The p53 Mutation HandBook
By L. Hjortsberg, J.M. Rubio-Nevado, D. Hamroun, M. Claustre, C. Béroud and T. Soussi

What is the p53 Mutation HandBook?

The p53 Mutation Handbook is a compilation of multiple analyses performed using information from the UMD p53 Mutation database

Which release of the UMD TP53 database was used for these analyses?

Except when otherwise specified, the curated version of the 2008_R2 release of the UMD p53 mutation database was used.

What is the difference between the curated and uncurated version of the p53 database?

The curated version of the UMD TP53 database has been purged from artefactual data known to affect p53 mutation analysis. More information can be found on our website (http://p53.free.fr/Database/p53_database.html) or in our recent publication (Soussi, T., Asselain, B., Hamroun, D., Kato, S., Ishioka, C., Claustres, M. and Beroud, C. (2006) Meta-analysis of the p53 mutation database for mutant p53 biological activity reveals a methodological bias in mutation detection. Clin Cancer Res, 12, 62-69.)

How were the various analyses performed?

Using novel software, the entire UMD TP53 mutation database was automatically analyzed resulting in the p53 Mutation Handbook as an output.

What type of information can be found in the p53 Mutation HandBook?

The p53 Mutation Handbook presents an analysis of TP53 mutation distribution and mutational events in the most frequent human cancers.

It also contains helpful reference pages about the human p53 sequence and how each codon of the protein is mutated in human cancer.

No text accompanies the various analyses

The p53 mutation handbook is not intended to be a manuscript. The handbook provides crude data and figures that are open for interpretation and/or discussion by anyone. Data / figures included in this handbook can be used and reproduced freely by anyone as long as the reference to the p53 mutation handbook is indicated.

What is the reference of the p53 Mutation HandBook?

L. Hjortsberg, J.M. Rubio-Nevado, D. Hamroun, C. Béroud, M. Claustre and T Soussi,. The p53 Mutation handbook 2.0, available online; http://p53.free.fr

What is the audience for this handBook?

Every scientist interested in p53 mutations or more globally in mutation analysis in human cancer.

What if I need a specific analysis which is not included in this p53 Mutation handbook?

Just send us an email (p53@free.fr) and, if your request is feasible, the analysis will be performed and added to the handbook.

You can also make suggestions via our Forum (http://p53.free.fr/Forum)

What is the future of the p53 Mutation HandBook?

More analyses and novel information will be added to the next version. Stay tuned!

Version History

2.0 October 2008

Update with the 2008 release of the UMD p53 database

Add new analysis

Add strategy of analysis for the most frequent cancer

1.1 March 2007

Modification of the CpG mutation analysis page 68 and 69

1.0

Release of the p53 Mutation HandBook, February 2007

Summary of analysis

Number of studies	Number of publications
Number of tumors	Total number of tumors with at least one p53 mutation
Number of mutations	Total number of mutations (several tumors have more than 1 mutations)
Number of tumors with 1 mutation	Self explanatory
Number of tumors with 2 mutations	Self explanatory
Number of tumors with more than 2 mutation	Self explanatory
In studies *	Number of studies that have a normal behavior upon the curation process
Out studies 95*	Number of studies that have an abnormal behavior upon the curation process using a 95% CI
Out studies 99*	Number of studies that have an abnormal behavior upon the curation process using a 99% CI

*: The curation process is fully decsribed in this section and also in:

Soussi, T., Asselain, B., Hamroun, D., Kato, S., Ishioka, C., Claustres, M. and Beroud, C. (2006) Meta-analysis of the p53 mutation database for mutant p53 biological activity reveals a methodologic bias in mutation detection. Clin Cancer Res, 12, 62-69.

Strategy of analysis

The first p53 mutations were described in 1989 in colon tumours and lung cancer cell lines. In the same year, Nigro et al. surveyed the p53 status of several tumour types and showed that p53 mutations are a frequent event in human tumorigenesis . The initial observation that these mutations were predominantly localized in exons 5 to 8 led to the common belief that the majority of mutations were localized in this region. This assumption has turned out to be false as 13.6% of p53 mutations are outside this region.

Analysis of studies that screened the entire p53 gene shows that focusing on exons 5 to 8 leads to an unacceptable bias. About 10-15 % of mutations are located outside of exons 5-8, with a significant number of mutations in exon 4, exon 10 and, to a lesser extent, exon 9. This bias can be observed in all of the various cancers, but also for each specific cancer, indicating that differences are not due to the particular distribution of mutations for a given type of cancer. Furthermore, analysis of p53 mutations found in exons 4, 9 and 10 shows that they contain a significantly greater number of frameshift or nonsense mutations than those in exons 4-8 Such null mutations are usually not detected by immunohistochemical analysis because no protein is produced.

Another possible source of bias concerns splice-site mutations. These types of mutations are thought to be rather infrequent (about 2%) and their effects have not been well characterized, but in a recent study, Varley

et al. reported germline splice-site mutations in 7 of 40 families (17.5%) with Li-Fraumeni Syndrome , and splicing was altered in 6 cases. Is it possible that the real incidence of splice-site mutations is closer to this figure, and that it has been underestimated in the past because splice junctions are rarely analysed.
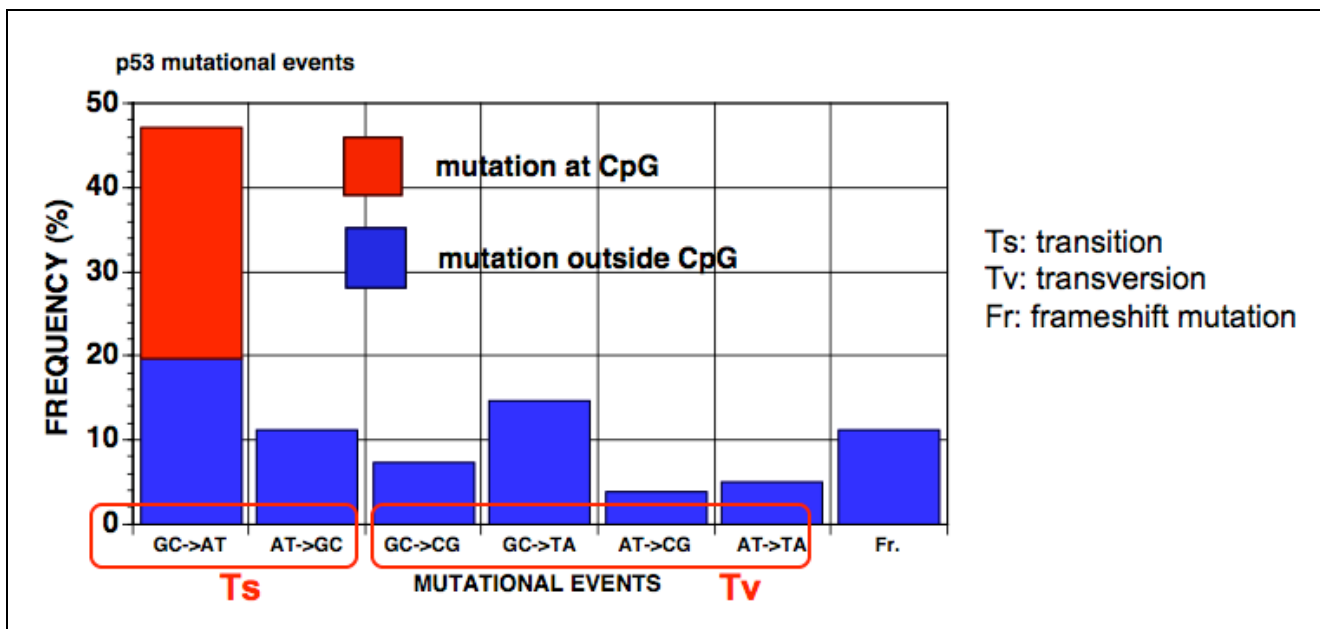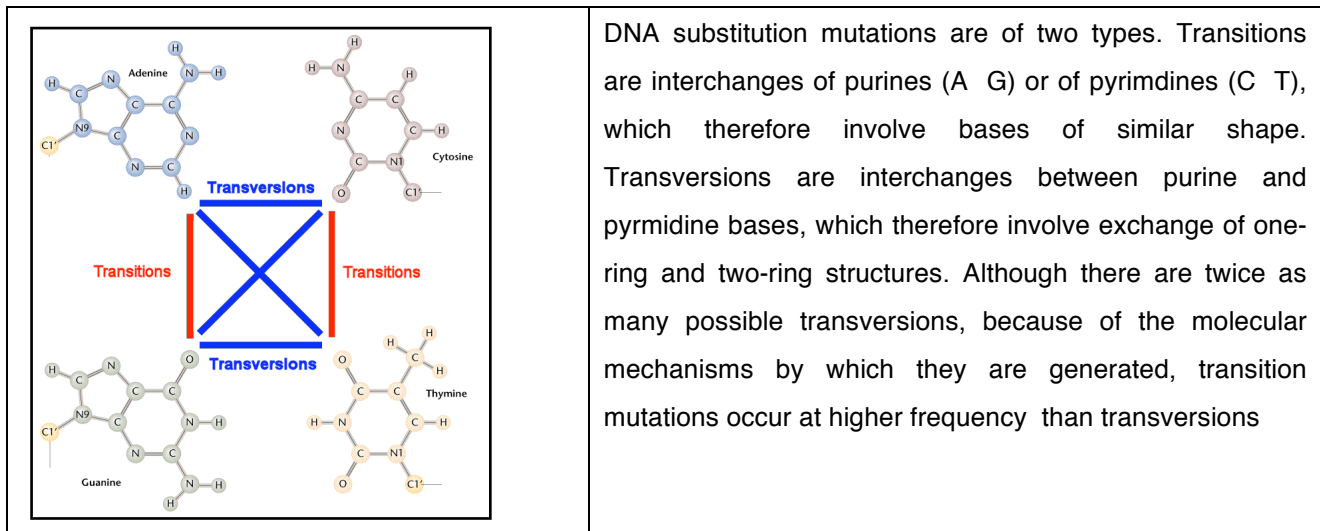
Only mutations that have been analyzed by sequencing (sanger or DNA chips) are included in the detabase. Mutations found by RSM (restriction site mutation) or similar methods have not been included in the database

Prescreening

Many prescreening methodologies have been used to increase the sensitivity of detection of mutations and to concentrate the sequencing exclusively on the mutant exon

SSCP	Single Strand Conformation Polymorphism
DGGE/CDGE	Denaturing gradient gel electrophoresis/ Constant denaturant gel electrophoresis
Yeast Assay	
IHC	Immunohistochemistry
dHPLC	Denaturing High Performance Liquid Chromatography
Other	Other methodology such as cleavase, RNase protection

Spectrum of p53 mutations in various types of tumors, how to read them.

DNA substitution mutations are of two types. Transitions are interchanges of purines (A G) or of pyrimdines (C T), which therefore involve bases of similar shape. Transversions are interchanges between purine and pyrmidine bases, which therefore involve exchange of one-ring and two-ring structures. Although there are twice as many possible transversions, because of the molecular mechanisms by which they are generated, transition mutations occur at higher frequency than transversions


A predominance of the GC->AT transition at the CpG dinucleotide (colon, ovary brain, or leukemia) is the consequence of spontaneous deamination of 5-methylcytosine.

A high frequency of GC->TA transversion (Lung, Head and neck or HCC) is strongly indicative of exposure to exogenous carcinogens.

CpG dinucleotide mutates at a high rate because cytosine is vulnerable to deamination. Cytosines in CpG dinucleotides are often methylated, and deamination of 5-methylcytosine (5mC) produces thymidine. Deamination of unmethylated cytosine produces uracil (U), which can be removed by uracil glycosylase, but 5mC deamination generates thymine (T), which cannot be processed by this enzyme. The consequence in humans is that the mutation rate from 5mC to T is 10-fold to 50-fold higher than other transitions.

Distribution of p53 mutations
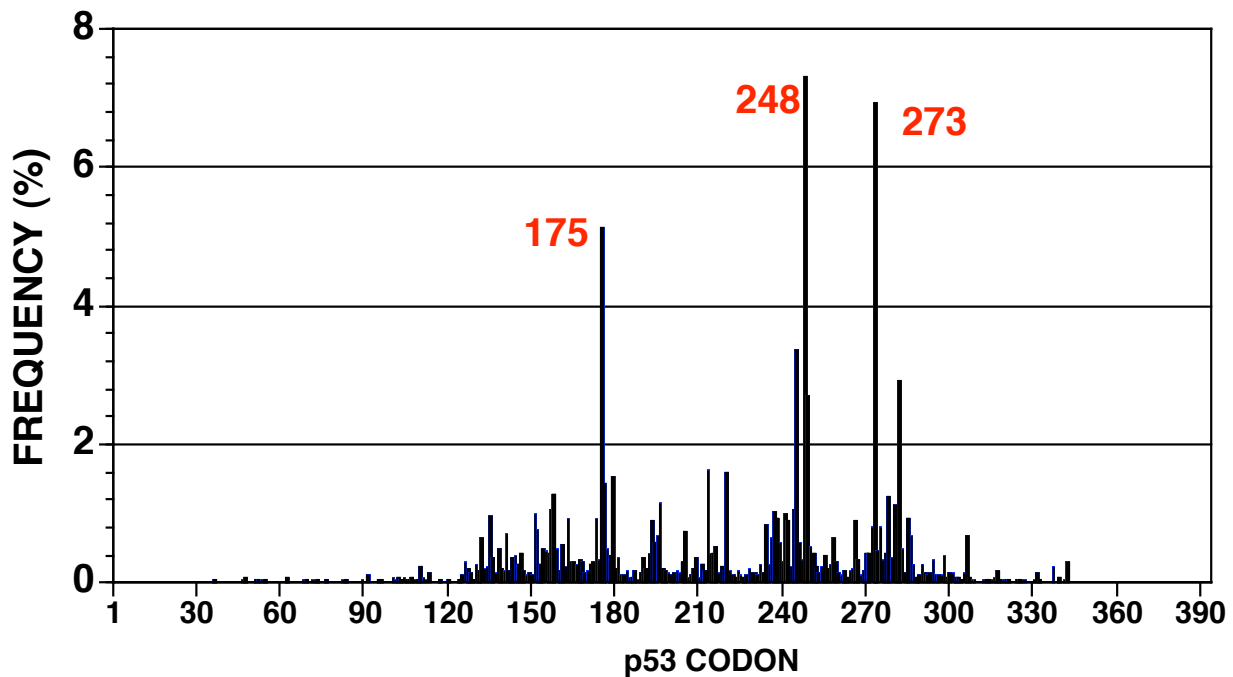
The human p53 protein consists of 393 amino acids with 5 evolutionarily conserved domains (I to V). Domains II to V correspond to the DNA binding domain which is the target for p53 mutations.

90 % of p53 mutations occur in the central region which harbors four of the five highly conserved evolutionary domains. X-ray crystallography of p53-DNA complexes shows that this region is essential for the p53-DNA interaction [Cho, 1994, #3218]. However, this distribution might be slightly biased since most investigations have focused exclusively on this region of the p53 gene.

More recent studies on all the coding exons (exons 2 through 11) show that a considerable number of mutations are found in exons 4 and 10. Mutations in exons 5-8 are significantly different from those found in exons 4, 9 (see exon distribution below).

Distribution of p53 mutations in the various functional domains of p53.
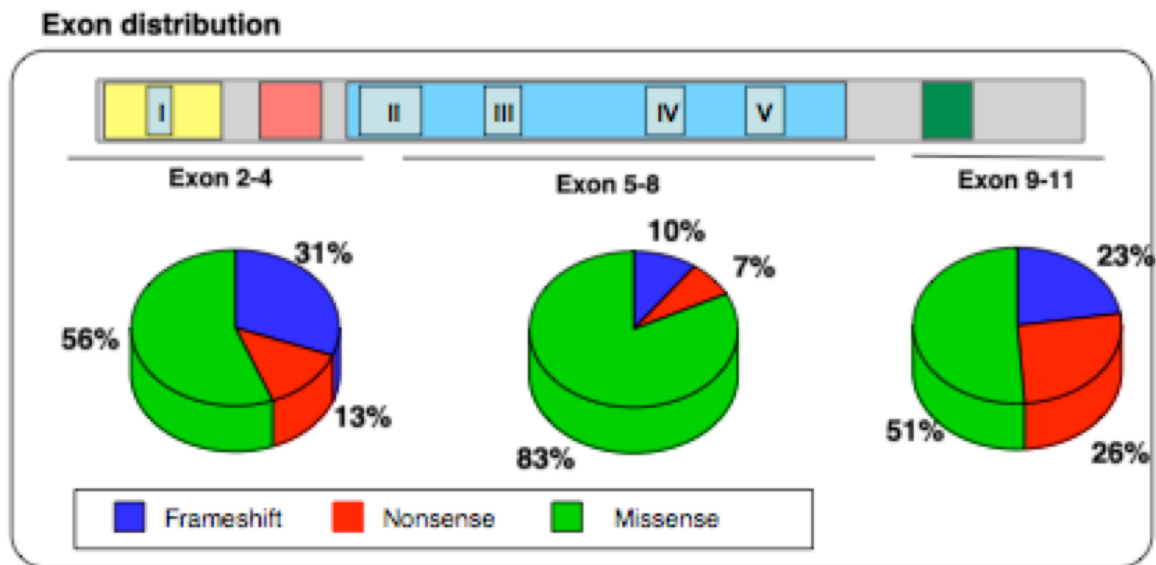
The higher frequency of frameshift mutations between exon 2-4 and exon 5-8 domains is statistically significant (p<0.0001).

The p53 protein

Human p53 protein (Hp53) can be divided into five domains, each corresponding to specific functions:

i) The amino-terminus part 1-42 contains the acidic transactivation domain and the mdm2 protein binding site. It also contains the Highly Conserved Domain I (HCD I) (**Yellow**)

II) Region 40-92 contains series repeated proline residues that are conserved in the majority of p53. it also contains a second transactivation domain (**Red**).

III) The central region (101-306) contains the DNA binding domain. It is the target of 90% of p53 mutations found in human cancers. It contains HCD II to V (**Blue**).

IV) The oligomerization domain (307-355, TET) consists of a beta-strand, followed by an alpha-helix necessary for dimerization, as p53 is composed of a dimer of two dimers. A nuclear export signal (NES) is localized in this oligomerization domain (**Green**).

V) The carboxy-terminus of p53 (356-393) contains 3 nuclear localization signals (NLS) and a non-specific DNA binding domain that binds to damaged DNA. This region is also involved in downregulation of DNA binding of the central domain

**Meta analysis and exclusion critera: a brief explanation**

Methodology

The mean and 95% confidence interval (CI) of the biological activity of all mutants was calculated by using the transactivational activity measured on the WAF1 promoter. For data analysis and presentation of the results, we used a similar approach to that used for meta-analyses comparing clinical trials. For each cancer, the mean and 95% CI of p53 activity in each publication were graphically displayed. The reference value corresponds to the mean and 95% CI of all studies for the specific cancer. In this statistical analysis, the width of the 95% CI depends on both the scatter of the individual values (SD) and the sample size: the width of the 95% CI increases as the sample size decreases. Only publications reporting 10 or more mutations were analyzed in this study in order to ensure significant results. Cancers with >500 published mutations were analyzed, corresponding to the 10 most frequent cancers.

Results

Most publications display a homogeneous distribution with a 95% CI, which includes the mean value of the activity for all studies combined for a specific type of cancer 54 out of range studies have been identified : in these publications, the distribution of p53 mutant activity significantly differs from the average as their CI does not include the global mean value. A deeper analysis of these publications shows that they have some commun features such as :

- Multiple mutations in the same tumour
- High frequency of polymorphic changes
- High frequency of novel mutations previously undescribed
- Low frequency of mutations at hot spot position

Among these excluded studies, there is the Gao publication in lung cancer that has been known to cause several problems in the analysis and interpretation of the epidemiological analysis of the p53 mutation database in lung cancer (see below NSCLC) Therefore, we believe that curation of the UMD p53 mutations database will lead to a better set of data for the analysis of p53 mutations
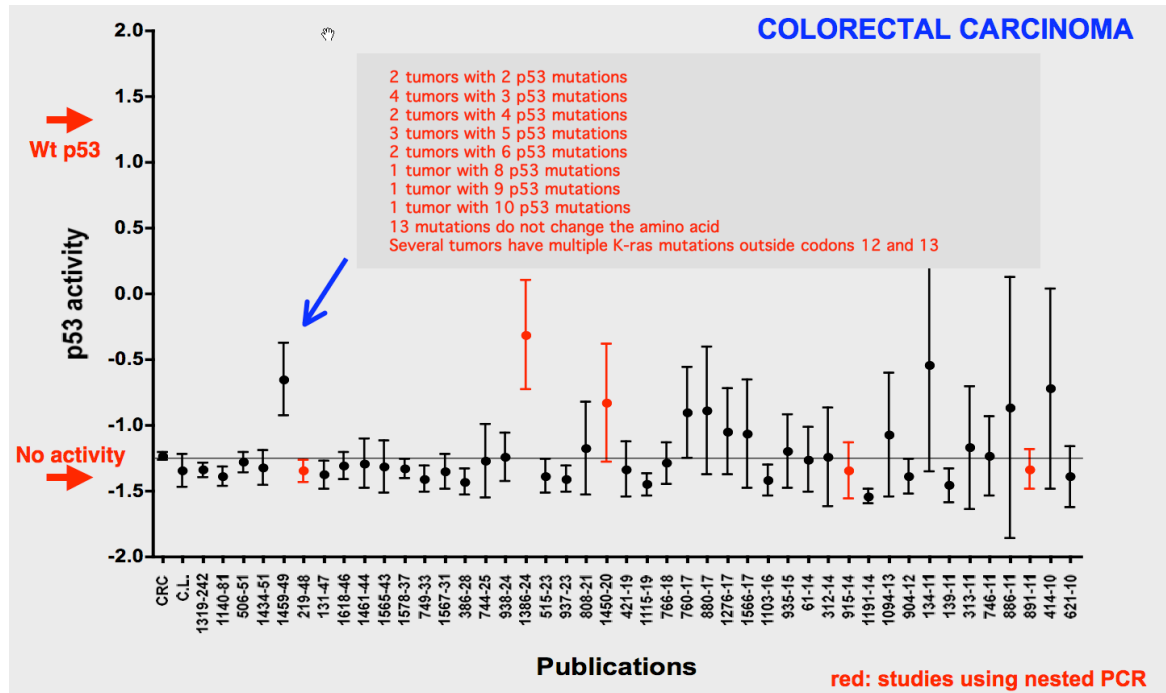
Meta-analysis of p53 loss of function in CRC. Dot and bars: mean and 95% CI of mean p53 activity as measured by transactivation with the WAF1 promoter. The mean and 95% CI of p53 activity for all studies combined for a specific type of cancer is shown on the far left of each graph. The horizontal line shows the mean of the combined studies. The publication code is indicated on the x-axis: the first number is an anonymous ID for the publication and the second number indicates the number of p53 mutants included in this study. Studies are presented from left to right in decreasing order of number of p53 mutants. The y-axis corresponds to p53 transactivation activity, with a value of -1.5 for the negative control and a value of 2.5 for 100% of wt activity.
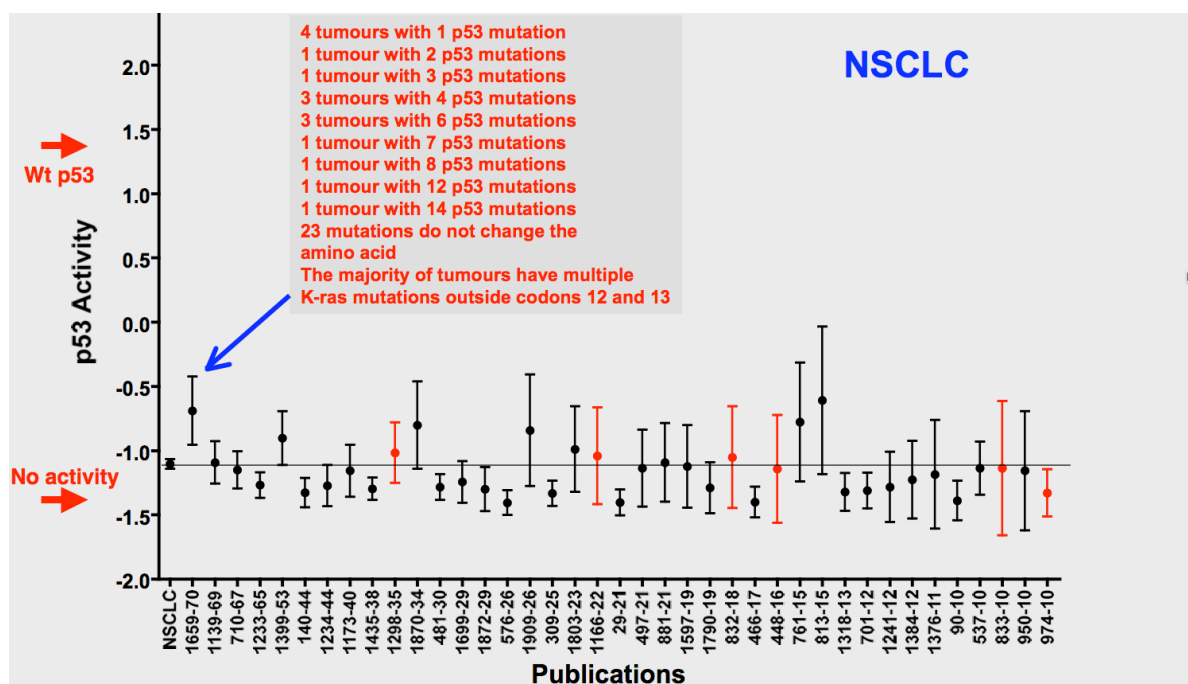
Meta-analysis of p53 loss of function in NSCLC. Same methodology as above. 2000-70 is well known to be artefactual

