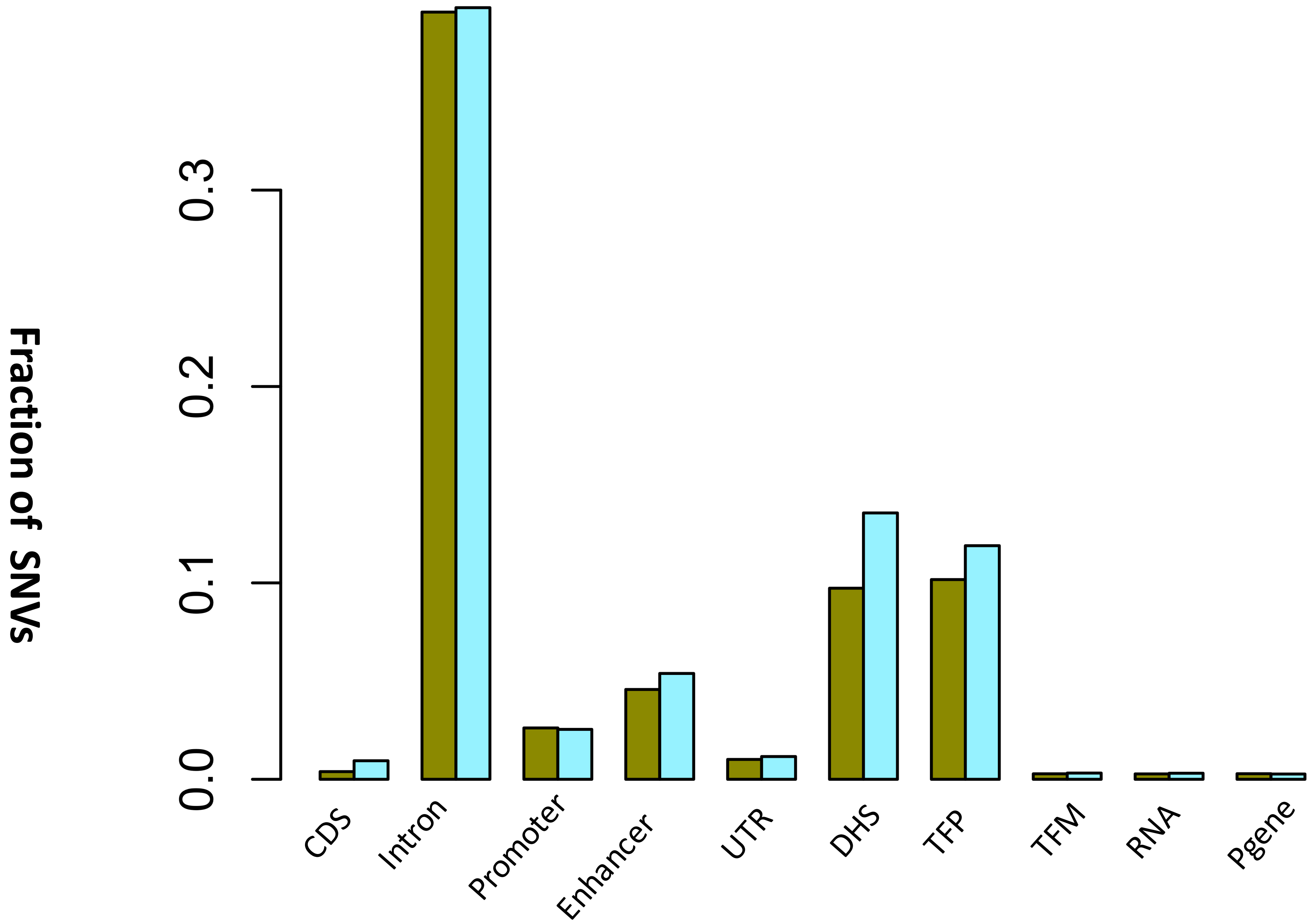
Somatic INDELs across 20 IBC Samples



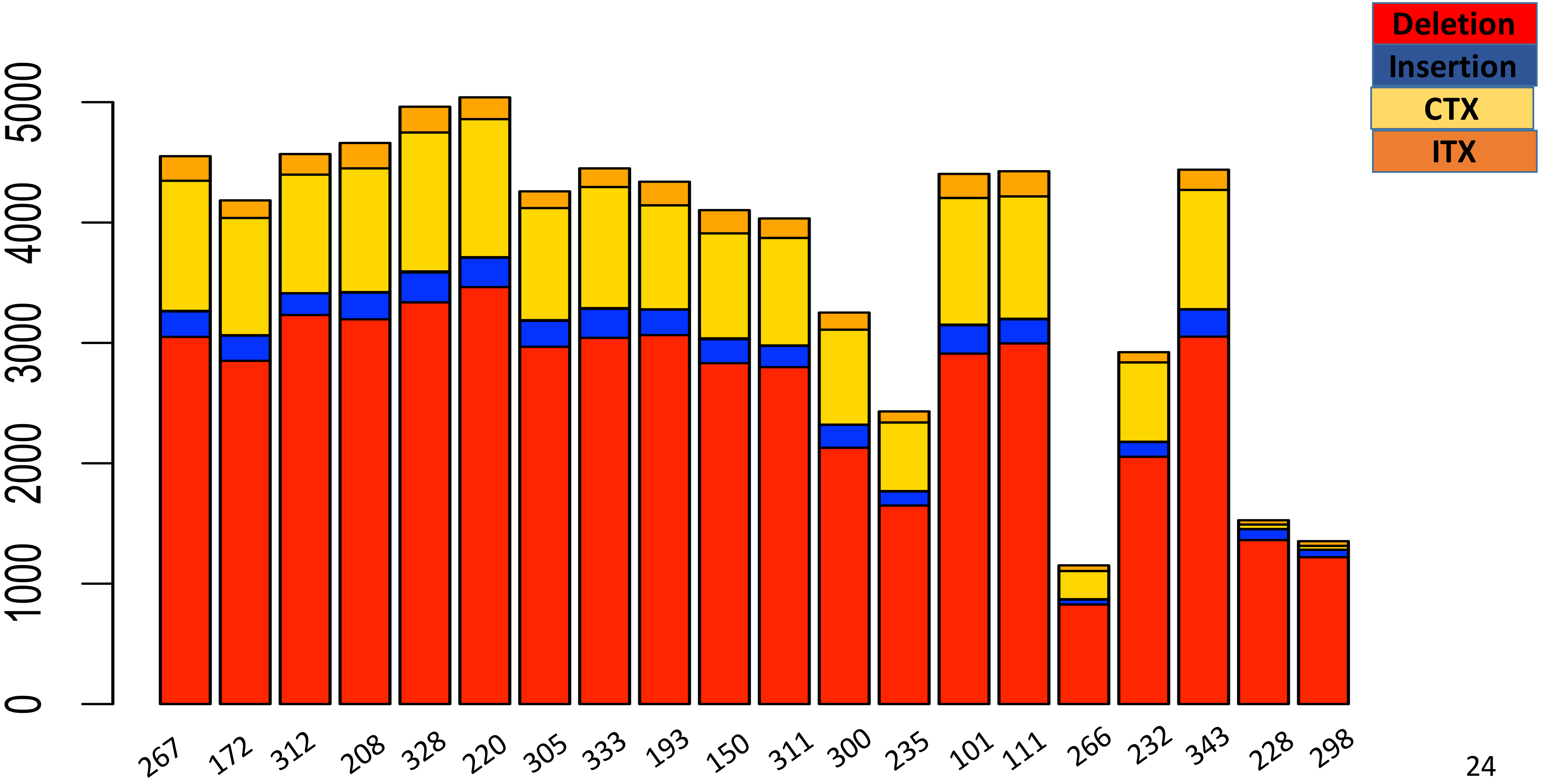
Somatic SNPs across non-IBC Samples



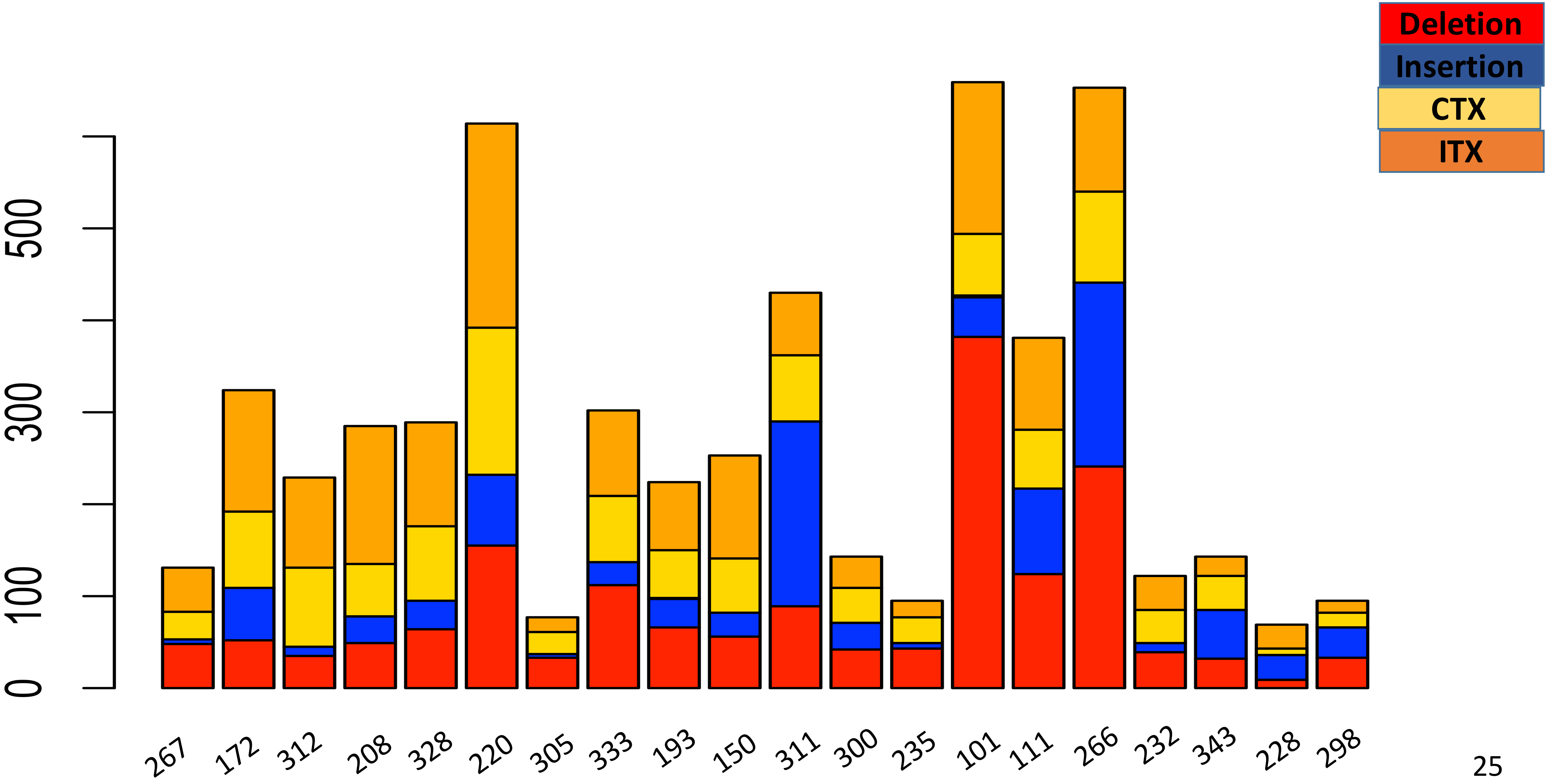
Annotation of Somatic SNPs across 20 IBC Samples



Germline SVs across 20 IBC Samples



Somatic SVs across 20 IBC Samples



Future Directions

Finish somatic CNV calling on IBC samples

Leverage the variant data to compare IBC and non-IBC samples.

Acknowledgment

Xiaotong
Rob
Arif
Mark Gerstein
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