# Frequency of p53 mutations in various cancers
## Data from the 2008R2 release of the UMD database
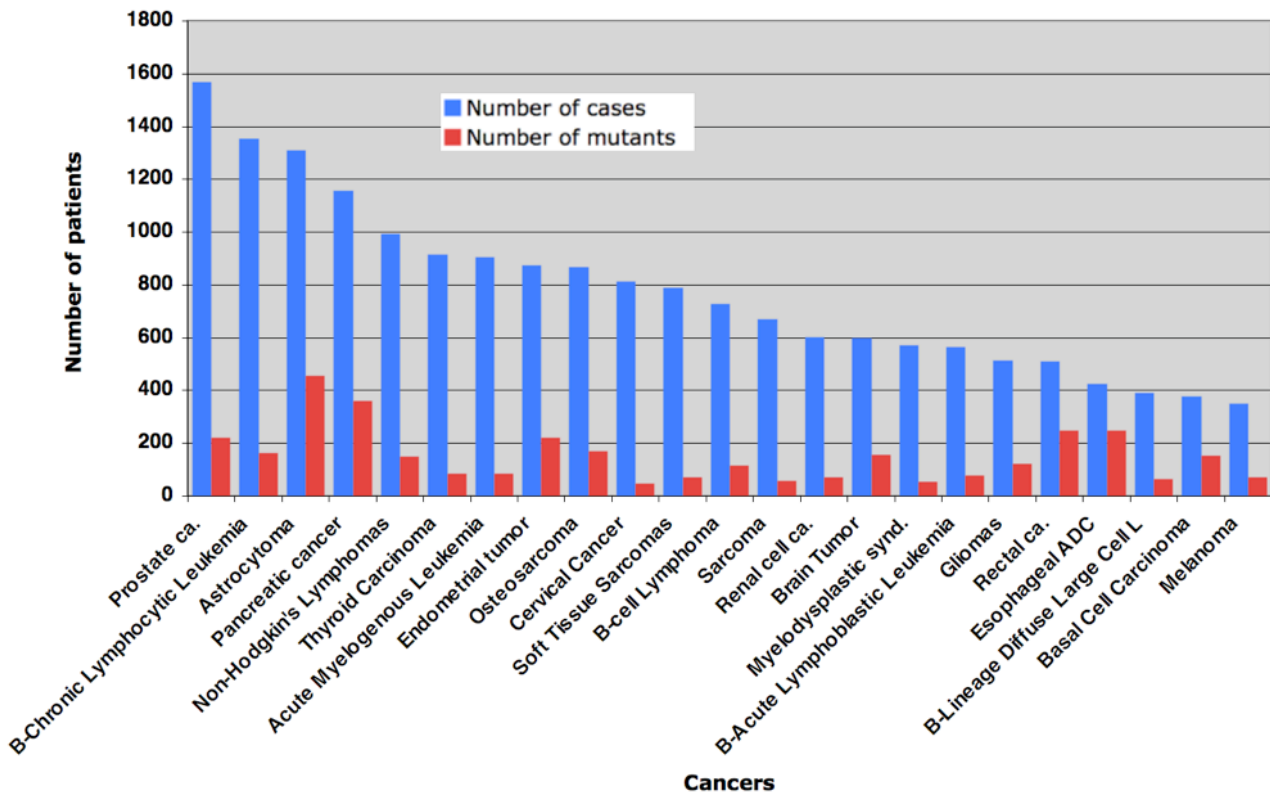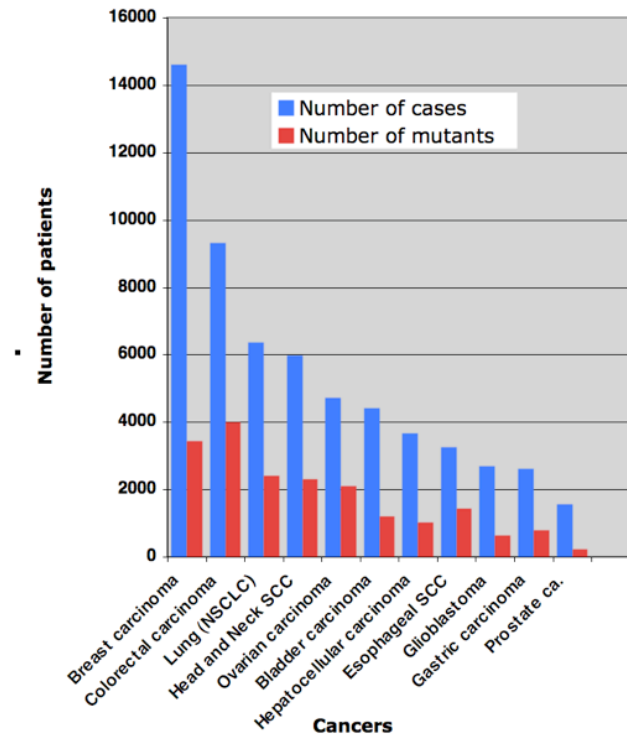
Cancer	Number of cancer	Number of Mutant	Frequency
Breast carcinoma	14389	3390	23.56
Colorectal carcinoma	9183	3967	43.2
Lung (NSCLC)	6126	2314	37.77
Head and Neck SCC	5654	2185	38.65
Ovarian carcinoma	4401	1997	45.38
Bladder carcinoma	4271	1156	27.07
Hepatocellular carcinoma	3327	945	28.4
Glioblastoma	2706	633	23.39
Gastric carcinoma	2467	739	29.96
Esophageal SCC	2444	1136	46.48
Prostate ca.	1395	205	14.7
Astrocytoma	1247	451	36.17
B-Chronic Lymphocytic Leukemia	1200	144	12
Pancreatic cancer	1107	342	30.89
Acute Myelogenous Leukemia	852	78	9.15
Osteosarcoma	816	158	19.36
Soft Tissue Sarcomas	791	73	9.23
Cervical Cancer	766	44	5.74
Endometrial tumor	724	184	25.41
Non-Hodgkin's Lymphomas	708	137	19.35
B-cell Lymphoma	638	101	15.83
Sarcoma	627	36	5.74
Thyroid Carcinoma	603	58	9.62
Brain Tumor	599	155	25.88
B-Acute Lymphoblastic Leukemia	564	77	13.65
Renal cell ca.	528	70	13.26
Gliomas	481	112	23.28
Esophageal ADC	424	248	58.49
Myelodysplastic synd.	422	29	6.87
B-Lineage Diffuse Large Cell L	357	59	16.53
Adult T-cell Leukemia	328	54	16.46
Skin Squamous Cell Carcinoma	312	132	42.31
Lung (SCLC)	288	148	51.39
Basal Cell Carcinoma	284	124	43.66
Follicular lymphoma	274	27	9.85
Rectal ca.	261	116	44.44
Urothelial TCC	260	111	42.69
Esophageal ADC (Barrett)	253	77	30.43
Colorectal adenoma	238	14	5.88
Nasopharyngeal carcinoma	232	34	14.66
Melanoma	210	54	25.71
Multiple Myeloma	209	20	9.57
Uterine cancer	189	71	37.57
Wilm's tumor	177	21	11.86
Hepatic angiosarcomas	169	5	2.96
Neuroblastoma	147	4	2.72
Mantle Cell Lymphoma	143	23	16.08
Oligodendroglioma	143	28	19.58
Urothelial ca.	143	73	51.05
Colorectal Carc. Metast.	142	77	54.23

p53 MUTATION DATABASE ANALYSIS

FREQUENCY OF GC->TA TRANSVERSION
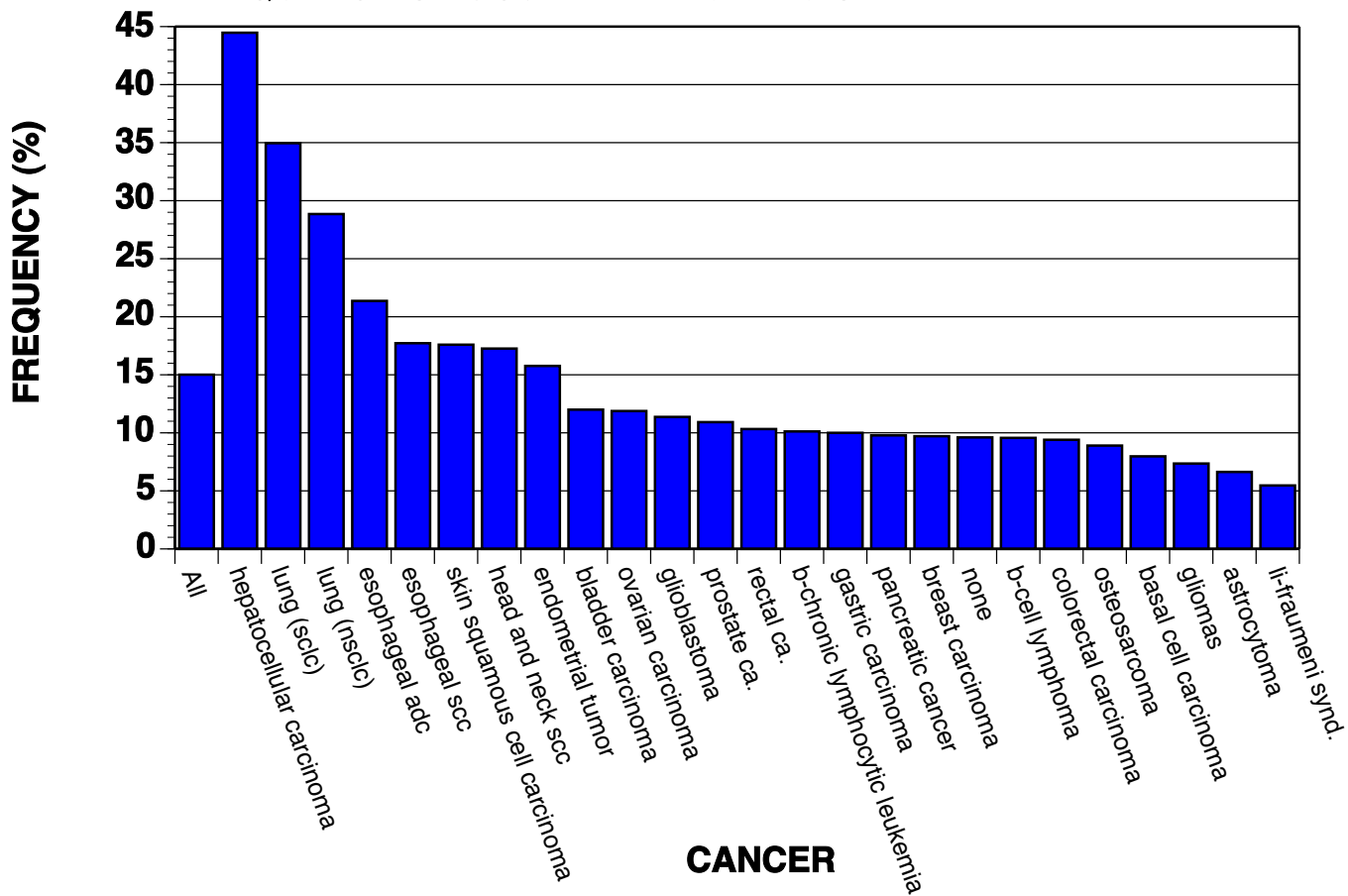
FREQUENCY OF GC->AT TRANSITION

mutation at CpG
mutation outside CpG
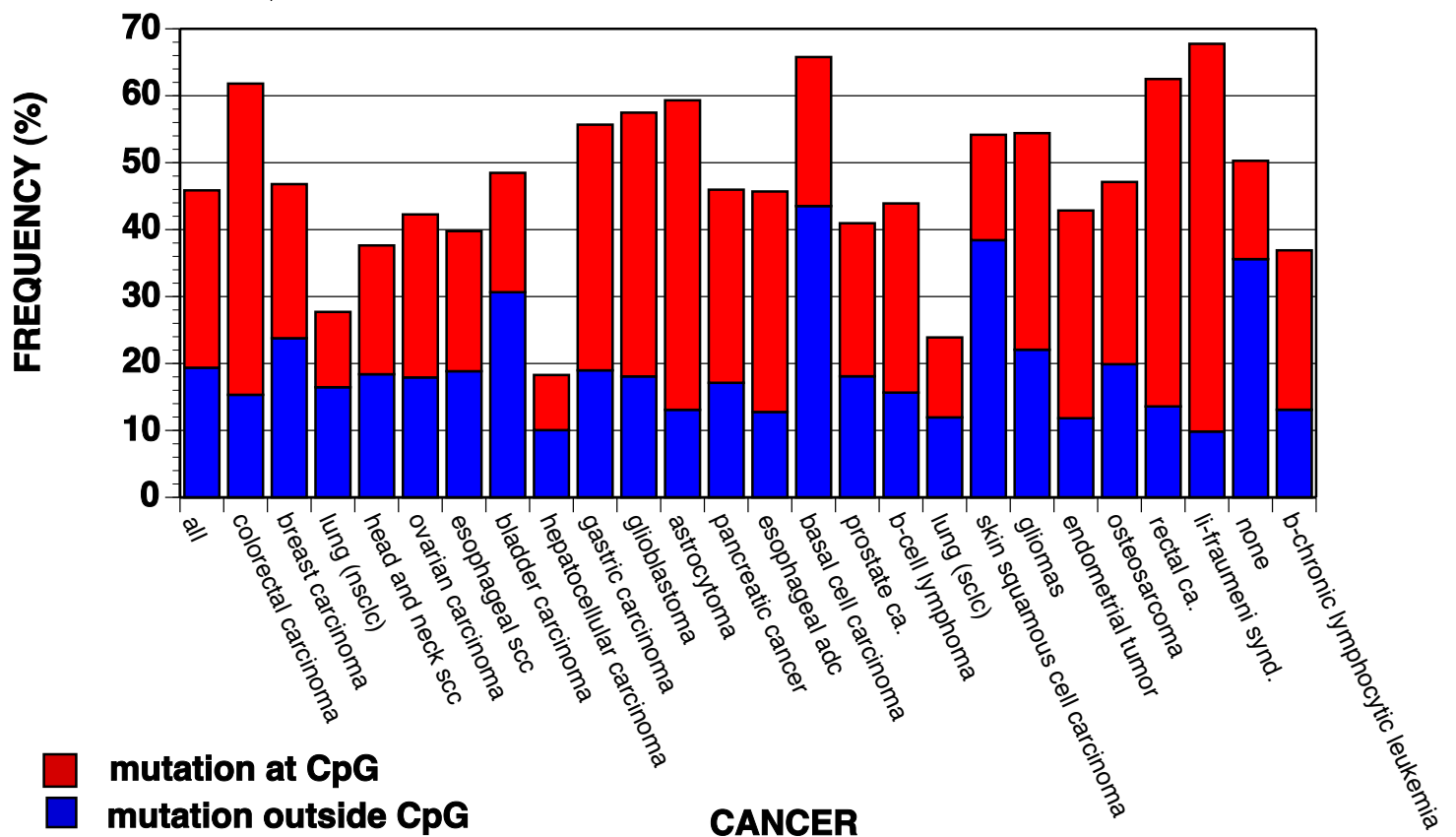
Analysis of GC->AT transition at CpG dinucleotide in the TP53 gene

The 42 CpG dinucleotide of the p53 gene are methylated in normal tissue [Tornaletti and Pfeifer, 1995].
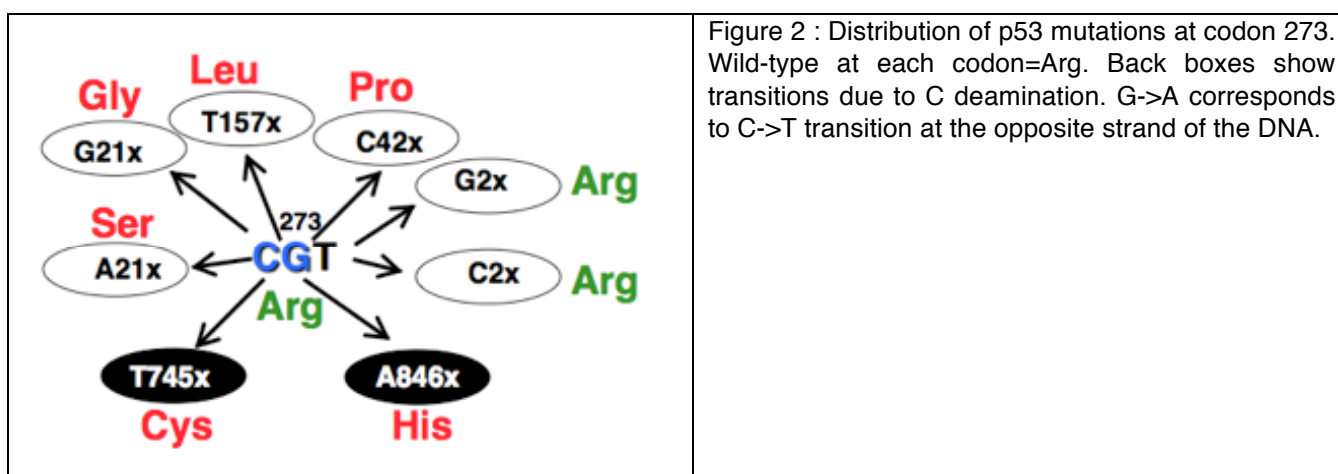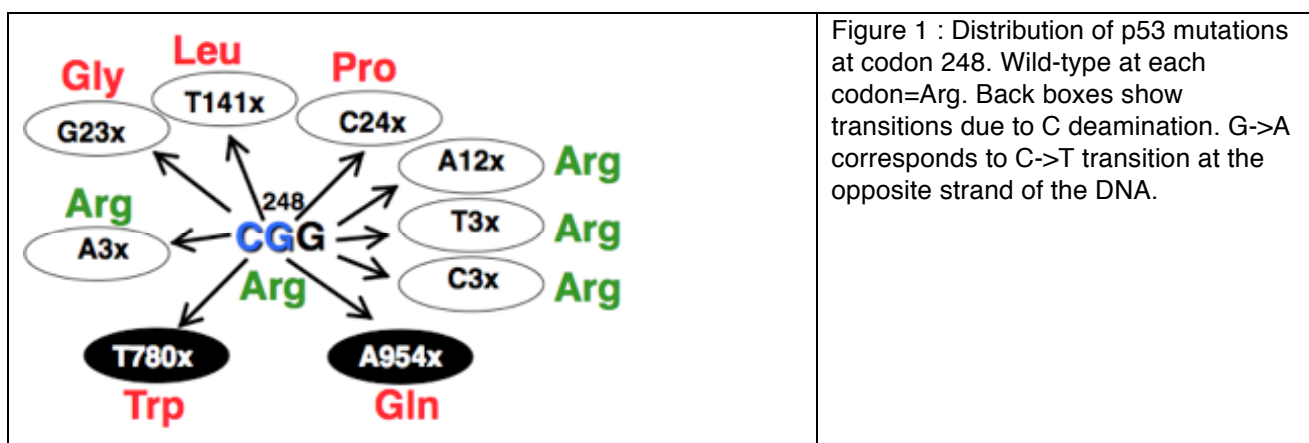It is generally assumed that the higher deamination rate of 5-methylcytosine leading to a T/G mismatch that is not efficiently repaired could lead to this high rate of transversion in the p53 gene. Deamination of cytosine leads to a U/G mismatch that could be removed more efficiently. Although attractive, this hypothesis has not been formally demonstrated and several lines of evidence suggest that other models should also be investigated. Various studies have demonstrated that exogenous carcinogens, such as BPDE or UV sunlight, have a greater affinity for methylated CpG dinucleo- tides than their unmethylated counterparts [Denisenko et al., 1997; You et al., 1999]. It is conceivable that endogenous mutagens, derived from an altered cell metabolism, could also target methylated CpG dinucleotide leading to a high rate of transition

These CpG can occur in three forms in the coding sequence of the gene: **CGN**, **NCG**, or **NNC GNN**, that will be called type I, II and III, respectively.

A table with the position, frequency and remaining activity of every mtant p53 at CpG site is shown a the end of this section

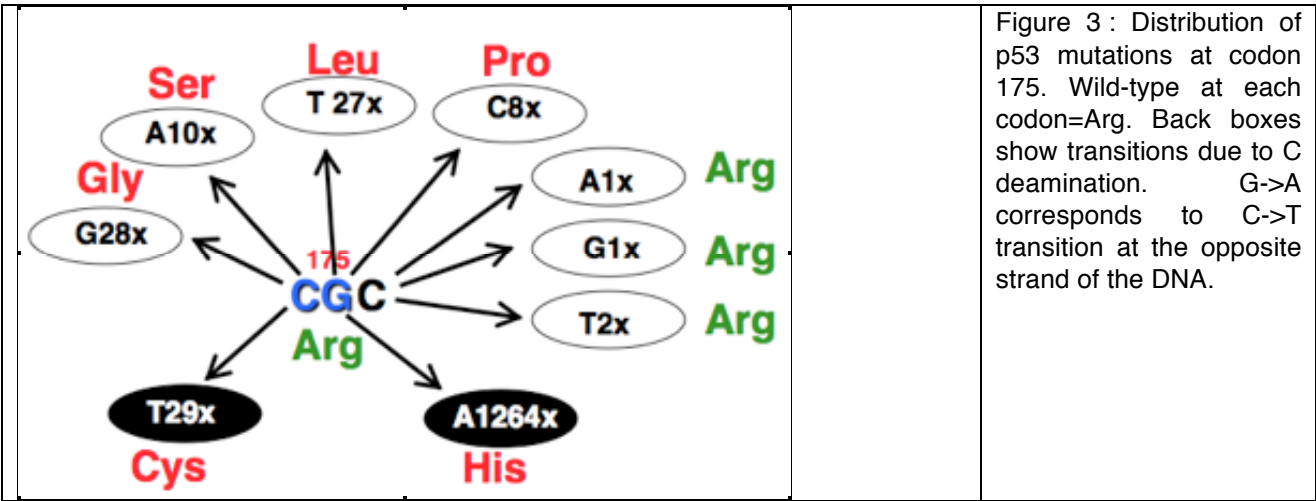### CpG and p53 mutations at hot spot codons

Examination of transitions at the 42 CpG of the p53 gene clearly shows a high degree of heterogeneity both for the frequency of mutations and also for the pattern of mutation between the two residues, (Figures 1-5). Targeting of the two C residues in both strands of a CpG dinucleotide is expected to occur and to be repaired at a similar rate. Examination of the frequency of transition at the two hot spot codons, 248 and 273 (type I CpG), confirms this expectation as there is roughly the same number of C>T and G>A substitutions (figure 1 and 2).

Figure 1 : Distribution of p53 mutations at codon 248. Wild-type at each codon=Arg. Back boxes show transitions due to C deamination. G->A corresponds to C->T transition at the opposite strand of the DNA.

Figure 2 : Distribution of p53 mutations at codon 273. Wild-type at each codon=Arg. Back boxes show transitions due to C deamination. G->A corresponds to C->T transition at the opposite strand of the DNA.

On the other hand, examination of an other hot spot codons, 175 shows a marked disequilibrium in the distribution of mutations (figure 3). Similar findings are observed for codons 196, 213, 282, and 306 that present a lower frequency of mutation (figure . It is essential to keep in mind that these mutations are not a true representation of the rate of p53 gene mutation, as only alterations that lead to a growth advantage for tumor progression will be selected. It is likely that some transitions at specific CpG dinucleotides will not lead to a

selectable alteration. In 1994, we already reported this disequilibrium for codon 175, as it was already obvious in a mutation database composed of only a few hundred mutations.

The G>A transition at codon 175 leads to an arginine substituted for an histidine. The biochemical and biological function of this mutant (R175H) is totally impaired. The C>T transition leads to an arginine substituted for a cysteine (R175C). In all studies performed to date, this substitution does not inactivate p53 activity [Ory et al., 1994], indicating that only inactivating p53 mutations are selected during the transformation process.

Figure 3 : Distribution of p53 mutations at codon 175. Wild-type at each codon=Arg. Back boxes show transitions due to C deamination. G->A corresponds to C->T transition at the opposite strand of the DNA.

Transition at type I CpG

Transition at type I CpG always leads to amino acid substitution whether it is the first or the second base that is changed (specific targeting of the first C will lead to a C to T transition on the transcribed strand; targeting of the second C, on the opposite strand, will lead to a similar event that will be translated as a G4A transition on the transcribed stranded).
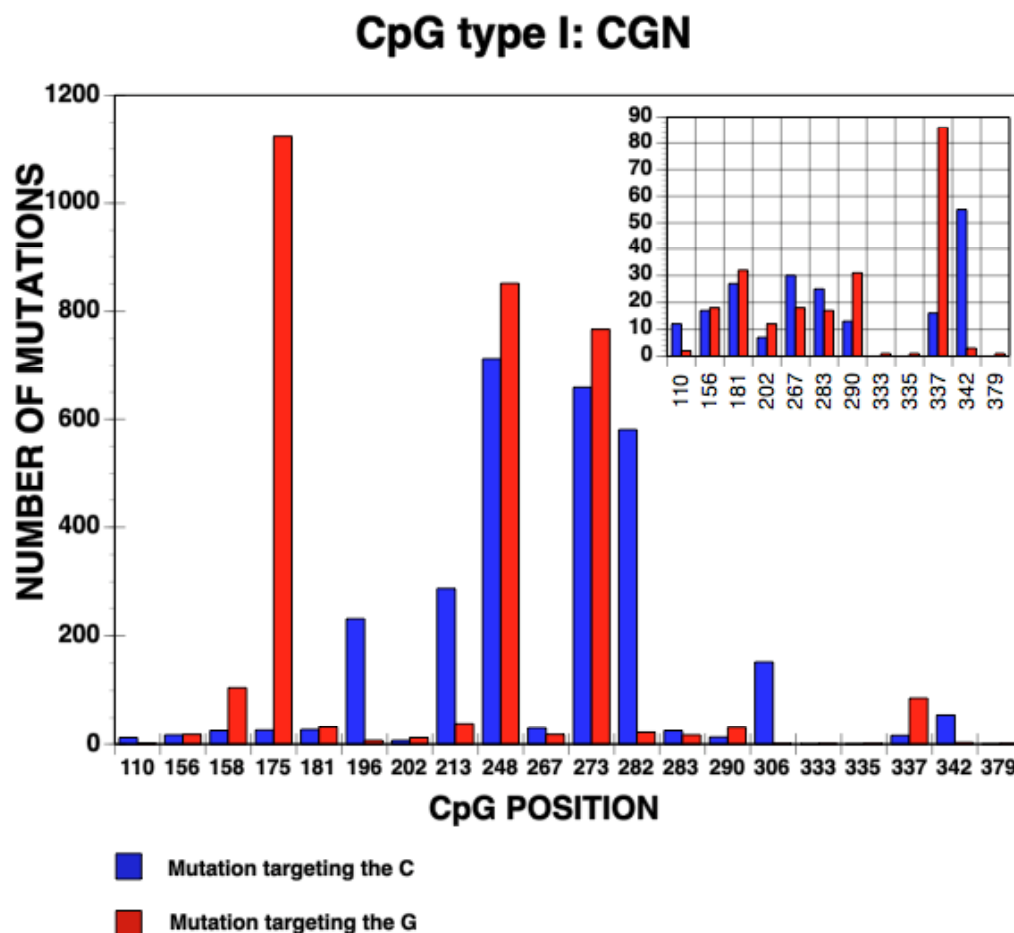
For type I CpG codons, such as 175, 196, 213 and 282, 18, 5, 25, and 18 mutants have been identified at the underrepresented position, respectively. Seven of the 18 G->A mutants at position 282 are found in tumors containing more than one p53 mutation. In each case, these second mutations correspond to well-known inactivating mutations. Multiple mutations in a single tumor is an uncommon event for the p53 gene, as the most frequent mechanism appears to be a single mutation in one allele and loss of the second allele due to partial or complete deletion of chromosome 17. Less than 0.5% of tumors harbor multiple mutations. These observations strongly suggest that G->A mutants at position 282 are not true driving mutations per se, but passenger mutations that could have been co- selected with a second mutation constituting the true driving force for p53 inactivation. For the remaining 11 cases, it is possible that the true mutation may not have been detected, as most of these studies only examined exons 5 to 8. Similar comments may apply to codons 175, 196, and 213.

Transition at type II CpG

Transition at type II CpG will only lead to mutation when the C is modified, as mutation of the G residue does not change the amino acid residue due to degeneration of the genetic code.
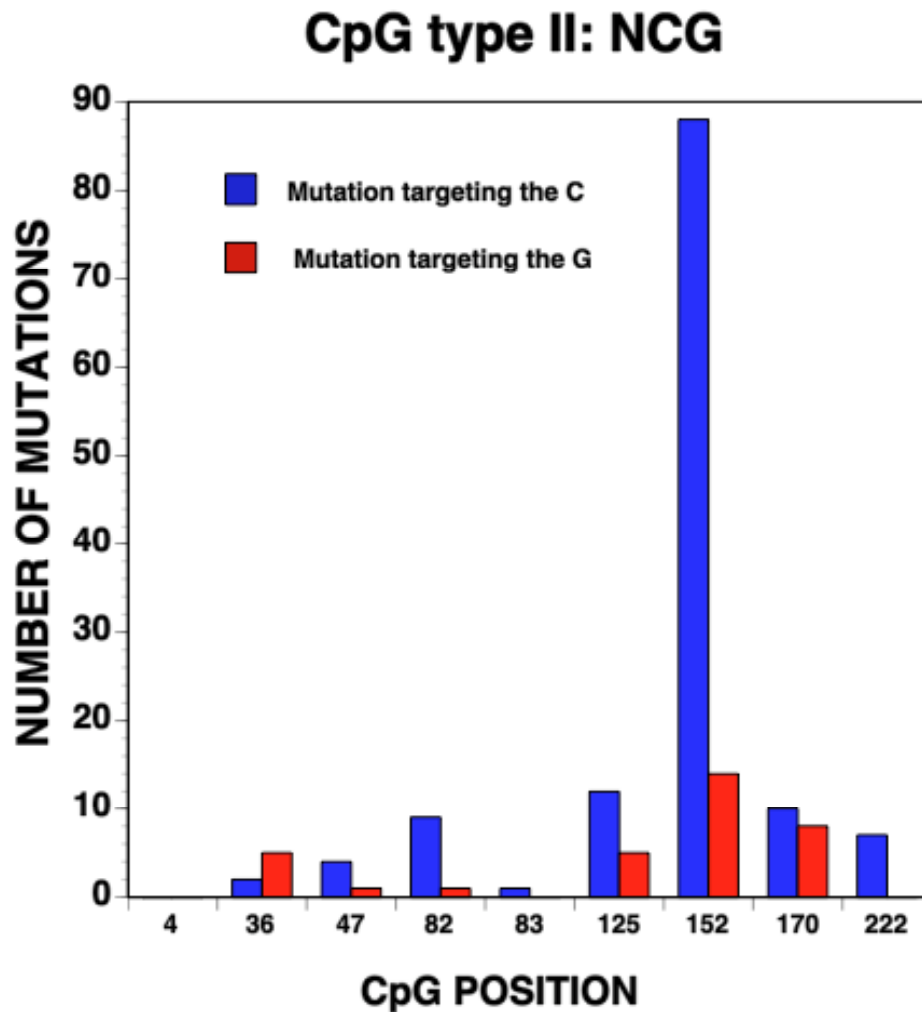
The frequency of p53 mutations at these CpG is very low, except for codon 152. Although the C>T transition leads to an inactivating mutation, the G->A transition does not change the identity of the proline residue. Nevertheless, 11 tumors harbor this neutral mutation. Five of them are found in tumors containing more than one p53 mutation. In each case, these second mutations correspond to well-known inactivating mutations indicating that these C->T transition are passenger mutations.

Transition at type III CpG

Transition at type III CpG will only lead to a change of the amino residue when the G is modified. The frequency of p53 mutations at these CpG is very low, except for codon 245. The hotspot G245S mutant found more than 400 times in the database is well known to be inactive.

CpG type III: NNC GNN
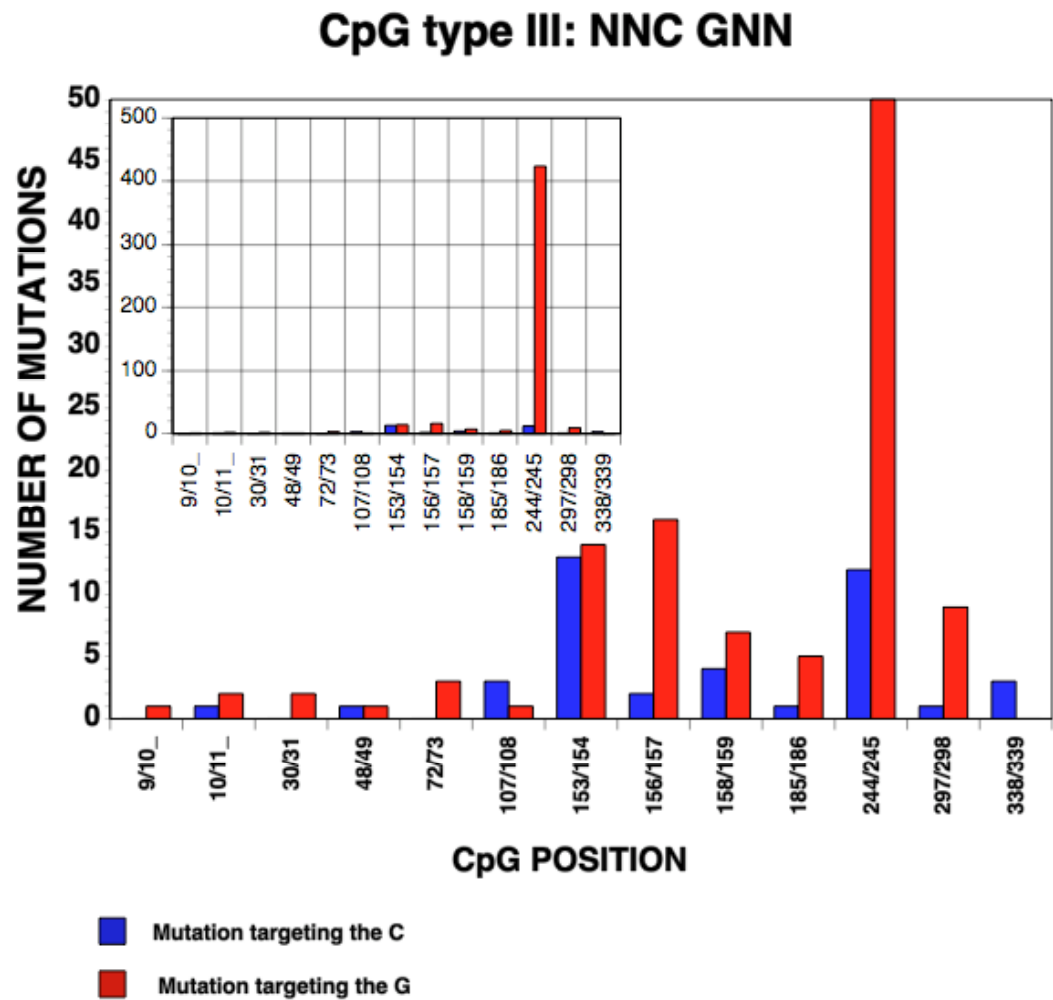
Only frequent p53 mutant are inactive
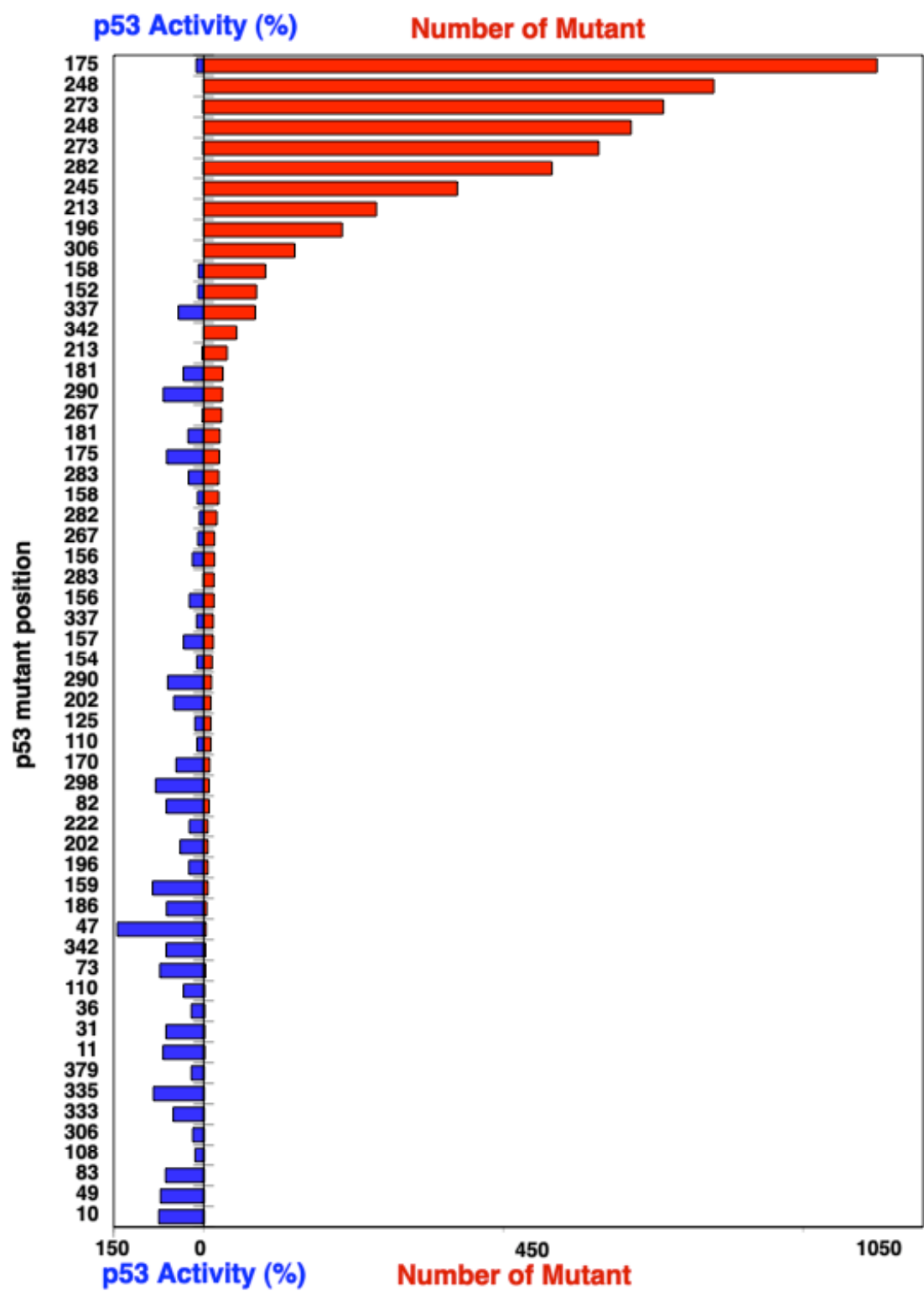
CpG MUTATION AND LOSS OF p53 ACTIVITY

POS:	Codon position (1 to 393)
WT:	Normal base sequence of the codon in which the mutation occurred
Mut:	Sequence of the mutated codon
WT AA:	Wild type amino acid
Mut:	Mutant amino acid.
Event:	Mutational event:
Number:	Number of reccord in the database
WAF1:	Activity of the mutant p53 using a waf1 reporter gene (%)
	ND: No mutant activity available
	NR: Not Relevant
Code:	▇ Polymorphism ▇ Mutant

	Mutation name	Pos.	WT	Mut.	WT AA	Mut. AA	Event	Number	WAF1	Code
1	p.Pro4Leu	4	CCG	CTG	Pro	Leu	C->T	0	39.5	
1	p.Pro4Pro	4	CCG	CCA	Pro	Pro	G->A	0	NR	
2	p.Ser9Ser	9	AGC	AGT	Ser	Ser	C->T	0	NR	
2	p.Val10Ile	10	GTC	ATC	Val	Ile	G->A	1	74.84	
3	p.Val10Val	10	GTC	GTT	Val	Val	C->T	0	NR	
3	p.Glu11Lys	11	GAG	AAG	Glu	Lys	G->A	1	67.82	
4	p.Asn30Asn	30	AAC	AAT	Asn	Asn	C->T	0	NR	
4	p.Val31Ile	31	GTT	ATT	Val	Ile	G->A	2	62.79	
5	p.Pro36Leu	36	CCG	CTG	Pro	Leu	C->T	2	20.58	
5	p.Pro36Pro	36	CCG	CCA	Pro	Pro	G->A	5	NR	
6	p.Pro47Leu	47	CCG	CTG	Pro	Leu	C->T	4	144.03	
6	p.Pro47Pro	47	CCG	CCA	Pro	Pro	G->A	1	NR	
7	p.Asp48Asp	48	GAC	GAT	Asp	Asp	C->T	1	NR	
7	p.Asp49Asn	49	GAT	AAT	Asp	Asn	G->A	1	72	
8	p.Arg72Cys	72	CGC	TGC	Arg	Cys	C->T	0	ND	
8	p.Arg72His	72	CGC	CAC	Arg	His	G->A	0	ND	
9	p.Pro72Pro	72	CCC	CCT	Pro	Pro	C->T	0	NR	
9	p.Val73Met	73	GTG	ATG	Val	Met	G->A	3	72.99	
10	p.Pro82Leu	82	CCG	CTG	Pro	Leu	C->T	8	62.23	
10	p.Pro82Pro	82	CCG	CCA	Pro	Pro	G->A	1	NR	
11	p.Ala83Val	83	GCG	GTG	Ala	Val	C->T	1	63.55	
11	p.Ala83Ala	83	GCG	GCA	Ala	Ala	G->A	0	NR	
12	p.Tyr107Tyr	107	TAC	TAT	Tyr	Tyr	C->T	3	NR	
12	p.Gly108Ser	108	GGT	AGT	Gly	Ser	G->A	1	14.27	
13	p.Arg110Cys	110	CGT	TGT	Arg	Cys	C->T	12	10.91	
13	p.Arg110His	110	CGT	CAT	Arg	His	G->A	2	33.67	
14	p.Thr125Met	125	ACG	ATG	Thr	Met	C->T	11	14.64	
14	p.Thr125Thr	125	ACG	ACA	Thr	Thr	G->A	4	NR	
15	p.Pro152Leu	152	CCG	CTG	Pro	Leu	C->T	80	9.52	
15	p.Pro152Pro	152	CCG	CCA	Pro	Pro	G->A	14	NR	
16	p.Pro153Pro	153	CCC	CCT	Pro	Pro	C->T	12	NR	
16	p.Gly154Ser	154	GGC	AGC	Gly	Ser	G->A	12	11.47	
17	p.Arg156Cys	156	CGC	TGC	Arg	Cys	C->T	8	23.94	
17	p.Arg156His	156	CGC	CAC	Arg	His	G->A	16	18.55	
18	p.Arg156Arg	156	CGC	CGT	Arg	Arg	C->T	1	NR	
18	p.Val157Ile	157	GTC	ATC	Val	Ile	G->A	13	33.57	
19	p.Arg158Cys	158	CGC	TGC	Arg	Cys	C->T	24	10.06	

19	p.Arg158His	158	CGC	CAC	Arg	His	G->A	102	8.78	
20	p.Arg158Arg	158	CGC	CGT	Arg	Arg	C->T	4	NR	
20	p.Ala159Thr	159	GCC	ACC	Ala	Thr	G->A	7	85.26	
20	p.Thr170Met	170	ACG	ATG	Thr	Met	C->T	9	46.08	
21	p.Thr170Thr	170	ACG	ACA	Thr	Thr	G->A	8	NR	
21	p.Arg175Cys	175	CGC	TGC	Arg	Cys	C->T	25	61.6	
22	p.Arg175His	175	CGC	CAC	Arg	His	G->A	1102	12.41	
22	p.Arg181Cys	181	CGC	TGC	Arg	Cys	C->T	26	26.1	
23	p.Arg181His	181	CGC	CAC	Arg	His	G->A	30	34.07	
23	p.Ser185Ser	185	AGC	AGT	Ser	Ser	C->T	1	NR	
24	p.Asp186Asn	186	GAT	AAT	Asp	Asn	G->A	3	61.8	
24	p.Arg196Stop	196	CGA	TGA	Arg	Stop	C->T	229	0	
25	p.Arg196Gln	196	CGA	CAA	Arg	Gln	G->A	7	24.56	
25	p.Arg202Cys	202	CGT	TGT	Arg	Cys	C->T	5	39.25	
26	p.Arg202His	202	CGT	CAT	Arg	His	G->A	8	49.84	
26	p.Arg213Stop	213	CGA	TGA	Arg	Stop	C->T	281	0	
27	p.Arg213Gln	213	CGA	CAA	Arg	Gln	G->A	39	2.19	
27	p.Pro222Leu	222	CCG	CTG	Pro	Leu	C->T	6	23.96	
27	p.Pro222Pro	222	CCG	CCA	Pro	Pro	G->A	0	NR	
28	p.Gly244Gly	244	GGC	GGT	Gly	Gly	C->T	11	NR	
28	p.Gly245Ser	245	GGC	AGC	Gly	Ser	G->A	420	0	
29	p.Arg248Trp	248	CGG	TGG	Arg	Trp	C->T	705	0	
29	p.Arg248Gln	248	CGG	CAG	Arg	Gln	G->A	838	0	
30	p.Arg267Trp	267	CGG	TGG	Arg	Trp	C->T	30	1.68	
30	p.Arg267Gln	267	CGG	CAG	Arg	Gln	G->A	13	9.75	
31	p.Arg273Cys	273	CGT	TGT	Arg	Cys	C->T	648	0.91	
31	p.Arg273His	273	CGT	CAT	Arg	His	G->A	759	1.01	
32	p.Arg282Trp	282	CGG	TGG	Arg	Trp	C->T	572	0.55	
32	p.Arg282Gln	282	CGG	CAG	Arg	Gln	G->A	22	7.18	
33	p.Arg283Cys	283	CGC	TGC	Arg	Cys	C->T	25	25.27	
33	p.Arg283His	283	CGC	CAC	Arg	His	G->A	17	0.46	
34	p.Arg290Cys	290	CGC	TGC	Arg	Cys	C->T	11	60.02	
34	p.Arg290His	290	CGC	CAC	Arg	His	G->A	24	67.3	
35	p.His297His	297	CAC	CAT	His	His	C->T	1	NR	
35	p.Glu298Lys	298	GAG	AAG	Glu	Lys	G->A	5	80.15	
36	p.Arg306Stop	306	CGA	TGA	Arg	Stop	C->T	150	0	
36	p.Arg306Gln	306	CGA	CAA	Arg	Gln	G->A	1	18.22	
37	p.Arg333Cys	333	CGT	TGT	Arg	Cys	C->T	0	ND	
37	p.Arg333His	333	CGT	CAT	Arg	His	G->A	1	50.76	
38	p.Arg335Cys	335	CGT	TGT	Arg	Cys	C->T	0	ND	
38	p.Arg335His	335	CGT	CAT	Arg	His	G->A	1	83.88	
39	p.Arg337Cys	337	CGC	TGC	Arg	Cys	C->T	16	11.86	
39	p.Arg337His	337	CGC	CAC	Arg	His	G->A	86	42.17	
40	p.Phe338Phe	338	TTC	TTT	Phe	Phe	C->T	3	NR	
40	p.Glu339Lys	339	GAG	AAG	Glu	Lys	G->A	0	ND	
41	p.Arg342Stop	342	CGA	TGA	Arg	Stop	C->T	55	0	
41	p.Arg342Gln	342	CGA	CAA	Arg	Gln	G->A	3	62.39	
42	p.Arg379Cys	379	CGC	TGC	Arg	Cys	G->A	1	48	
42	p.Arg379His	379	CGC	CAC	Arg	His	C->T	1	55	

DISTRIBUTION OF p53 MUTATION

Amino acids residues are shown using both 3 or 1 letter abbreviation

Yellow: codon number	White: wt codon	Light orange: 3 letter aa	light blue: 1 letter aa

The last lane shows the number of mutations found at this position in the UMD p53 database
The frequency of p53 mutations is colored coded:

Red: between 1 and 10 mutations	Green: between 11 and 100 mutations	Blue: > 100 mutations

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
ATG	GAG	GAG	CCG	CAG	TCA	GAT	CCT	AGC	GTC	GAG	CCC	CCT	CTG	AGT	CAG	GAA	ACA	TTT	TCA
Met	Glu	Glu	Pro	Gln	Ser	Asp	Pro	Ser	Val	Glu	Pro	Pro	Leu	Ser	Gln	Glu	Thr	Phe	Ser
M	E	E	P	Q	S	D	P	S	V	E	P	P	L	S	Q	E	T	F	S
0	2	0	0	2	1	1	1	0	2	12	1	1	0	1	1	1	1	0	0

21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
GAC	CTA	TGG	AAA	CTA	CTT	CCT	GAA	AAC	AAC	GTT	CTG	TCC	CCC	TTG	CCG	TCC	CAA	GCA	ATG
Asp	Leu	Trp	Lys	Leu	Leu	Pro	Glu	Asn	Asn	Val	Leu	Ser	Pro	Leu	Pro	Ser	Gln	Ala	Met
D	L	W	K	L	L	P	E	N	N	V	L	S	P	L	P	S	Q	A	M
1	1	0	1	1	3	2	2	3	1	2	1	3	1	5	10	4	6	2	2

41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60
GAT	GAT	TTG	ATG	CTG	TCC	CCG	GAC	GAT	ATT	GAA	CAA	TGG	TTC	ACT	GAA	GAC	CCA	GGT	CCA
Asp	Asp	Leu	Met	Leu	Ser	Pro	Asp	Asp	Iso	Glu	Gln	Trp	Phe	Thr	Glu	Asp	Pro	Gly	Pro
D	D	L	M	L	S	P	D	D	I	E	Q	W	F	T	E	D	P	G	P
7	2	4	5	2	16	8	4	9	3	9	13	21	12	2	8	3	1	7	6

61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80
GAT	GAA	GCT	CCC	AGA	ATG	CCA	GAG	GCT	GCT	CCC	CCC	GTG	GCC	CCT	GCA	CCA	GCA	GCT	CCT
Asp	Glu	Ala	Pro	Arg	Met	Pro	Glu	Ala	Ala	Pro	Pro	Val	Ala	Pro	Ala	Pro	Ala	Ala	Pro
D	E	A	P	R	M	P	E	A	A	P	P	V	A	P	A	P	A	A	P
8	24	6	2	14	2	11	14	10	5	9	CCG	12	6	8	18	7	1	3	5
											Arg								
											R								
											11								

81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100
ACA	CCG	GCG	GCC	CCT	GCA	CCA	GCC	CCC	TCC	TGG	CCC	CTG	TCA	TCT	TCT	GTC	CCT	TCC	CAG
Thr	Pro	Ala	Ala	Pro	Ala	Pro	Ala	Pro	Ser	Trp	Pro	Leu	Ser	Ser	Ser	Val	Pro	Ser	Gln
T	P	A	A	P	A	P	A	P	S	W	P	L	S	S	S	V	P	S	Q
5	15	9	11	10	3	4	12	40	5	29	8	5	8	8	9	4	14	5	19

101	102	103	104	105	106	107	108	109	110	111	112	113	114	115	116	117	118	119	120
AAA	ACC	TAC	CAG	GGC	AGC	TAC	GGT	TTC	CGT	CTG	GGC	TTC	TTG	CAT	TCT	GGG	ACA	GCC	AAG
Lys	Thr	Tyr	Gln	Gly	Ser	Tyr	Gly	Phe	Arg	Leu	Gly	Phe	Leu	His	Ser	Gly	Thr	Ala	Lys
K	T	Y	Q	G	S	Y	G	F	R	L	G	F	L	H	S	G	T	A	K
11	19	13	30	19	13	21	14	11	67	22	13	32	4	5	8	14	3	8	18

121	122	123	124	125	126	127	128	129	130	131	132	133	134	135	136	137	138	139	140
TCT	GTG	ACT	TGC	ACG	TAC	TCC	CCT	GCC	CTC	AAC	AAG	ATG	TTT	TGC	CAA	CTG	GCC	AAG	ACC
Ser	Val	Thr	Cys	Thr	Tyr	Ser	Pro	Ala	Leu	Asn	Lys	Met	Phe	Cys	Gln	Leu	Ala	Lys	Thr
S	V	T	C	T	Y	S	P	A	L	N	K	M	F	C	Q	L	A	K	T
8	9	5	16	38	89	65	32	24	81	56	190	57	64	252	102	36	110	55	46

141	142	143	144	145	146	147	148	149	150	151	152	153	154	155	156	157	158	159	160
TGC	CCT	GTG	CAG	CTG	TGG	GTT	GAT	TCC	ACA	CCC	CCG	CCC	GGC	ACC	CGC	GTC	CGC	GCC	ATG
Cys	Pro	Val	Gln	Leu	Trp	Val	Asp	Ser	Thr	Pro	Pro	Pro	Gly	Thr	Arg	Val	Arg	Ala	Met
C	P	V	Q	L	W	V	D	S	T	P	P	P	G	T	R	V	R	A	M
195	48	98	122	72	124	54	31	47	42	266	213	74	133	140	132	298	330	151	50

161	162	163	164	165	166	167	168	169	170	171	172	173	174	175	176	177	178	179	180
GCC	ATC	TAC	AAG	CAG	TCA	CAG	CAC	ATG	ACG	GAG	GTT	GTG	AGG	CGC	TGC	CCC	CAC	CAT	GAG
Ala	Iso	Tyr	Lys	Gln	Ser	Gln	His	Met	Thr	Glu	Val	Val	Arg	Arg	Cys	Pro	His	His	Glu
A	I	Y	K	Q	S	Q	H	M	T	E	V	V	R	R	C	P	H	H	E
156	66	248	86	76	81	104	85	37	50	69	85	248	83	1375	427	137	97	416	55

181	182	183	184	185	186	187	188	189	190	191	192	193	194	195	196	197	198	199	200
CGC	TGC	TCA	GAT	AGC	GAT	GGT	CTG	GCC	CCT	CCT	CAG	CAT	CTT	ATC	CGA	GTG	GAA	GGA	AAT
Arg	Cys	Ser	Asp	Ser	Asp	Gly	Leu	Ala	Pro	Pro	Gln	His	Leu	Iso	Arg	Val	Glu	Gly	Asn
R	C	S	D	S	D	G	L	A	P	P	Q	H	L	I	R	V	E	G	N
55	34	45	56	24	25	42	15	46	105	55	128	254	148	192	313	52	55	43	29

201	202	203	204	205	206	207	208	209	210	211	212	213	214	215	216	217	218	219	220
TTG	CGT	GTG	GAG	TAT	TTG	GAT	GAC	AGA	AAC	ACT	TTT	CGA	CAT	AGT	GTG	GTG	GTG	CCC	TAT
Leu	Arg	Val	Glu	Tyr	Leu	Asp	Asp	Arg	Asn	Thr	Phe	CGG	His	Ser	Val	Val	Val	Pro	Tyr
L	R	V	E	Y	L	D	D	R	N	T	F	Arg	H	S	V	V	V	P	Y
36	51	45	88	195	25	30	54	100	29	71	48	R	109	118	138	49	75	47	451
												457							

221	222	223	224	225	226	227	228	229	230	231	232	233	234	235	236	237	238	239	240
GAG	CCG	CCT	GAG	GTT	GGC	TCT	GAC	TGT	ACC	ACC	ATC	CAC	TAC	AAC	TAC	ATG	TGT	AAC	AGT
Glu	Pro	Pro	Glu	Val	Gly	Ser	Asp	Cys	Thr	Thr	Iso	His	Tyr	Asn	Tyr	Met	Cys	Asn	Ser
E	P	P	E	V	G	S	D	C	T	T	I	H	Y	N	Y	M	C	N	S
50	35	26	59	29	39	38	54	51	40	30	71	39	224	81	170	267	249	164	88

241	242	243	244	245	246	247	248	249	250	251	252	253	254	255	256	257	258	259	260
Ser	Cys	Met	Gly	Gly	Met	Asn	Arg	Arg	Pro	Iso	Leu	Thr	Iso	Iso	Thr	Leu	Glu	Asp	Ser
S	C	M	G	G	M	N	R	R	P	I	L	T	I	I	T	L	E	D	S
TCC	TGC	ATG	GGC	GGC	ATG	AAC	CGG	AGG	CCC	ATC	CTC	ACC	ATC	ATC	ACA	CTG	GAA	GAC	TCC
259	248	81	277	921	157	96	1948	735	155	114	62	52	66	115	55	74	177	106	35

261	262	263	264	265	266	267	268	269	270	271	272	273	274	275	276	277	278	279	280
AGT	GGT	AAT	CTA	CTG	GGA	CGG	AAC	AGC	TTT	GAG	GTG	CGT	GTT	TGT	GCC	TGT	CCT	GGG	AGA
Ser	Gly	Asn	Leu	Leu	Gly	Arg	Asn	Ser	Phe	Glu	Val	Arg	Val	Cys	Ala	Cys	Pro	Gly	Arg
S	G	N	L	L	G	R	N	S	F	E	V	R	V	C	A	C	P	G	R
35	49	26	43	58	256	93	26	49	119	113	218	1832	120	225	88	122	337	95	297

281	282	283	284	285	286	287	288	289	290	291	292	293	294	295	296	297	298	299	300
GAC	CGG	CGC	ACA	GAG	GAA	GAG	AAT	CTC	CGC	AAG	AAA	GGG	GAG	CCT	CAC	CAC	GAG	CTG	CCC
Asp	Arg	Arg	Thr	Glu	Glu	Glu	Asn	Leu	Arg	Lys	Lys	Gly	Glu	Pro	His	His	Glu	Leu	Pro
D	R	R	T	E	E	E	N	L	R	K	K	G	E	P	H	H	E	L	P
222	790	138	37	245	181	77	24	35	88	43	37	50	110	31	39	26	111	29	41

301	302	303	304	305	306	307	308	309	310	311	312	313	314	315	316	317	318	319	320
CCA	GGG	AGC	ACT	AAG	CGA	GCA	CTG	CCC	AAC	AAC	ACC	AGC	TCC	TCT	CCC	CAG	CCA	AAG	AAG
Pro	Gly	Ser	Thr	Lys	Arg	Ala	Leu	Pro	Asn	Asn	Thr	Ser	Ser	Ser	Pro	Gln	Pro	Lys	Lys
P	G	S	T	K	R	A	L	P	N	N	T	S	S	S	P	Q	P	K	K
37	26	20	15	47	180	23	16	15	11	12	16	16	11	13	20	48	13	13	15

321	322	323	324	325	326	327	328	329	330	331	332	333	334	335	336	337	338	339	340
AAA	CCA	CTG	GAT	GGA	GAA	TAT	TTC	ACC	CTT	CAG	ATC	CGT	GGG	CGT	GAG	CGC	TTC	GAG	ATG
Lys	Pro	Leu	Asp	Gly	Glu	Tyr	Phe	Thr	Leu	Gln	Iso	Arg	Gly	Arg	Glu	Arg	Phe	Glu	Met
K	P	L	D	G	E	Y	F	T	L	Q	I	R	G	R	E	R	F	E	M
10	6	7	9	11	14	13	8	7	15	39	9	6	6	4	8	122	8	23	3

341	342	343	344	345	346	347	348	349	350	351	352	353	354	355	356	357	358	359	360
TTC	CGA	GAG	CTG	AAT	GAG	GCC	TTG	GAA	CTC	AAG	GAT	GCC	CAG	GCT	GGG	AAG	GAG	CCA	GGG
Phe	Arg	Glu	Leu	Asn	Glu	Ala	Leu	Glu	Leu	Lys	Asp	Ala	Gln	Ala	Gly	Lys	Glu	Pro	Gly
F	R	E	L	N	E	A	L	E	L	K	D	A	Q	A	G	K	E	P	G
11	103	9	5	2	6	5	4	10	1	0	2	1	3	2	5	0	3	1	6

361	362	363	364	365	366	367	368	369	370	371	372	373	374	375	376	377	378	379	380
GGG	AGC	AGG	GCT	CAC	TCC	AGC	CAC	CTG	AAG	TCC	AAA	AAG	GGT	CAG	TCT	ACC	TCC	CGC	CAT
Gly	Ser	Arg	Ala	His	Ser	Ser	His	Leu	Lys	Ser	Lys	Lys	Gly	Gln	Ser	Thr	Ser	Arg	His
G	S	R	A	H	S	S	H	L	K	S	K	K	G	Q	S	T	S	R	H
3	2	3	5	4	3	2	2	1	1	1	0	1	0	1	2	2	0	2	0

381	382	383	384	385	386	387	388	389	390	391	392	393
AAA	AAA	CTC	ATG	TTC	AAG	ACA	GAA	GGG	CCT	GAC	TCA	GAC
Lys	Lys	Leu	Met	Phe	Lys	Thr	Glu	Gly	Pro	Asp	Ser	Asp
K	K	L	M	F	K	T	E	G	P	D	S	D
2	0	0	0	1	0	1	0	2	1	0	3	2

p53 MUTATION DATABASE ANALYSIS

UV INDUCED MUTATION IN SKIN CANCER

TANDEM MUTATIONS
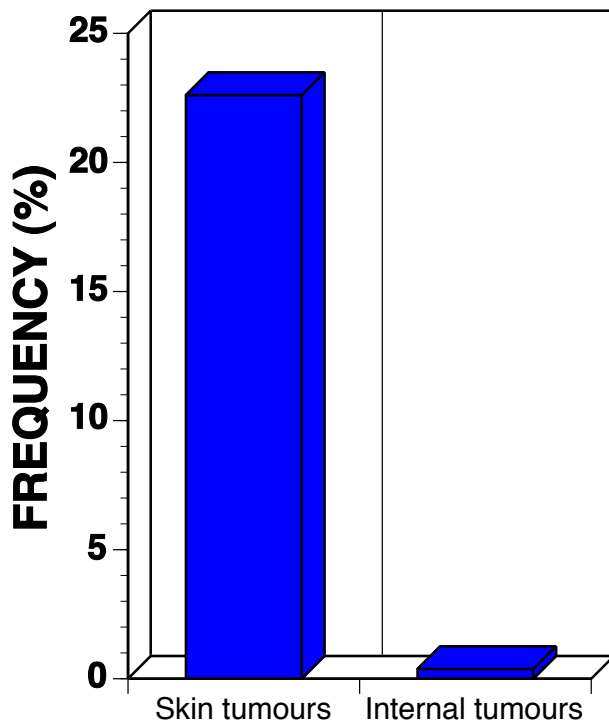
MUTATIONS AT Py-Py SITES
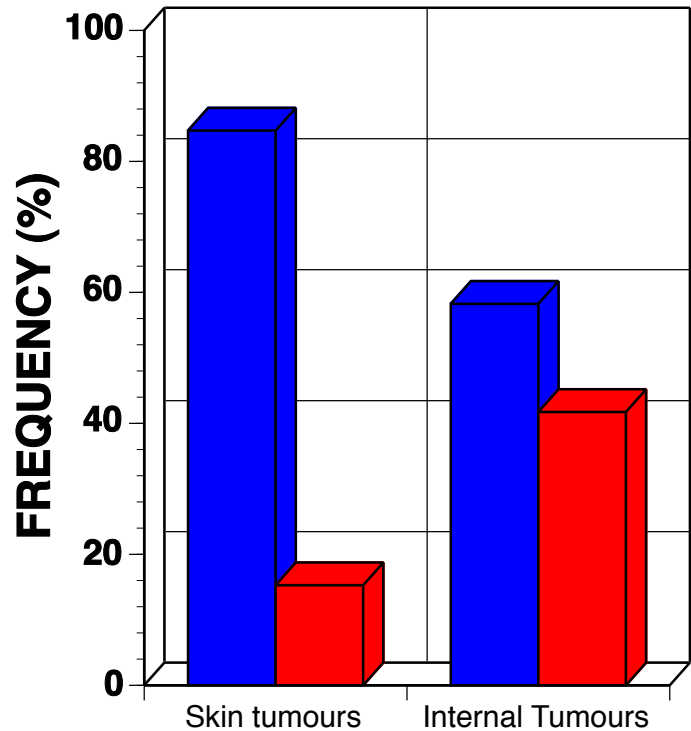
MUTATIONS AT DI-PYRIMIDINE SITES IN VARIOUS CANCER
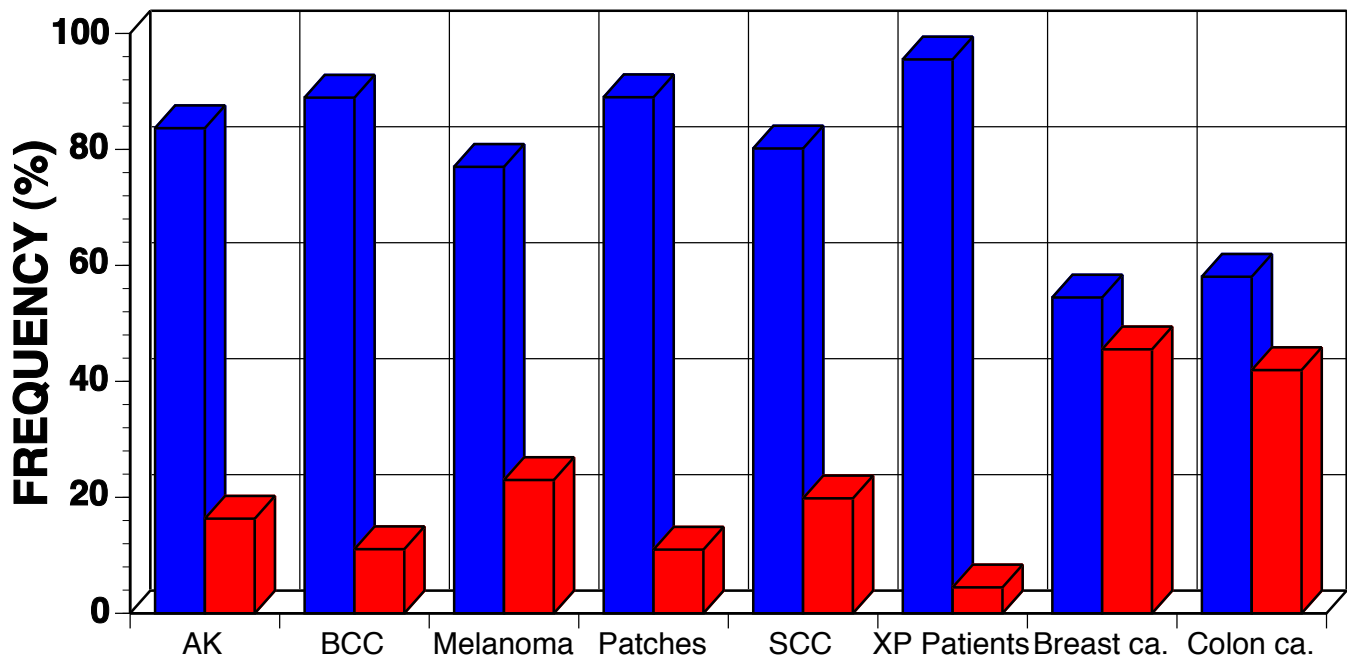
ACUTE MYELOID LEUKEMIA

Analysis summary

Number of studies	34
Number of tumors	107
Number of mutations	120
Number of tumors with 1 mutation	93
Number of tumors with 2 mutations	10
Number of tumors with more than 2 mutations	1
In studies	34
Out studies 95	0
Out studies 99	0

Strategy of analysis

Exon 2   Exon 3   Exon 4   Exon 5   Exon 6   Exon 7   Exon 8   Exon 9   Exon 10   Exon 11

Exon 5-8
7 studies

Exon 4-9
1 studies

Exon 2-11
6 studies
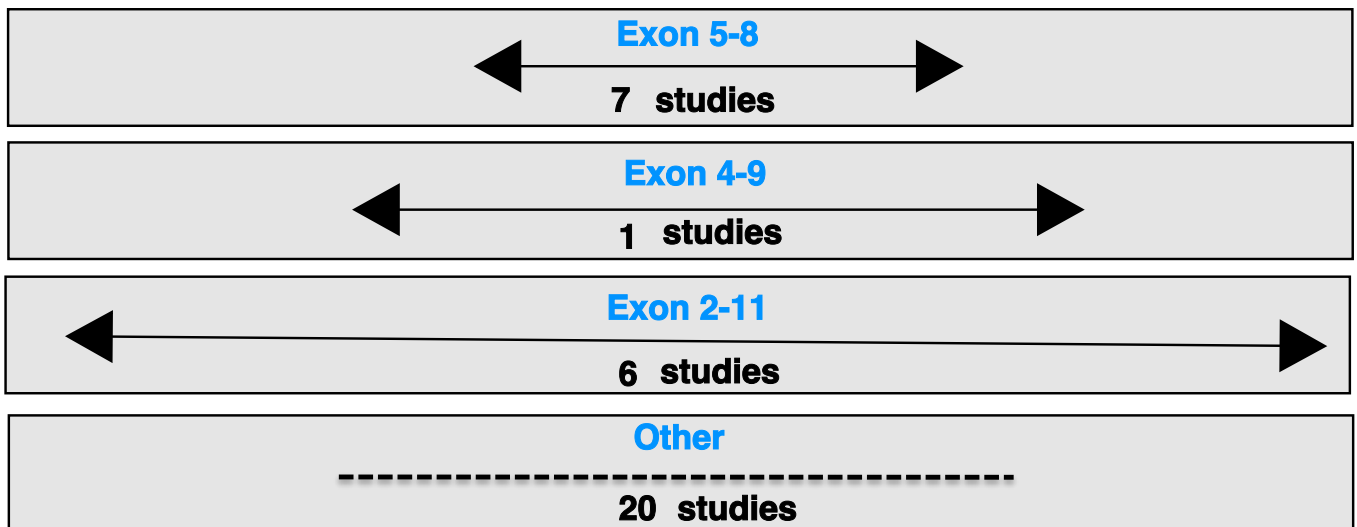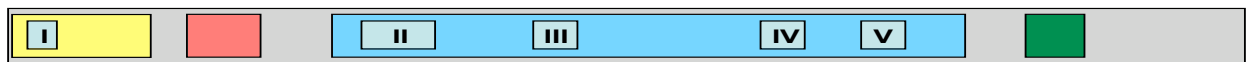
Other
20 studies

Prescreening

Studies with prescreening 17

SSCP	15	IHC	0
DGGE/CDGE	0	dHPLC	0
Yeast Assay	1	Other	1

Studies without prescreening 17

ACUTE MYELOID LEUKEMIA

p53 mutation frequency

Number of missense mutations	98	85%
Number of nonsense mutations	7	6%
Number of frameshift mutations	11	10%
Total number of mutations	116	100%
Number of polymorphisms	3	3%

p53 mutant frequency

Number of missense mutants	62	80%
Number of nonsense mutants	5	6%
Number of frameshift mutants	11	14%
Total number of mutants	78	100%
Number of polymorphisms	3	4%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
248	CGG	TGG	Arg	Trp	Ts	Yes	7
273	CGT	CAT	Arg	His	Ts	Yes	5
273	CGT	TGT	Arg	Cys	Ts	Yes	4
248	CGG	CAG	Arg	Gln	Ts	Yes	4
272	GTG	ATG	Val	Met	Ts	No	3
238	TGT	TAT	Cys	Tyr	Ts	No	3
175	CGC	CAC	Arg	His	Ts	Yes	3
220	TAT	TGT	Tyr	Cys	Ts	No	3
306	CGA	TGA	Arg	Stop	Ts	Yes	3
135	TGC	TCC	Cys	Ser	Tv	No	2

Exon Distribution

I		II	III	IV	V	

EXON 2-4　　　　**EXON 5-8**　　　　**EXON 9-11**

8%

6%

86%
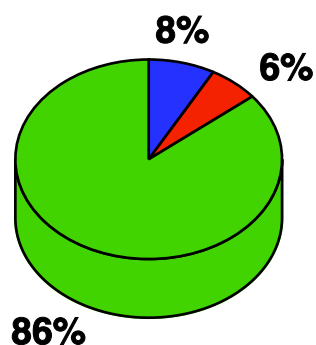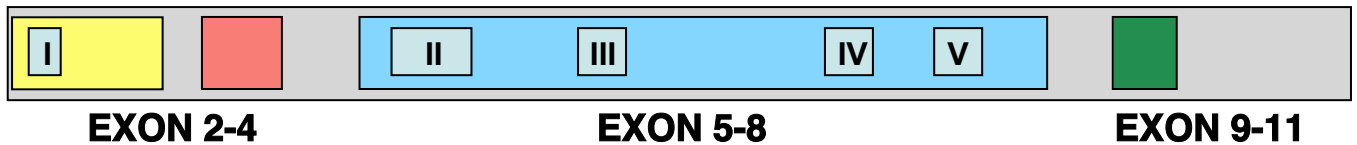
■ Frameshift　■ Nonsense　■ Missense

ACUTE MYELOID LEUKEMIA

p53 mutation distribution
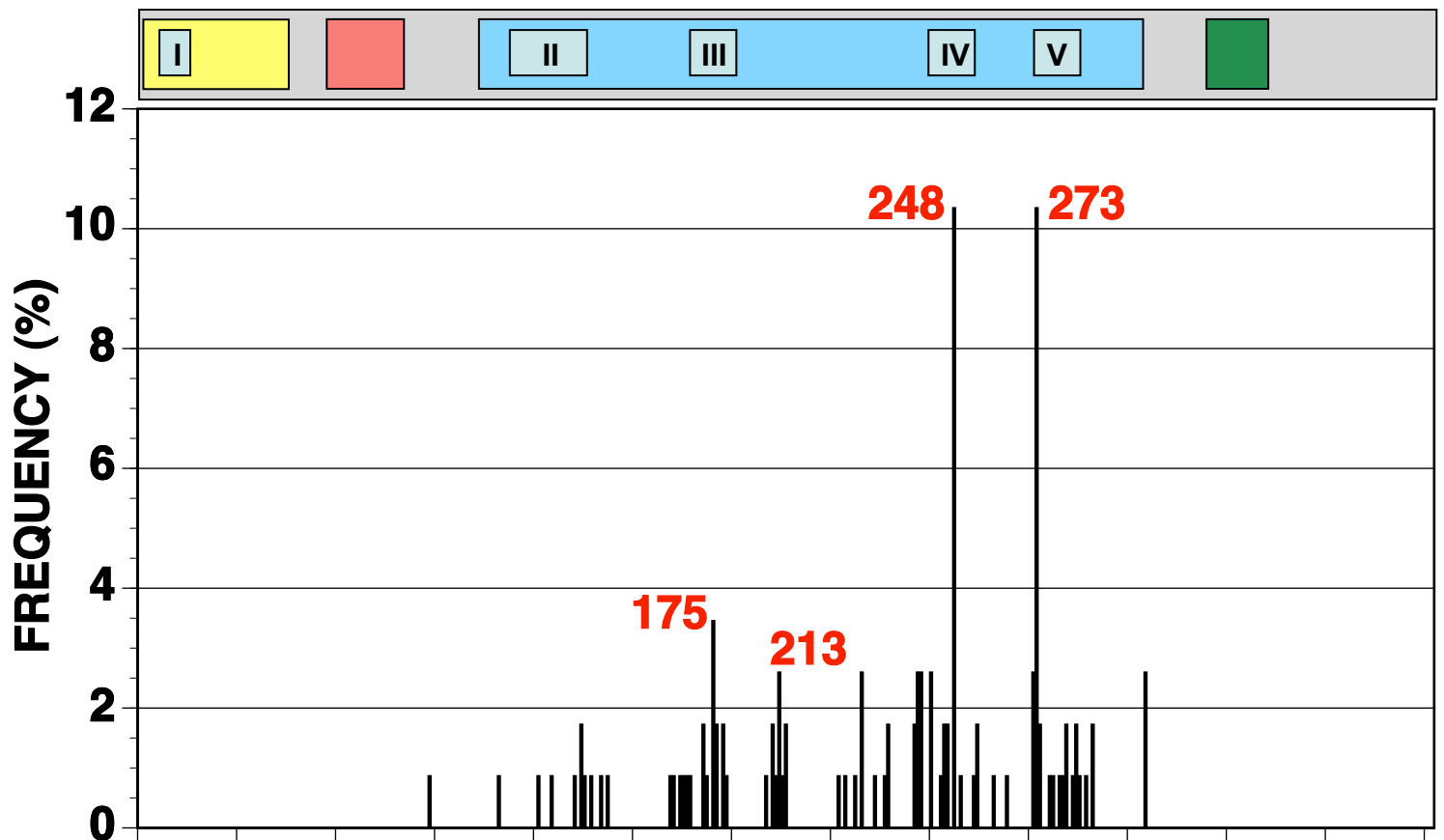
p53 mutational events
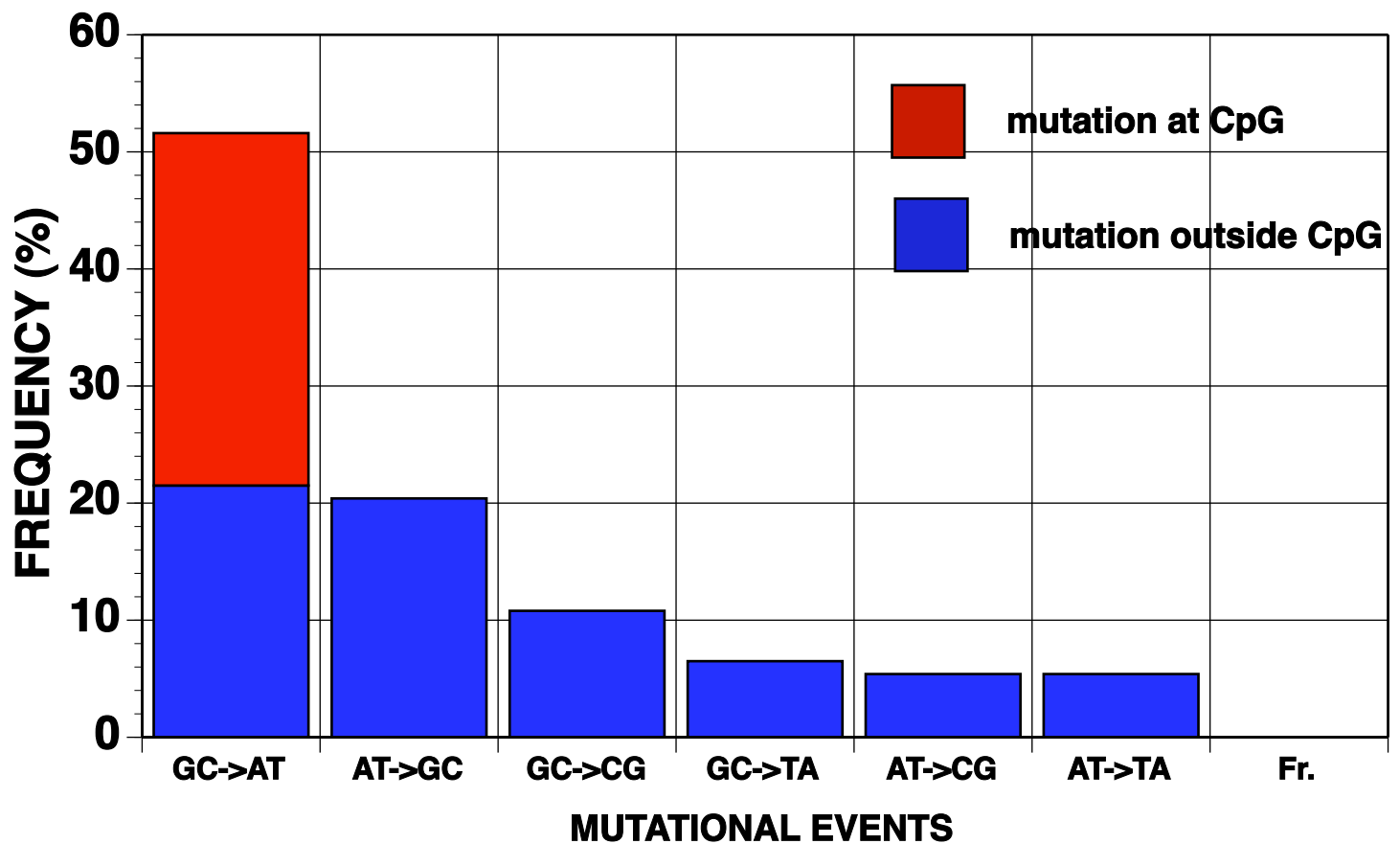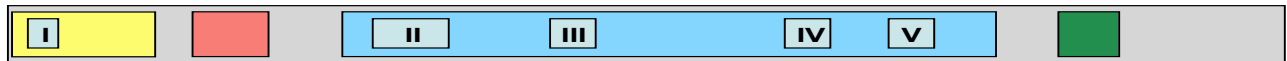
ASTROCYTOMA

Analysis summary

Number of studies	76
Number of tumors	529
Number of mutations	578
Number of tumors with 1 mutation	480
Number of tumors with 2 mutations	40
Number of tumors with more than 2 mutations	5
In studies	75
Out studies 95	0
Out studies 99	1

Strategy of analysis

Exon 2 Exon 3 Exon 4 Exon 5 Exon 6 Exon 7 Exon 8 Exon 9 Exon 10 Exon 11

Exon 5-8

32 studies

Exon 4-9

4 studies

Exon 2-11

10 studies

Other

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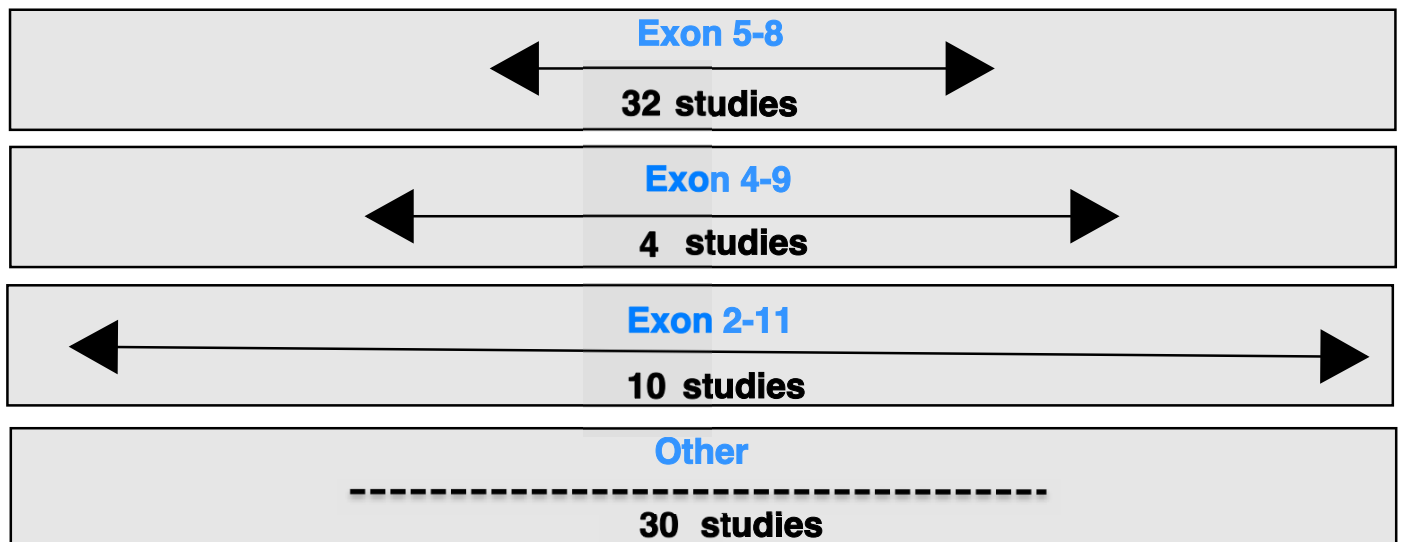
30 studies

Prescreening

Studies with prescreening	**47**				Studies without prescreening	**29**
SSCP	38		IHC	0		
DGGE/CDGE	5		dHPLC	0		
Yeast Assay	4		Other	1		

ASTROCYTOMA

p53 mutation frequency

Number of missense mutations	504	88%
Number of nonsense mutations	23	4%
Number of frameshift mutations	46	8%
Total number of mutations	573	100%
Number of polymorphisms	6	1%

p53 mutant frequency

Number of missense mutants	178	77%
Number of nonsense mutants	12	5%
Number of frameshift mutants	41	18%
Total number of mutants	231	100%
Number of polymorphisms	5	2%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
273	CGT	TGT	Arg	Cys	Ts	Yes	92
175	CGC	CAC	Arg	His	Ts	Yes	46
248	CGG	CAG	Arg	Gln	Ts	Yes	31
273	CGT	CAT	Arg	His	Ts	Yes	23
282	CGG	TGG	Arg	Trp	Ts	Yes	18
248	CGG	TGG	Arg	Trp	Ts	Yes	16
245	GGC	AGC	Gly	Ser	Ts	Yes	10
234	TAC	TGC	Tyr	Cys	Ts	No	8
179	CAT	CGT	His	Arg	Ts	No	7
163	TAC	TGC	Tyr	Cys	Ts	No	6

Exon Distribution
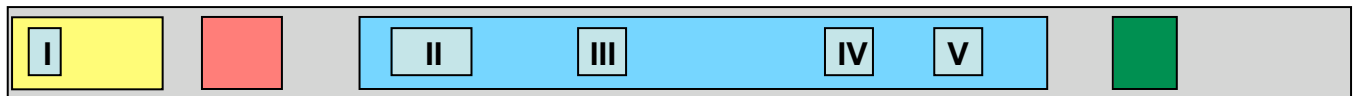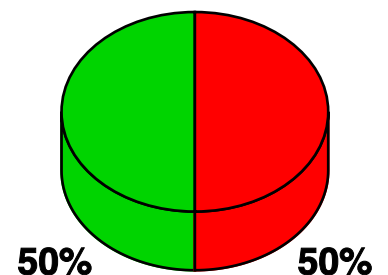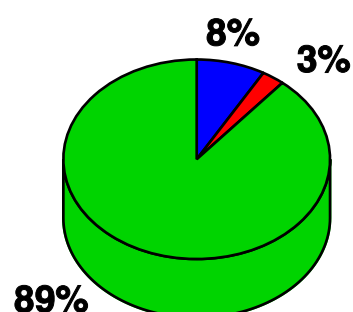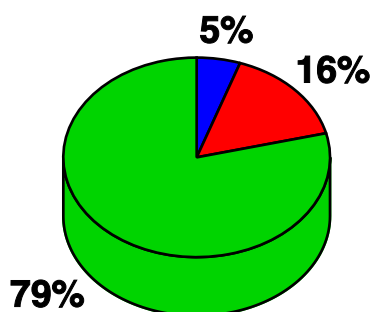
EXON 2-4: Frameshift 5%, Nonsense 16%, Missense 79%

EXON 5-8: Frameshift 8%, Nonsense 3%, Missense 89%

EXON 9-11: Missense 50%, Nonsense 50%

Legend: Frameshift (blue), Nonsense (red), Missense (green)

ASTROCYTOMA

p53 mutation distribution

273

175   248

FREQUENCY (%)

p53 CODON

p53 mutational events

FREQUENCY (%)

mutation at CpG

mutation outside CpG

MUTATIONAL EVENTS

GC->AT AT->GC GC->CG GC->TA AT->CG AT->TA Fr.
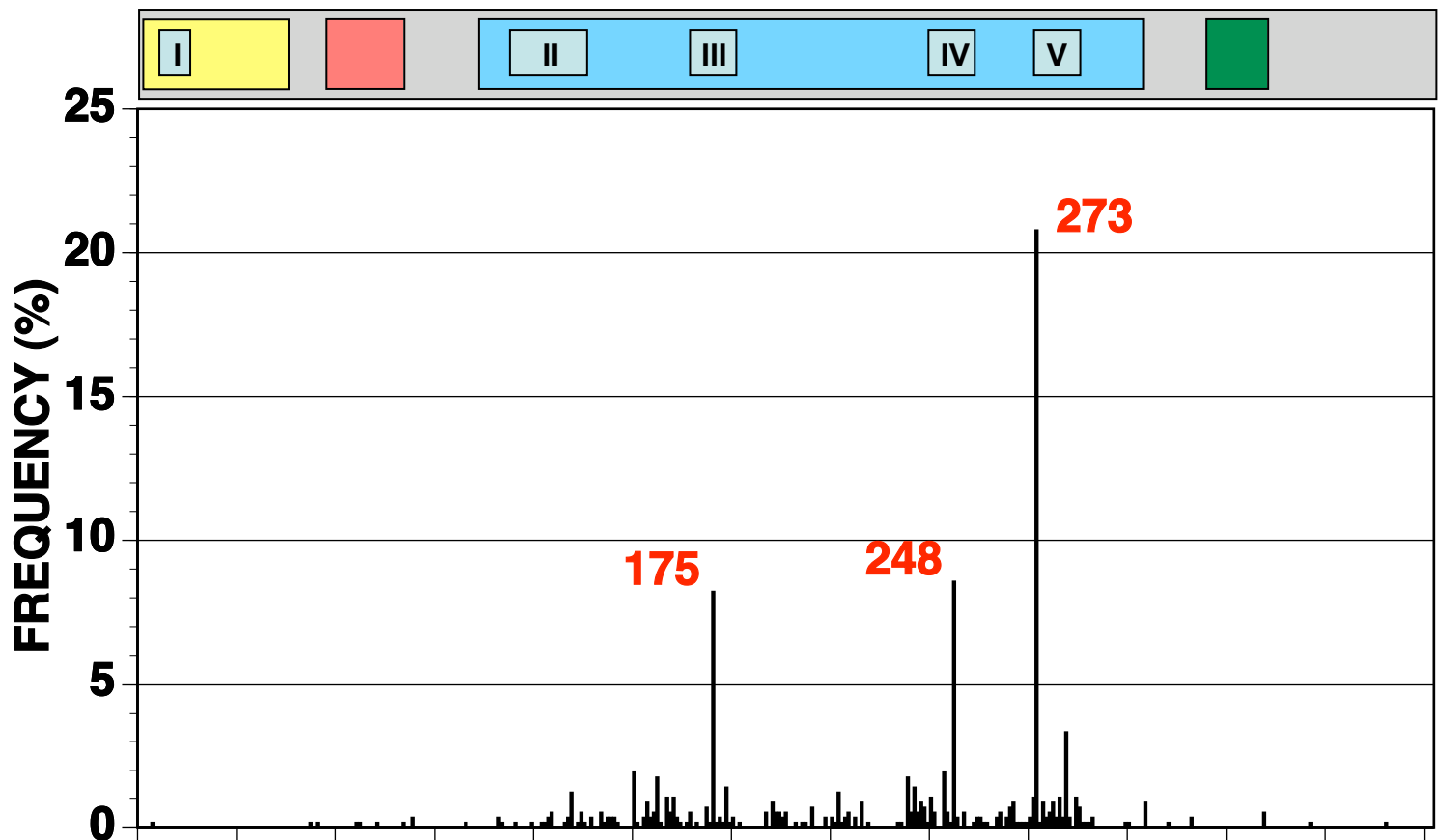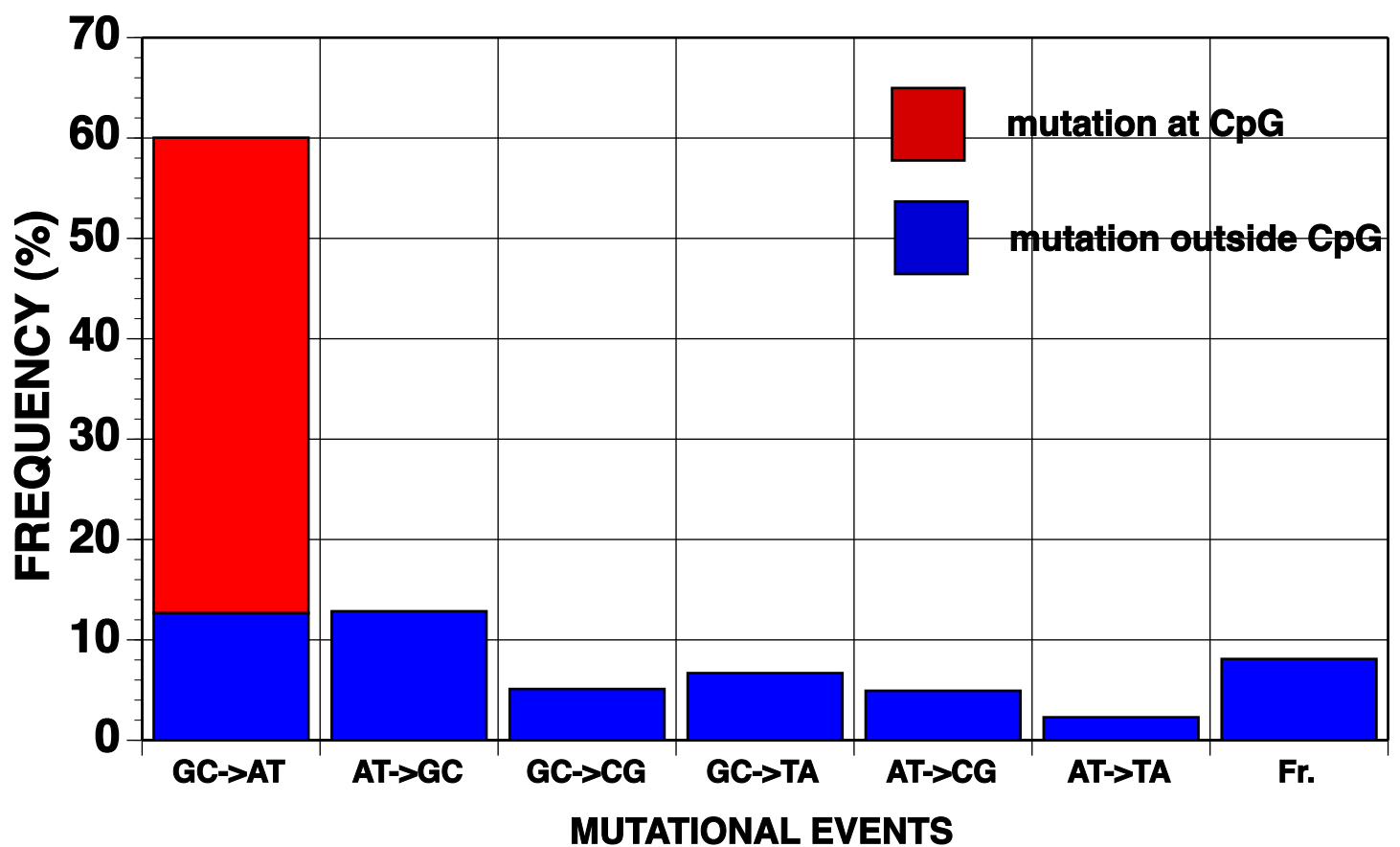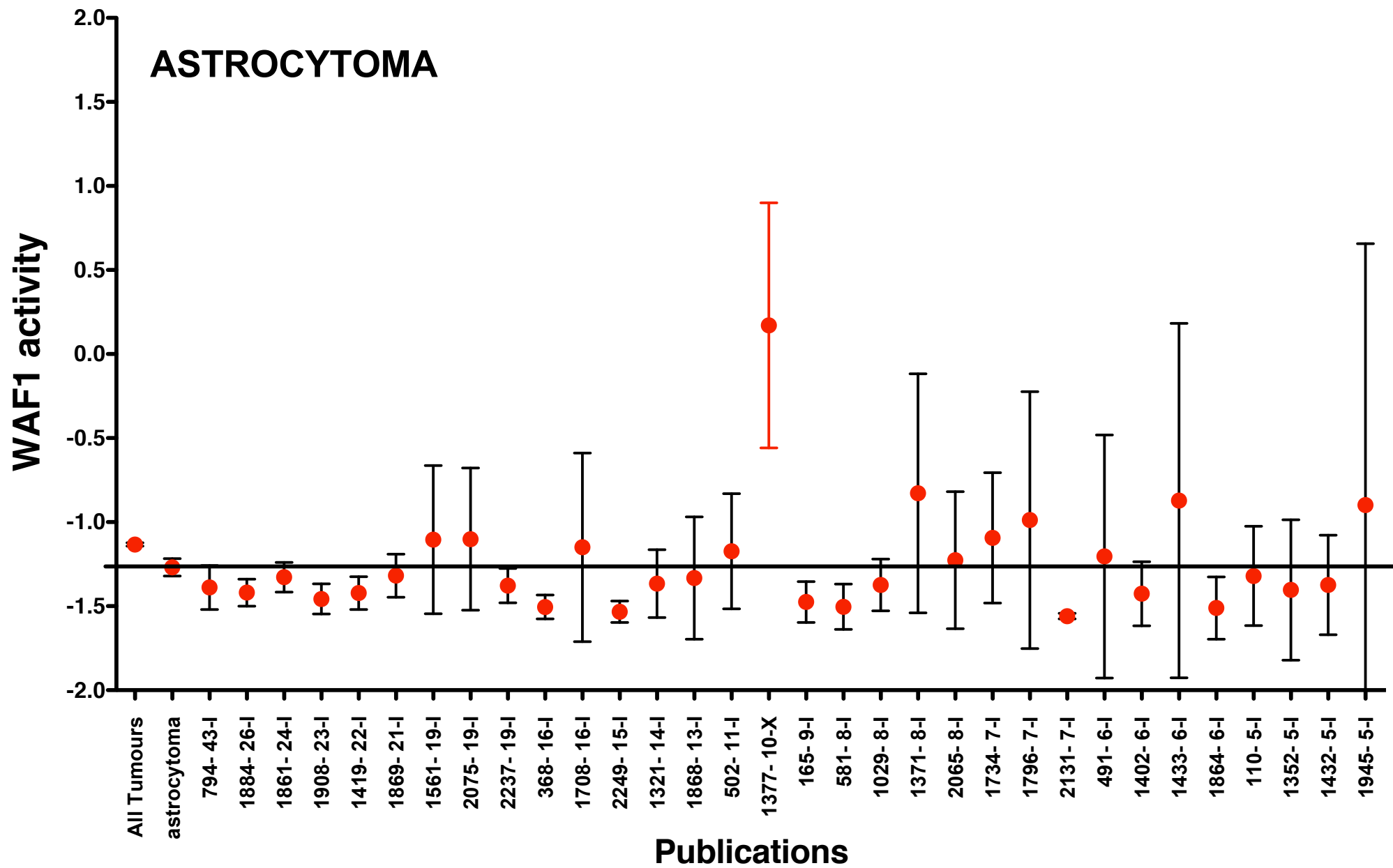
B-CELL LYMPHOMA

Analysis summary

Number of studies	39
Number of tumors	224
Number of mutations	240
Number of tumors with 1 mutation	205
Number of tumors with 2 mutations	14
Number of tumors with more than 2 mutations	1
In studies	37
Out studies 95	1
Out studies 99	1

Strategy of analysis

Exon 2 Exon 3 Exon 4 Exon 5 Exon 6 Exon 7 Exon 8 Exon 9 Exon 10 Exon 11

Exon 5-8
7 studies

Exon 4-9
3 studies

Exon 2-11
6 studies
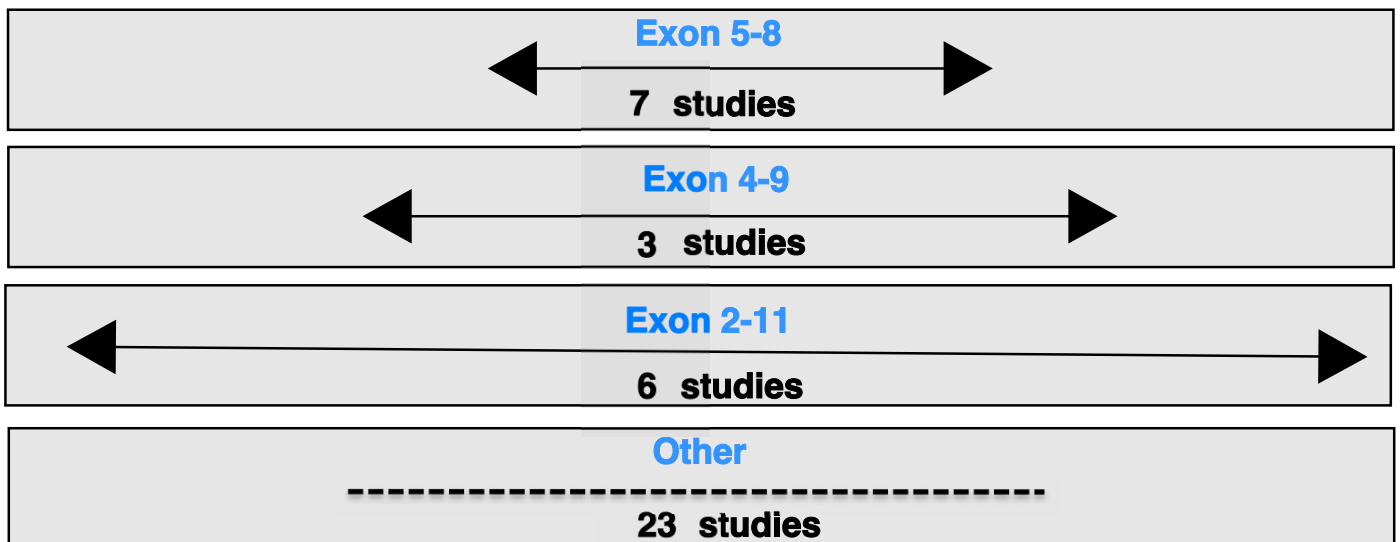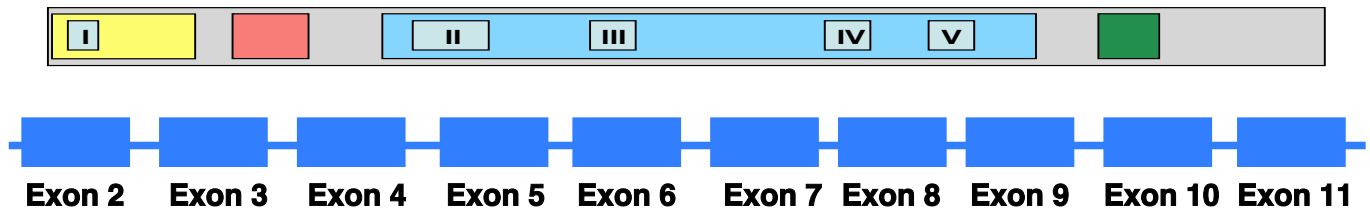
Other
- -
23 studies

Prescreening

Studies with prescreening   21

SSCP	16	**IHC**	0
DGGE/CDGE	3	**dHPLC**	1
Yeast Assay	1	**Other**	0

Studies without prescreening   18

B-CELL LYMPHOMA

p53 mutation frequency

Number of missense mutations	213	90%
Number of nonsense mutations	8	3%
Number of frameshift mutations	15	6%
Total number of mutations	236	100%
Number of polymorphisms	7	3%

p53 mutant frequency

Number of missense mutants	134	88%
Number of nonsense mutants	5	3%
Number of frameshift mutants	14	9%
Total number of mutants	153	100%
Number of polymorphisms	7	5%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
248	CGG	CAG	Arg	Gln	Ts	Yes	13
273	CGT	CAT	Arg	His	Ts	Yes	11
248	CGG	TGG	Arg	Trp	Ts	Yes	7
175	CGC	CAC	Arg	His	Ts	Yes	6
273	CGT	TGT	Arg	Cys	Ts	Yes	6
282	CGG	TGG	Arg	Trp	Ts	Yes	4
245	GGC	AGC	Gly	Ser	Ts	Yes	4
196	CGA	TGA	Arg	Stop	Ts	Yes	4
158	CGC	CAC	Arg	His	Ts	Yes	3
249	AGG	AGC	Arg	Ser	Tv	No	3

Exon Distribution
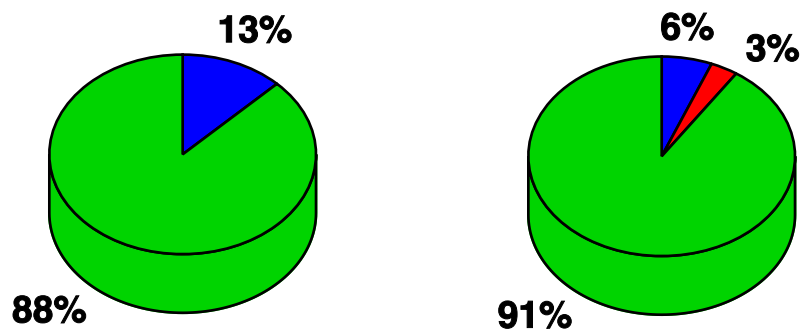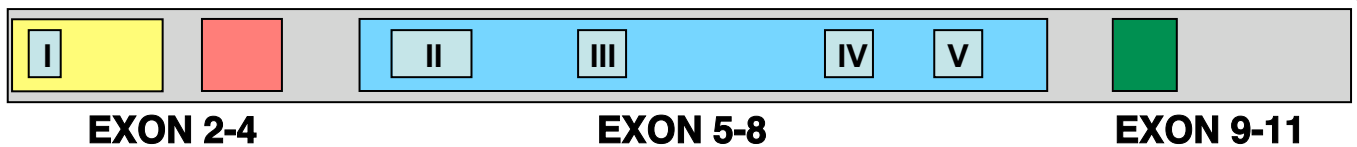
B-CELL LYMPHOMA

p53 mutation distribution
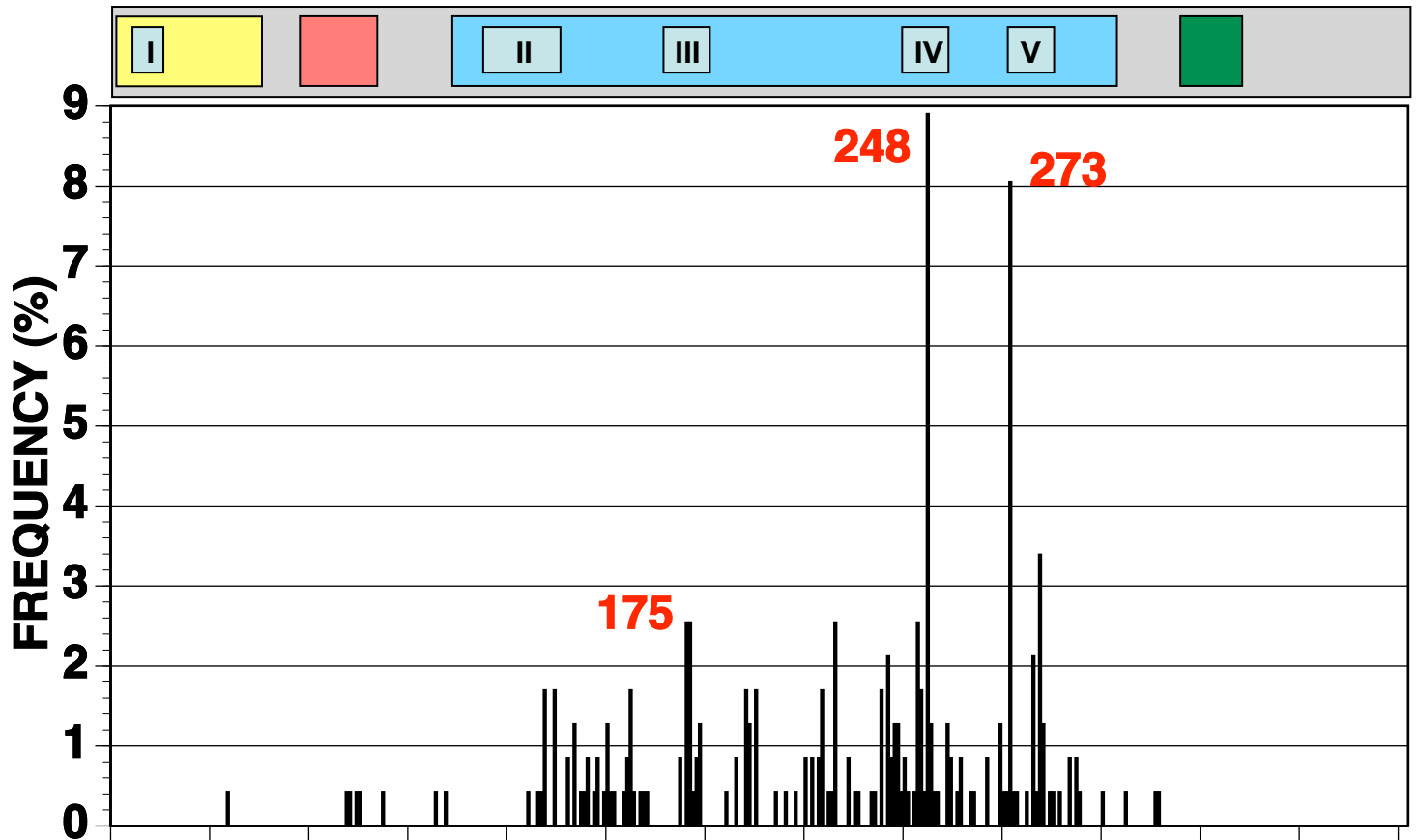
p53 mutational events
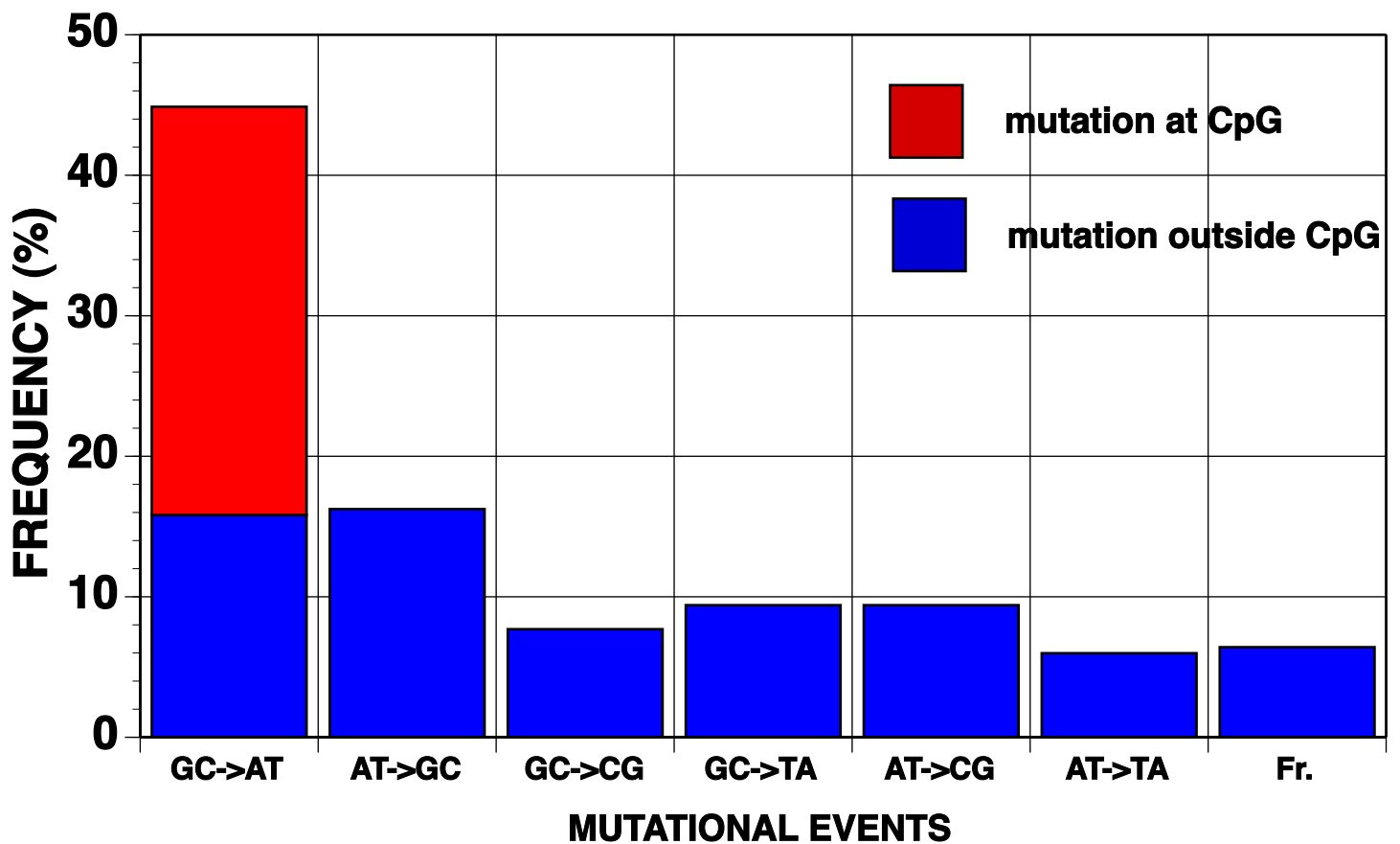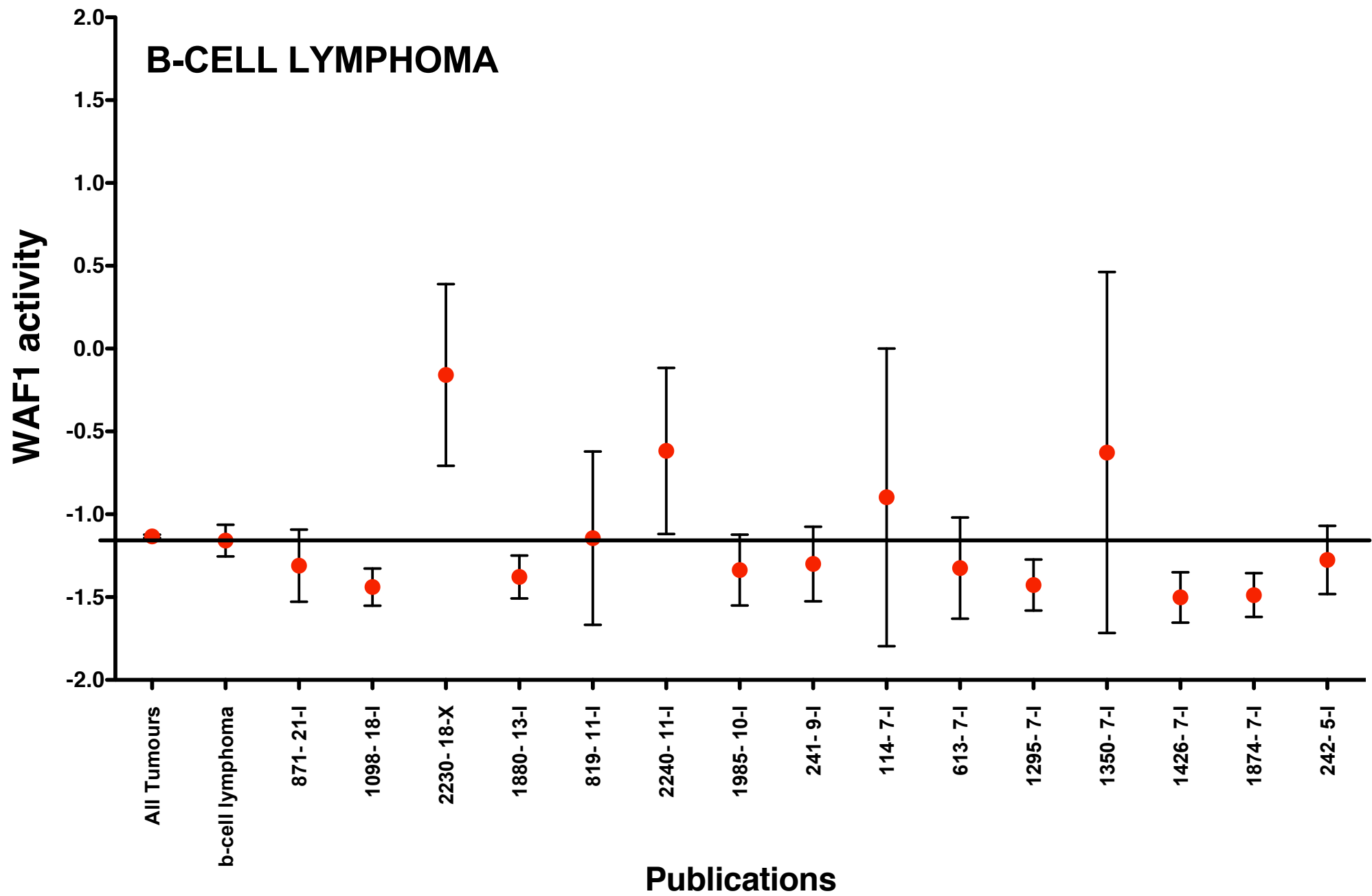
BASAL CELL CARCINOMA

Analysis summary

Number of studies	34
Number of tumors	217
Number of mutations	291
Number of tumors with 1 mutation	167
Number of tumors with 2 mutations	39
Number of tumors with more than 2 mutations	11
In studies	32
Out studies 95	2
Out studies 99	0

Strategy of analysis

Exon 2 Exon 3 Exon 4 Exon 5 Exon 6 Exon 7 Exon 8 Exon 9 Exon 10 Exon 11

Exon 5-8
8 studies

Exon 4-9
6 studies

Exon 2-11
6 studies
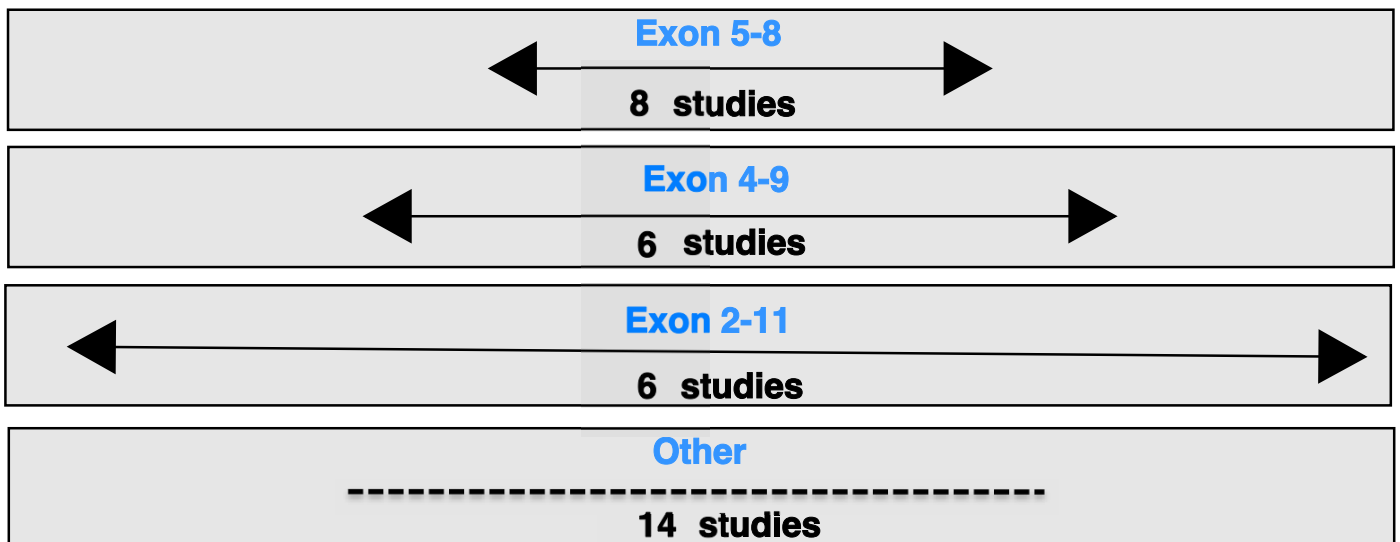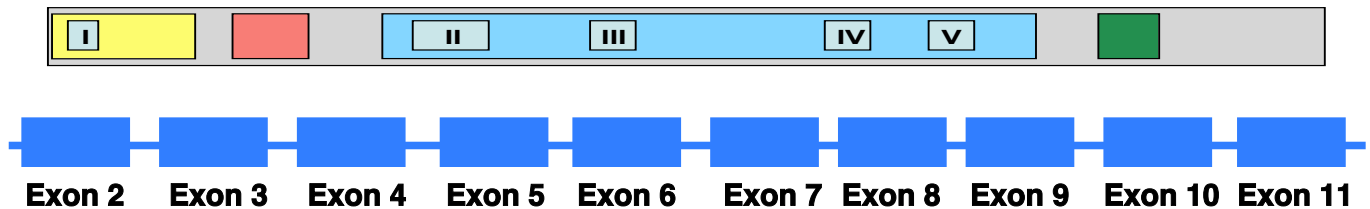
Other
----
14 studies

Prescreening

Studies with prescreening	**13**		Studies without prescreening	**21**

SSCP	12	IHC	0	
DGGE/CDGE	0	dHPLC	0	
Yeast Assay	0	Other	1	

BASAL CELL CARCINOMA

p53 mutation frequency

Number of missense mutations	241	83%
Number of nonsense mutations	35	12%
Number of frameshift mutations	15	5%
Total number of mutations	291	100%
Number of polymorphisms	27	9%

p53 mutant frequency

Number of missense mutants	113	84%
Number of nonsense mutants	10	7%
Number of frameshift mutants	12	9%
Total number of mutants	135	100%
Number of polymorphisms	15	11%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
196	CGA	TGA	Arg	Stop	Ts	Yes	15
282	CGG	TGG	Arg	Trp	Ts	Yes	11
177	CCC	CTC	Pro	Leu	Ts	No	10
248	CGG	TGG	Arg	Trp	Ts	Yes	10
179	CAT	TAT	His	Tyr	Ts	No	10
248	CGG	CAG	Arg	Gln	Ts	Yes	8
241	TCC	TTC	Ser	Phe	Ts	No	7
213	CGA	TGA	Arg	Stop	Ts	Yes	7
152	CCG	TCG	Pro	Ser	Ts	No	6
130	CTC	TTC	Leu	Phe	Ts	No	6

Exon Distribution

EXON 2-4: 43%, 36%, 21%

EXON 5-8: 3%, 10%, 86%

EXON 9-11: 43%, 57%

Legend: Frameshift (blue), Nonsense (red), Missense (green)
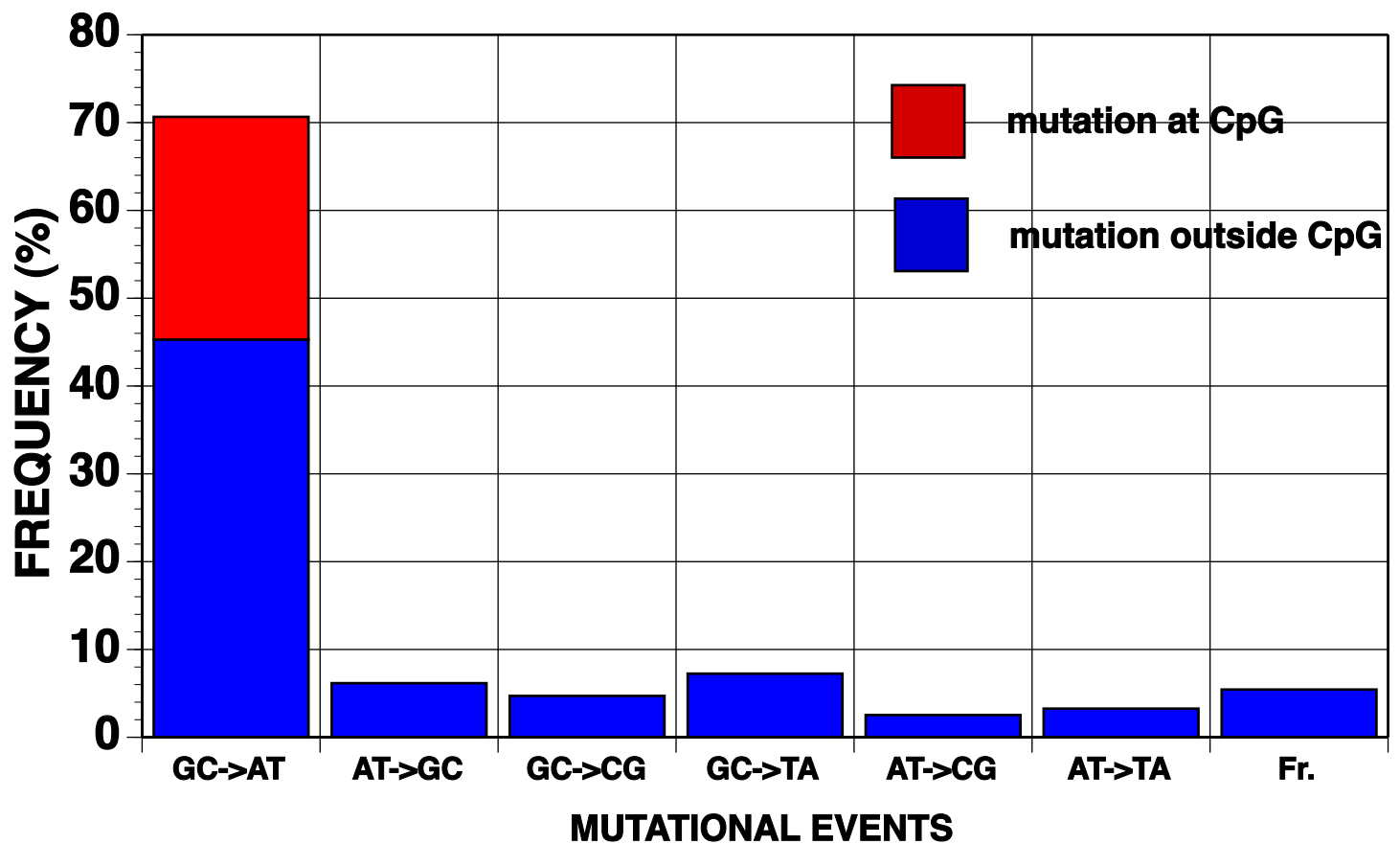
BASAL CELL CARCINOMA

BLADDER CANCER

Analysis summary

Number of studies	97
Number of tumors	1195
Number of mutations	1362
Number of tumors with 1 mutation	1034
Number of tumors with 2 mutations	130
Number of tumors with more than 2 mutations	20
In studies	92
Out studies 95	3
Out studies 99	2

Strategy of analysis

Exon 2 Exon 3 Exon 4 Exon 5 Exon 6 Exon 7 Exon 8 Exon 9 Exon 10 Exon 11

Exon 5-8
27 studies

Exon 4-9
13 studies

Exon 2-11
9 studies
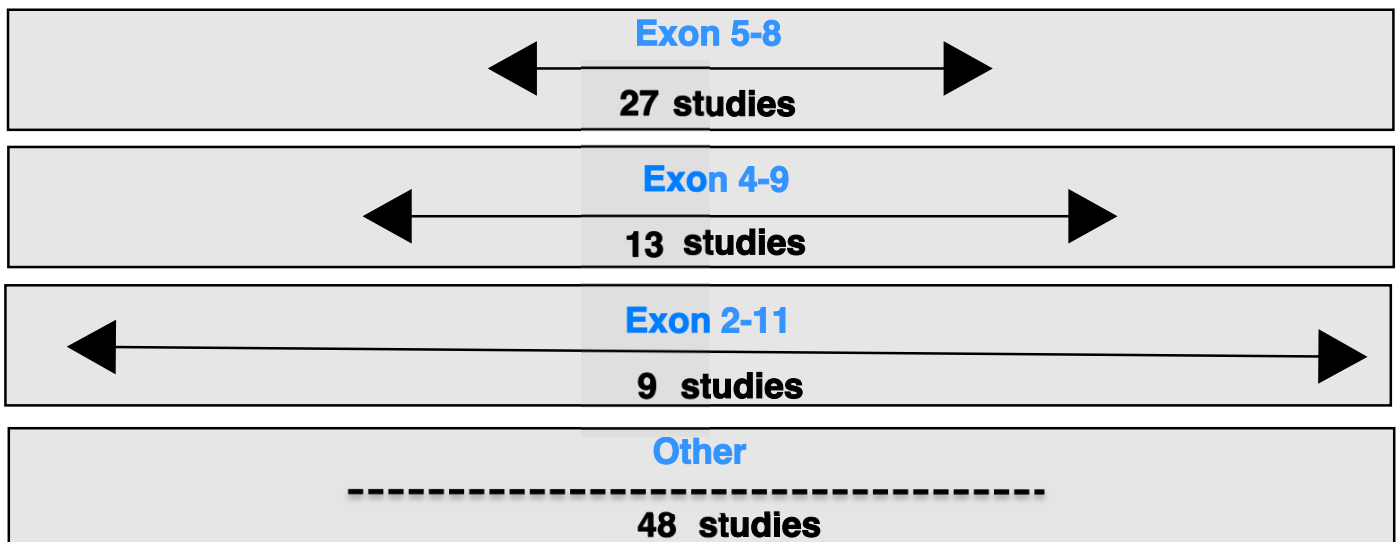
Other
----
48 studies

Prescreening

Studies with prescreening	59			Studies without prescreening	38
SSCP	45	IHC	1		
DGGE/CDGE	5	dHPLC	2		
Yeast Assay	5	Other	1		

BLADDER CARCINOMA

p53 mutation frequency

Number of missense mutations	1144	86%
Number of nonsense mutations	111	8%
Number of frameshift mutations	80	6%
Total number of mutations	1335	100%
Number of polymorphisms	92	7%

p53 mutant frequency

Number of missense mutants	443	81%
Number of nonsense mutants	38	7%
Number of frameshift mutants	68	12%
Total number of mutants	549	100%
Number of polymorphisms	66	12%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
285	GAG	AAG	Glu	Lys	Ts	No	63
248	CGG	CAA	Arg	Gln	Ts	No	46
280	AGA	ACA	Arg	Thr	Tv	No	35
175	CGC	CAC	Arg	His	Ts	Yes	33
220	TAT	TGT	Tyr	Cys	Ts	No	28
280	AGA	AAA	Arg	Lys	Ts	No	24
273	CGT	CAT	Arg	His	Ts	Yes	24
248	CGG	TGG	Arg	Trp	Ts	Yes	23
271	GAG	AAG	Glu	Lys	Ts	No	18
245	GGC	AGC	Gly	Ser	Ts	Yes	16

Exon Distribution
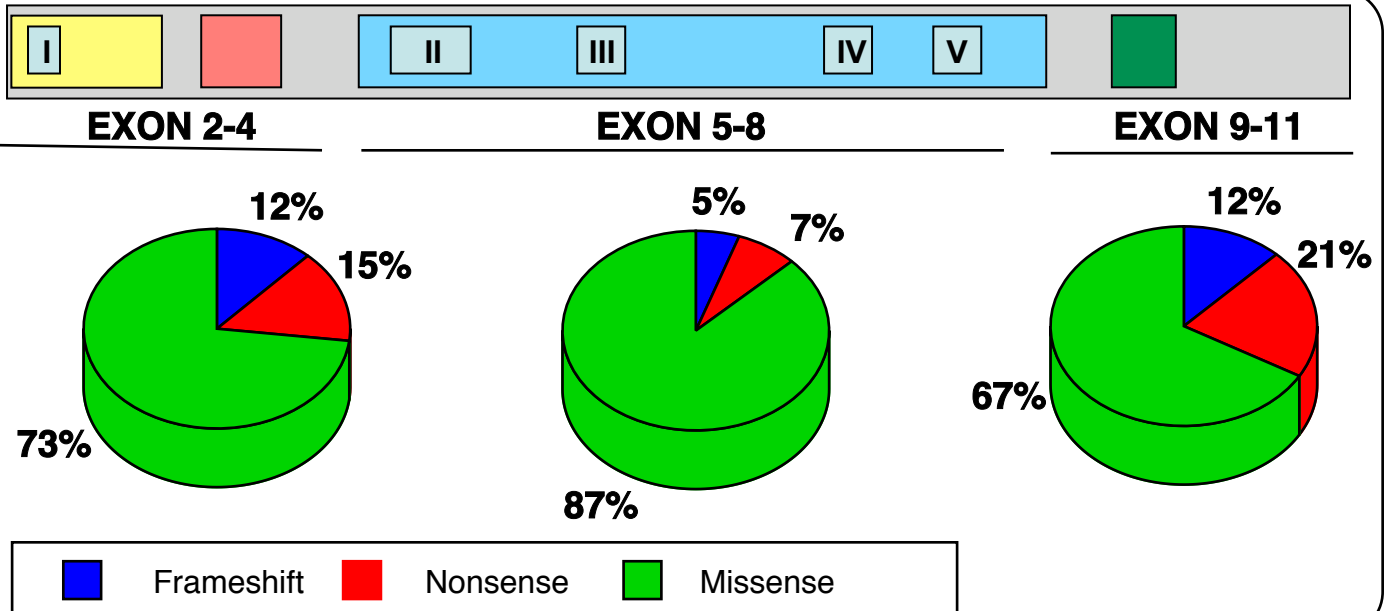
EXON 2-4 · EXON 5-8 · EXON 9-11

EXON 2-4: 12% Frameshift, 15% Nonsense, 73% Missense
EXON 5-8: 5% Frameshift, 7% Nonsense, 87% Missense
EXON 9-11: 12% Frameshift, 21% Nonsense, 67% Missense

Frameshift · Nonsense · Missense

BLADDER CARCINOMA

p53 mutation distribution
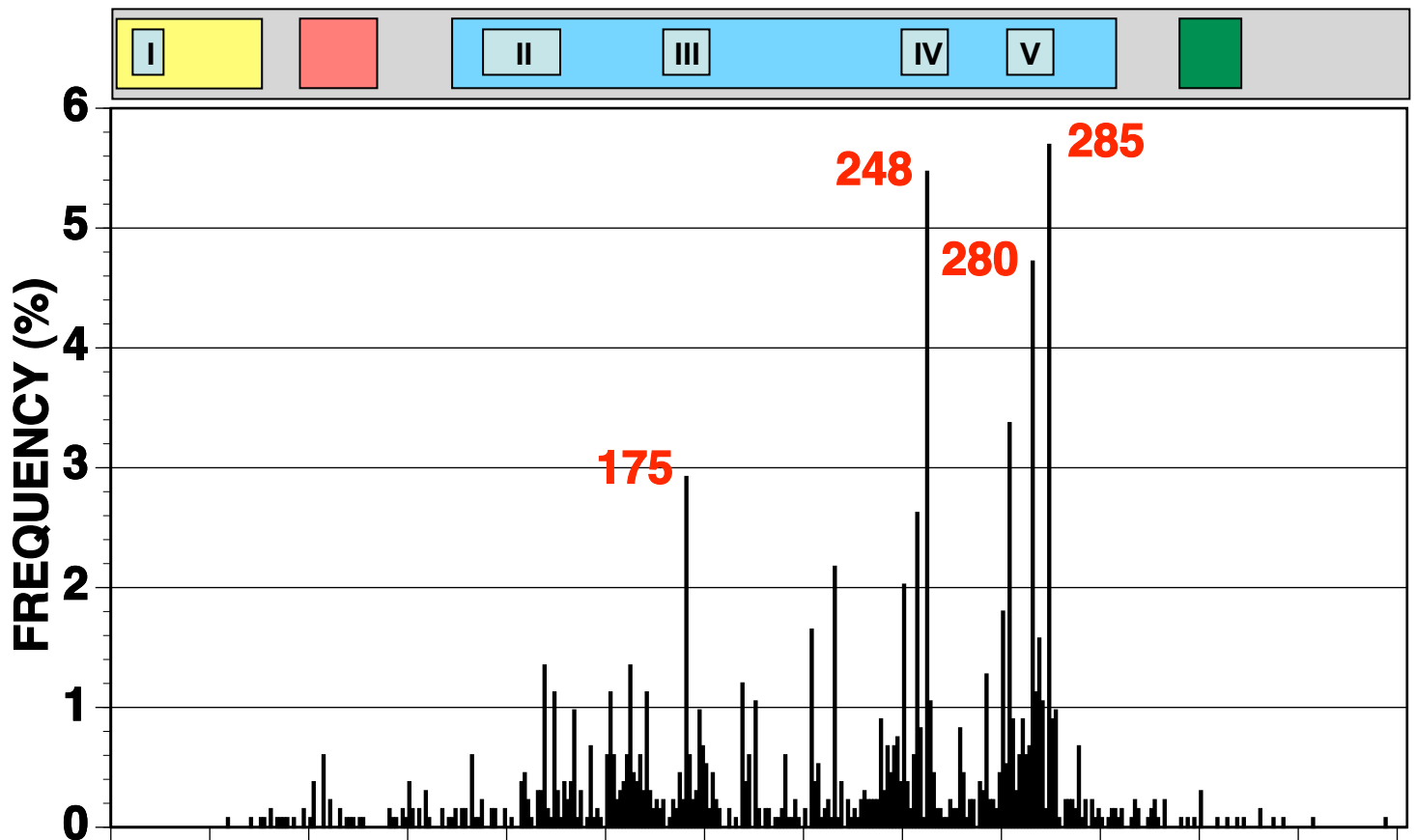
p53 CODON

p53 mutational events

MUTATIONAL EVENTS
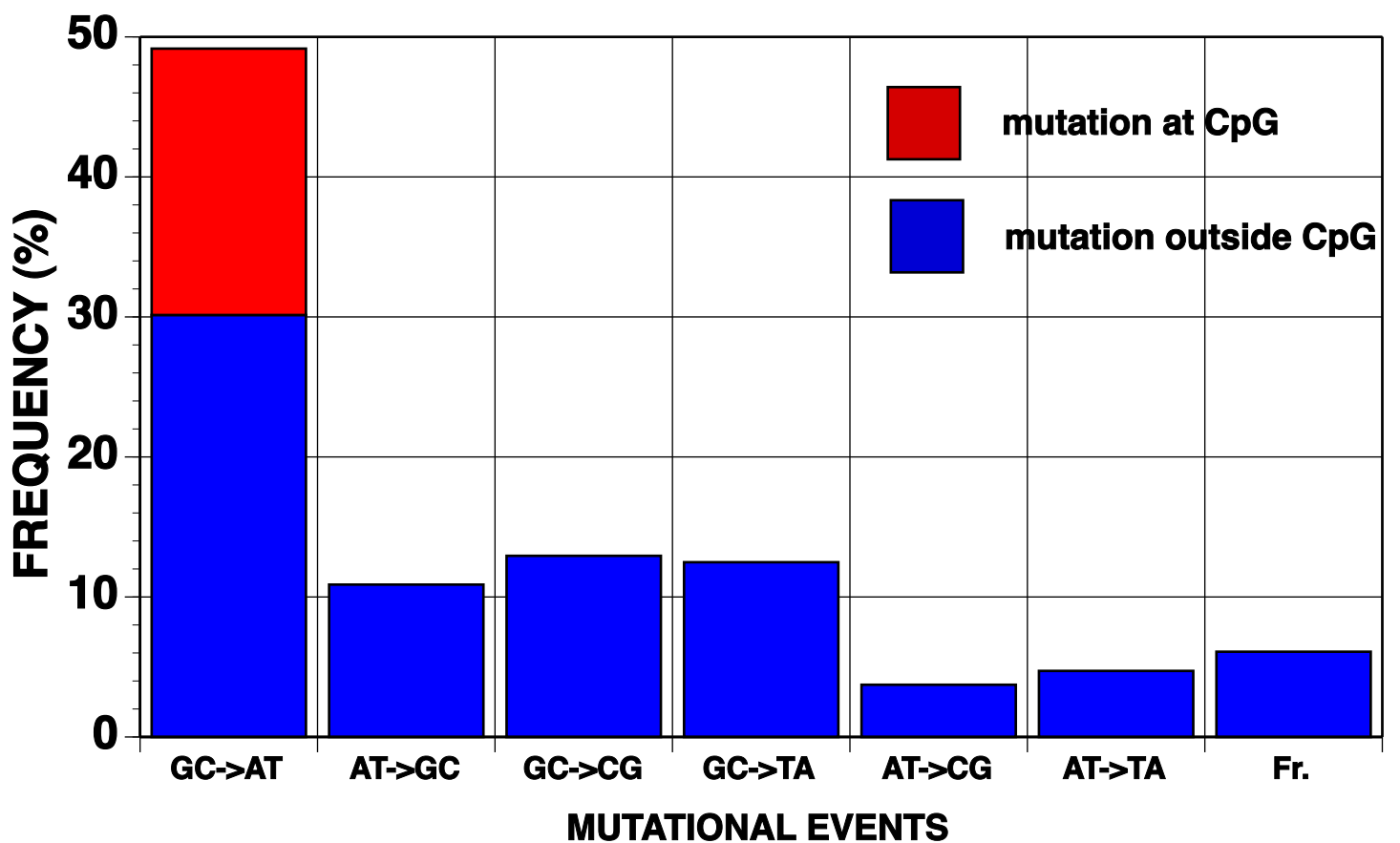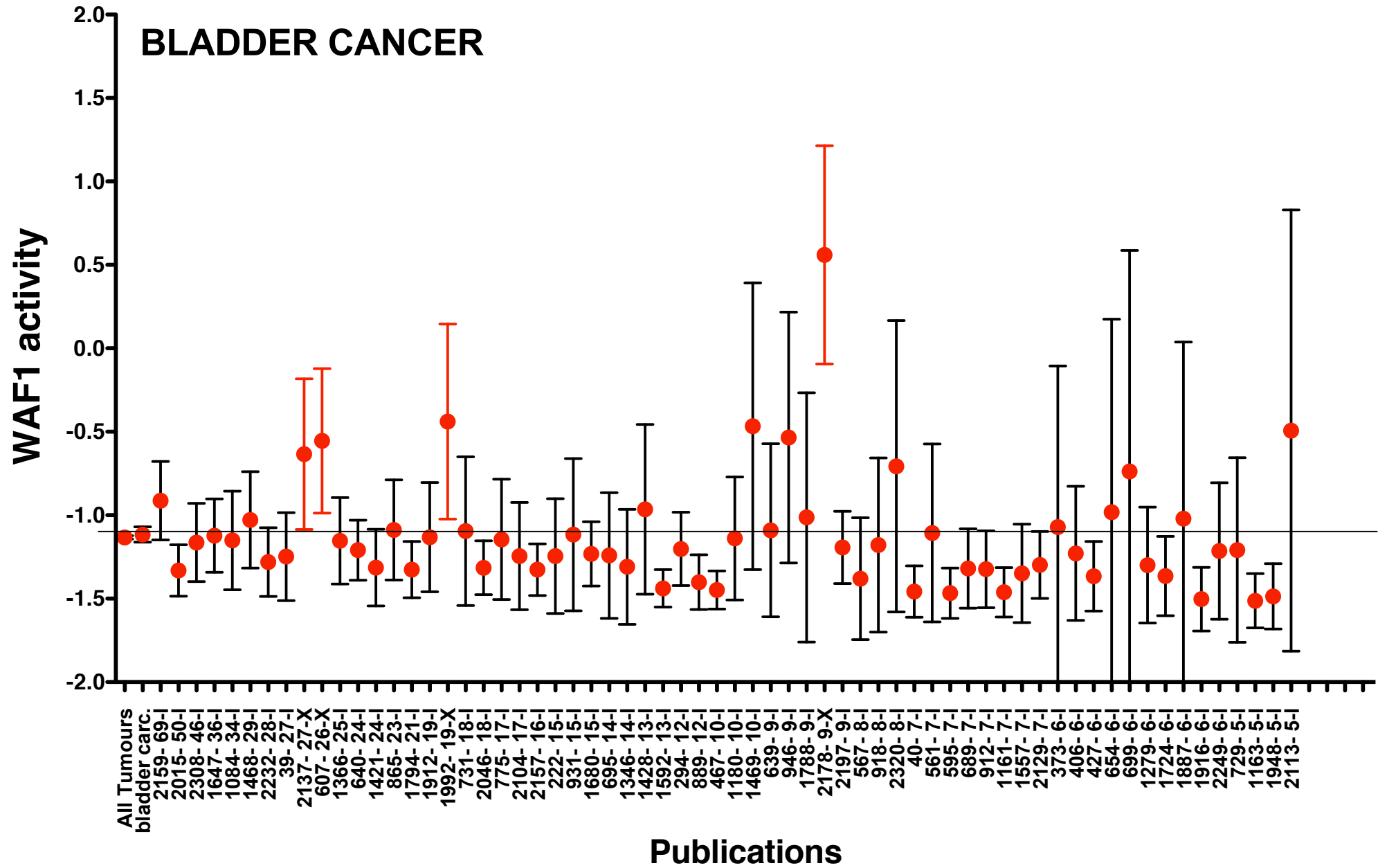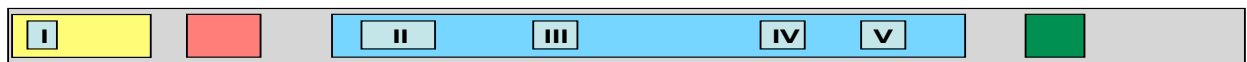
BREAST CARCINOMA

Analysis summary

Number of studies	204
Number of tumors	2822
Number of mutations	3110
Number of tumors with 1 mutation	2547
Number of tumors with 2 mutations	197
Number of tumors with more than 2 mutations	37
In studies	199
Out studies 95	1
Out studies 99	4

Strategy of analysis
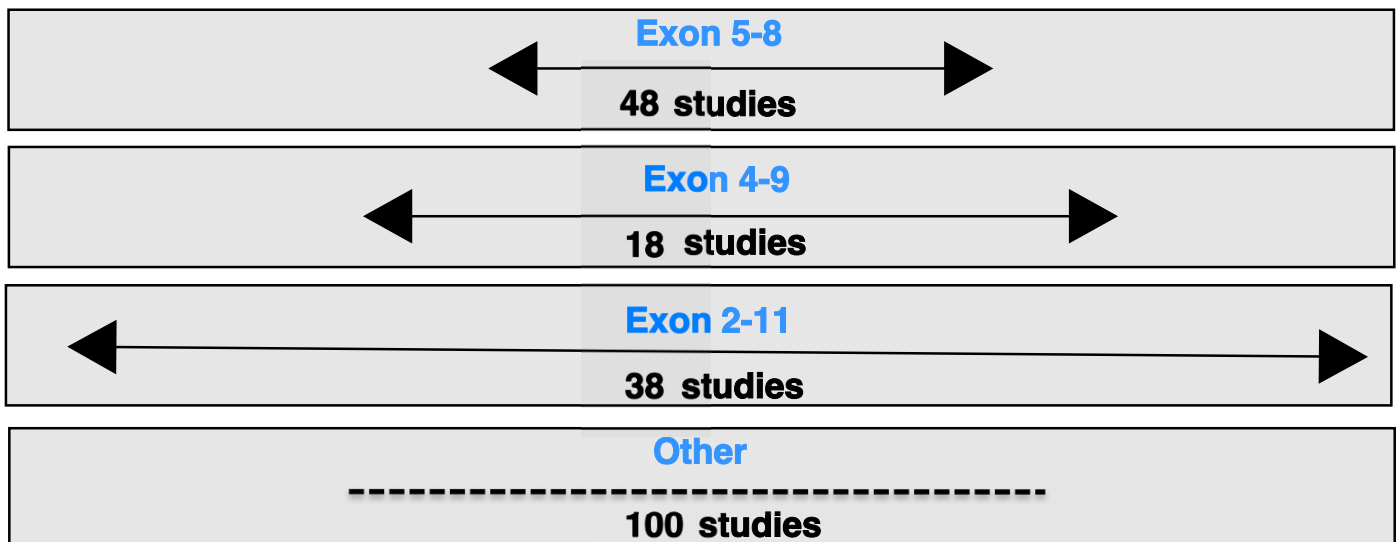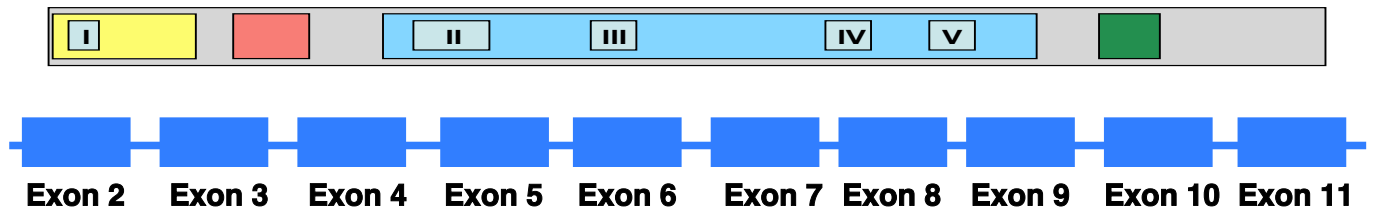
Exon 2 Exon 3 Exon 4 Exon 5 Exon 6 Exon 7 Exon 8 Exon 9 Exon 10 Exon 11

Exon 5-8
48 studies

Exon 4-9
18 studies

Exon 2-11
38 studies

Other
100 studies

Prescreening

Studies with prescreening	120		Studies without prescreening	84

SSCP	68	IHC	7	
DGGE/CDGE	28	dHPLC	1	
Yeast Assay	6	Other	13	

BREAST CARCINOMA

p53 mutation frequency

Number of missense mutations	2377	77%
Number of nonsense mutations	256	8%
Number of frameshift mutations	439	14%
Total number of mutations	3072	100%
Number of polymorphisms	183	6%

p53 mutant frequency

Number of missense mutants	668	70%
Number of nonsense mutants	52	5%
Number of frameshift mutants	240	25%
Total number of mutants	960	100%
Number of polymorphisms	100	10%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
175	CGC	CAC	Arg	His	Ts	Yes	117
248	CGG	CAG	Arg	Gln	Ts	Yes	116
273	CGT	CAT	Arg	His	Ts	Yes	100
248	CGG	TGG	Arg	Trp	Ts	Yes	80
273	CGT	TGT	Arg	Cys	Ts	Yes	45
220	TAT	TGT	Tyr	Cys	Ts	No	43
213	CGA	TGA	Arg	Stop	Ts	Yes	42
245	GGC	AGC	Gly	Ser	Ts	Yes	39
282	CGG	TGG	Arg	Trp	Ts	Yes	31
237	ATG	ATA	Met	Ile	Ts	No	30

Exon Distribution

EXON 2-4 — 48% Frameshift, 8% Nonsense, 45% Missense

EXON 5-8 — 12% Frameshift, 7% Nonsense, 81% Missense

EXON 9-11 — 25% Frameshift, 35% Nonsense, 40% Missense

Frameshift   Nonsense   Missense

BREAST CARCINOMA

p53 mutation distribution
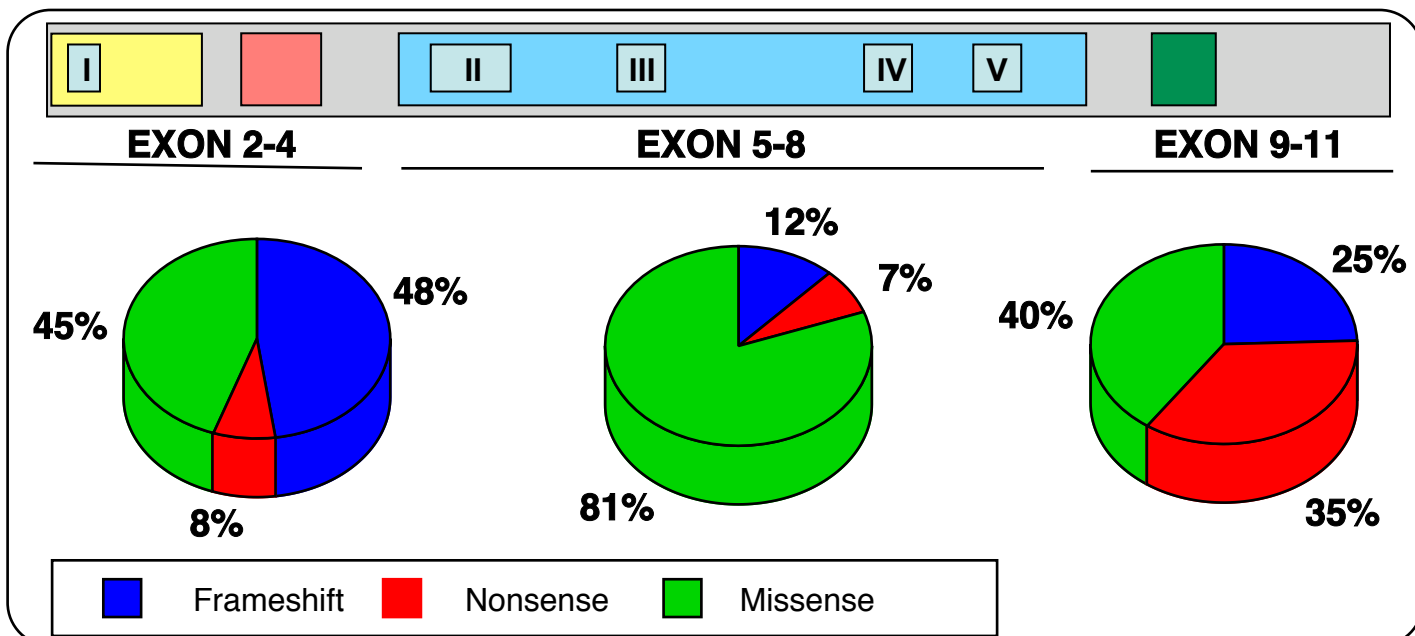
p53 CODON

p53 mutational events

- mutation at CpG
- mutation outside CpG
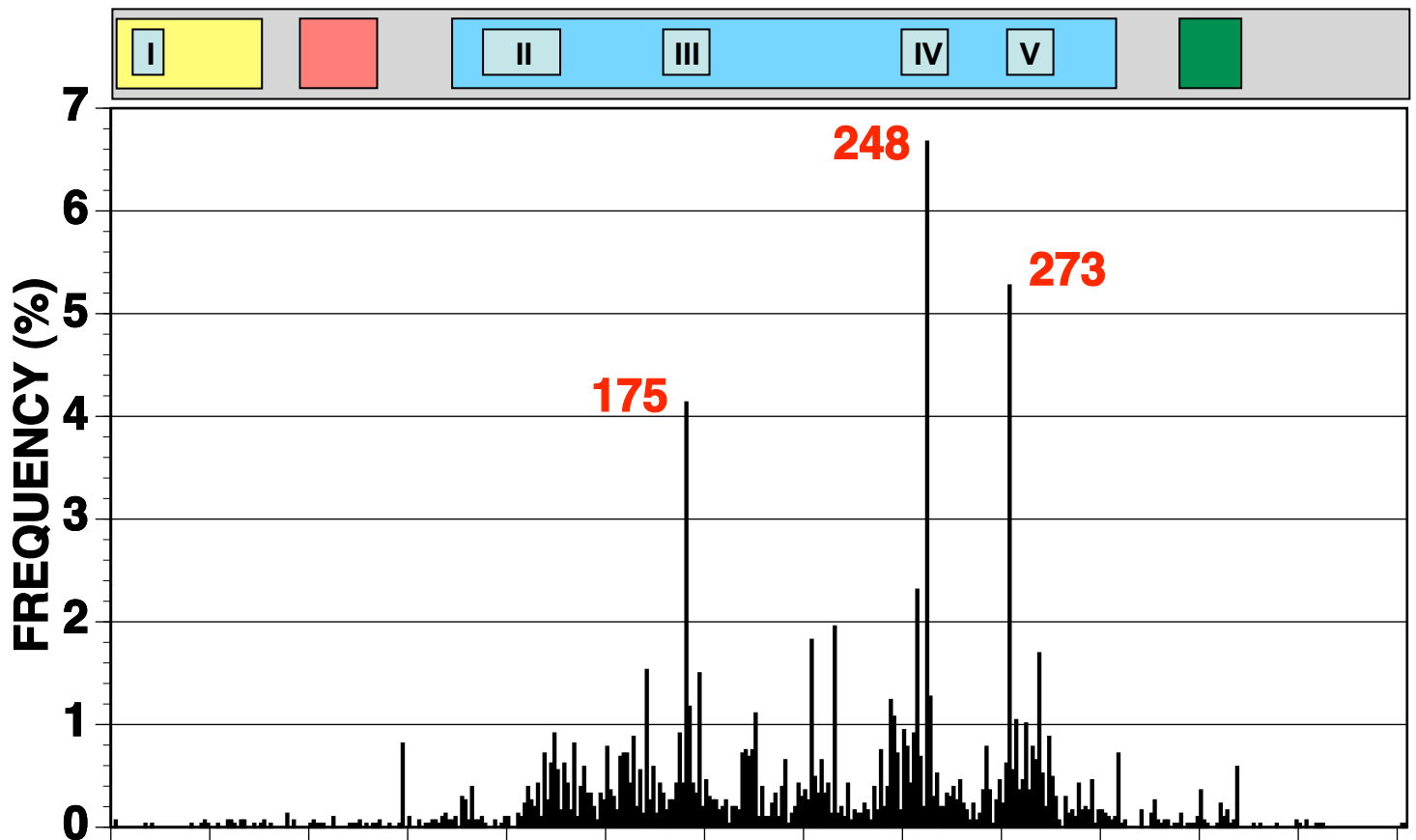
MUTATIONAL EVENTS
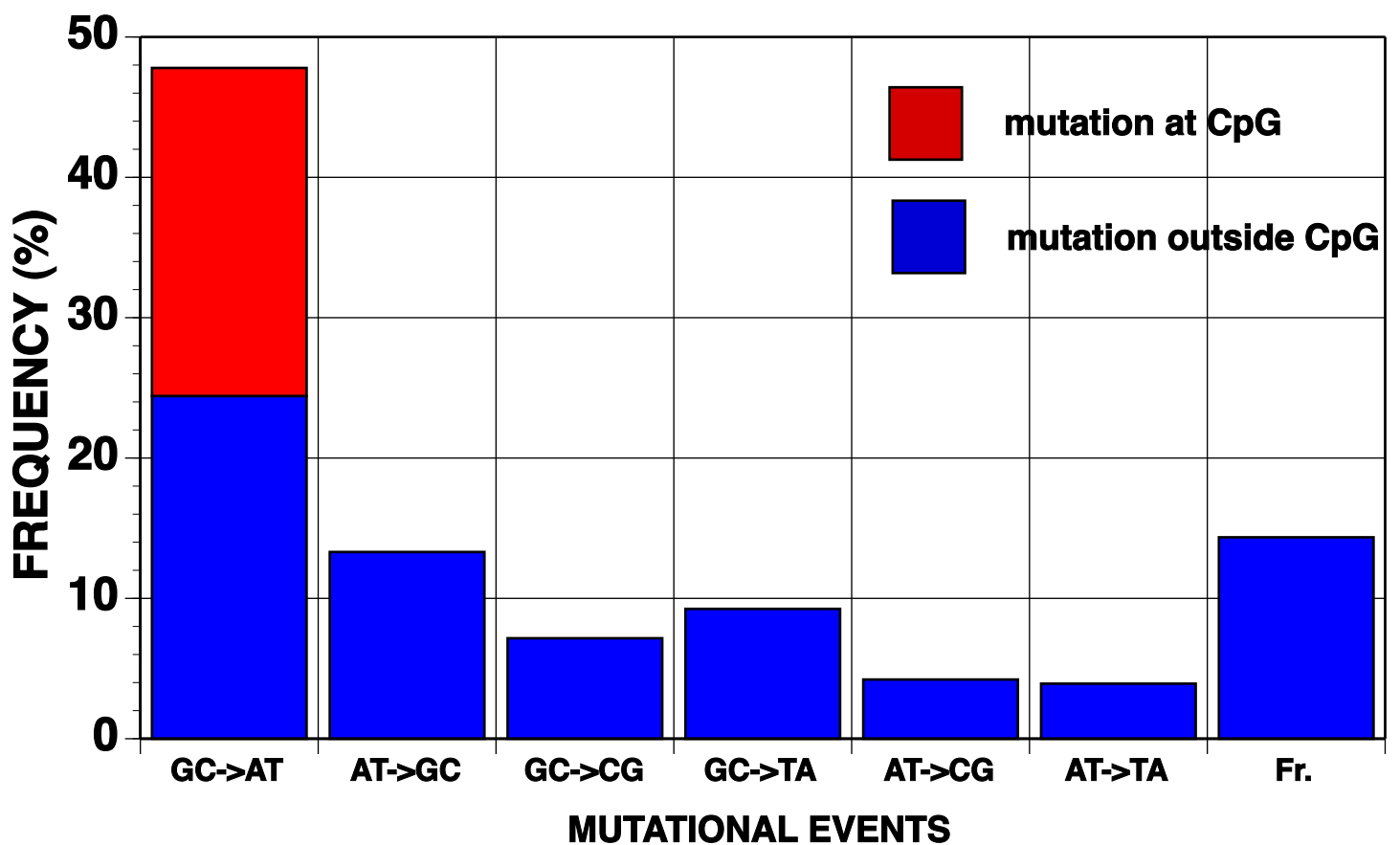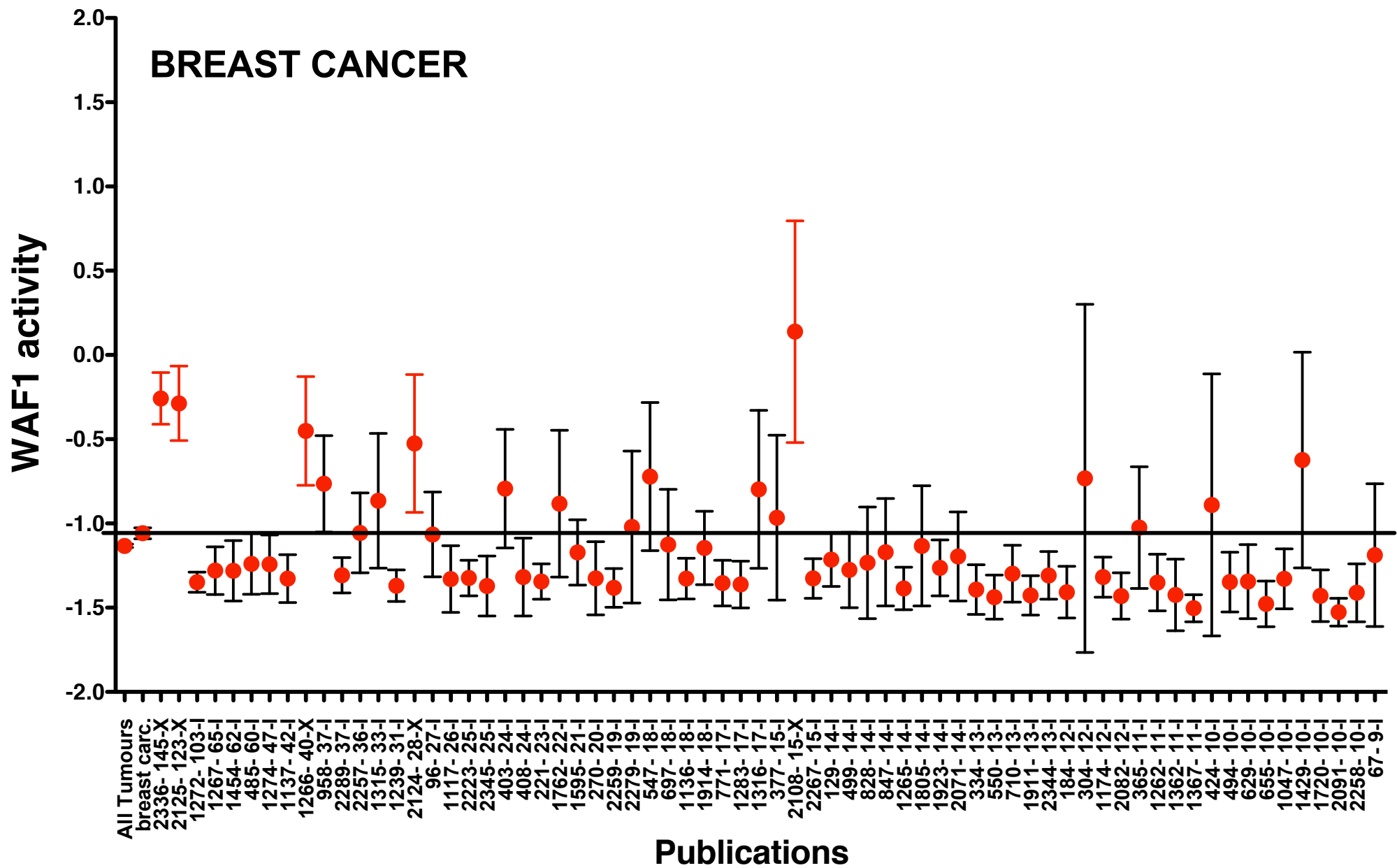
BURKITT LYMPHOMA

Analysis summary

Number of studies	22
Number of tumors	86
Number of mutations	97
Number of tumors with 1 mutation	73
Number of tumors with 2 mutations	10
Number of tumors with more than 2 mutations	0
In studies	22
Out studies 95	0
Out studies 99	0

Strategy of analysis

| I | | II | III | IV | V | |

Exon 2 Exon 3 Exon 4 Exon 5 Exon 6 Exon 7 Exon 8 Exon 9 Exon 10 Exon 11

Exon 5-8
6 studies

Exon 4-9
1 studies

Exon 2-11
3 studies

Other
12 studies

Prescreening
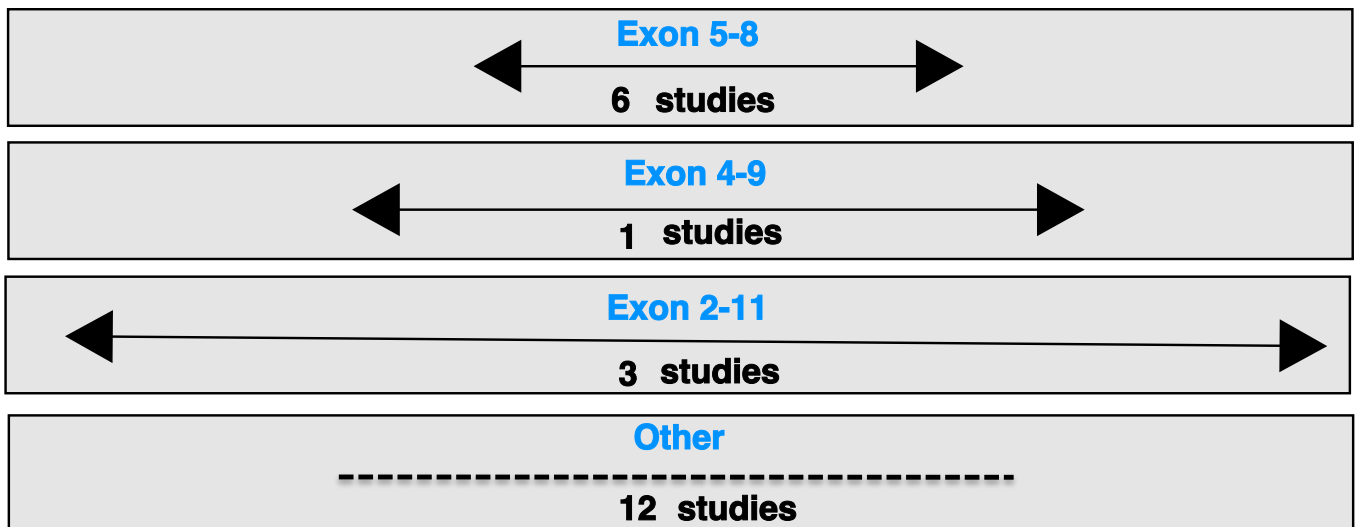
Studies with prescreening 12

Studies without prescreening 10

SSCP	11	IHC	0
DGGE/CDGE	1	dHPLC	0
Yeast Assay	0	Other	0

BURKITT LYMPHOMA

p53 mutation frequency

Number of missense mutations	77	84%
Number of nonsense mutations	8	9%
Number of frameshift mutations	7	8%
Total number of mutations	92	100%
Number of polymorphisms	0	0%

p53 mutant frequency

Number of missense mutants	51	84%
Number of nonsense mutants	4	7%
Number of frameshift mutants	6	10%
Total number of mutants	61	100%
Number of polymorphisms	0	0%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
248	CGG	CAG	Arg	Gln	Ts	Yes	8
273	CGT	TGT	Arg	Cys	Ts	Yes	4
213	CGA	TGA	Arg	Stop	Ts	Yes	4
175	CGC	CAC	Arg	His	Ts	Yes	4
158	CGC	CAC	Arg	His	Ts	Yes	4
282	CGG	TGG	Arg	Trp	Ts	Yes	3
238	TGT	TAT	Cys	Tyr	Ts	No	3
206	TTG	DEL1	Leu	Fs.	Fr	No	2
237	ATG	ATA	Met	Ile	Ts	No	2
248	CGG	TGG	Arg	Trp	Ts	Yes	2

Exon Distribution

EXON 2-4   EXON 5-8   EXON 9-11

8%   9%   84%
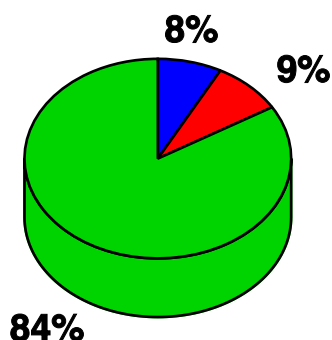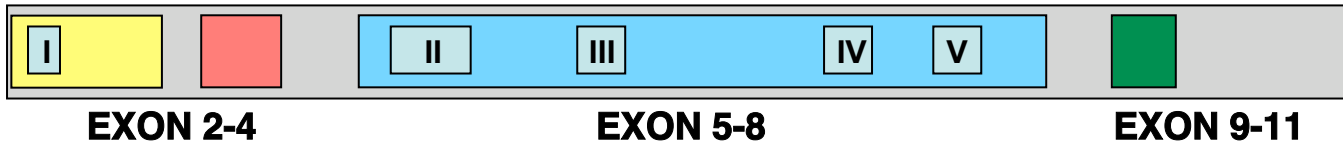
Frameshift   Nonsense   Missense

BURKITT LYMPHOMA

p53 mutation distribution
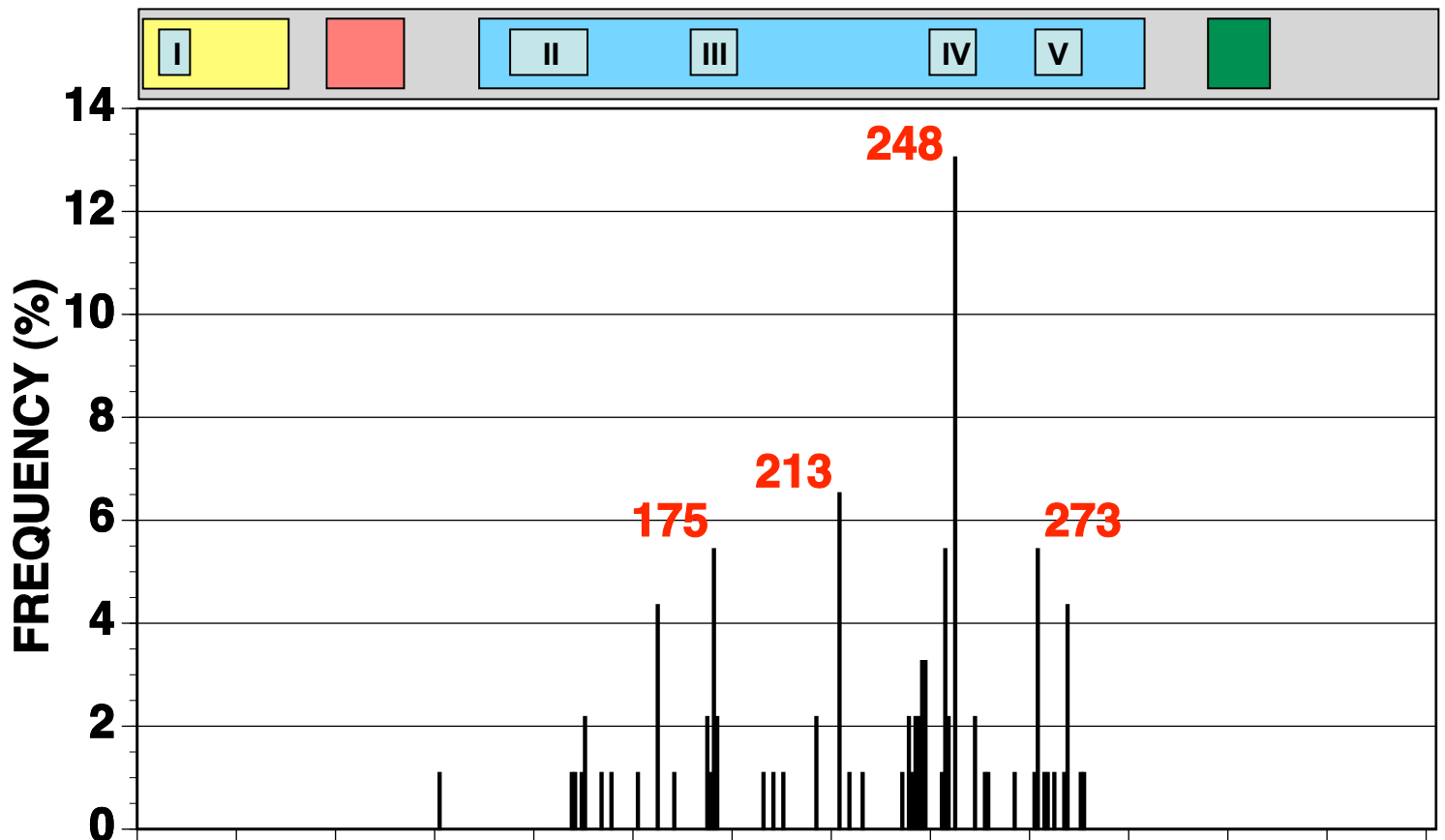
p53 mutational events
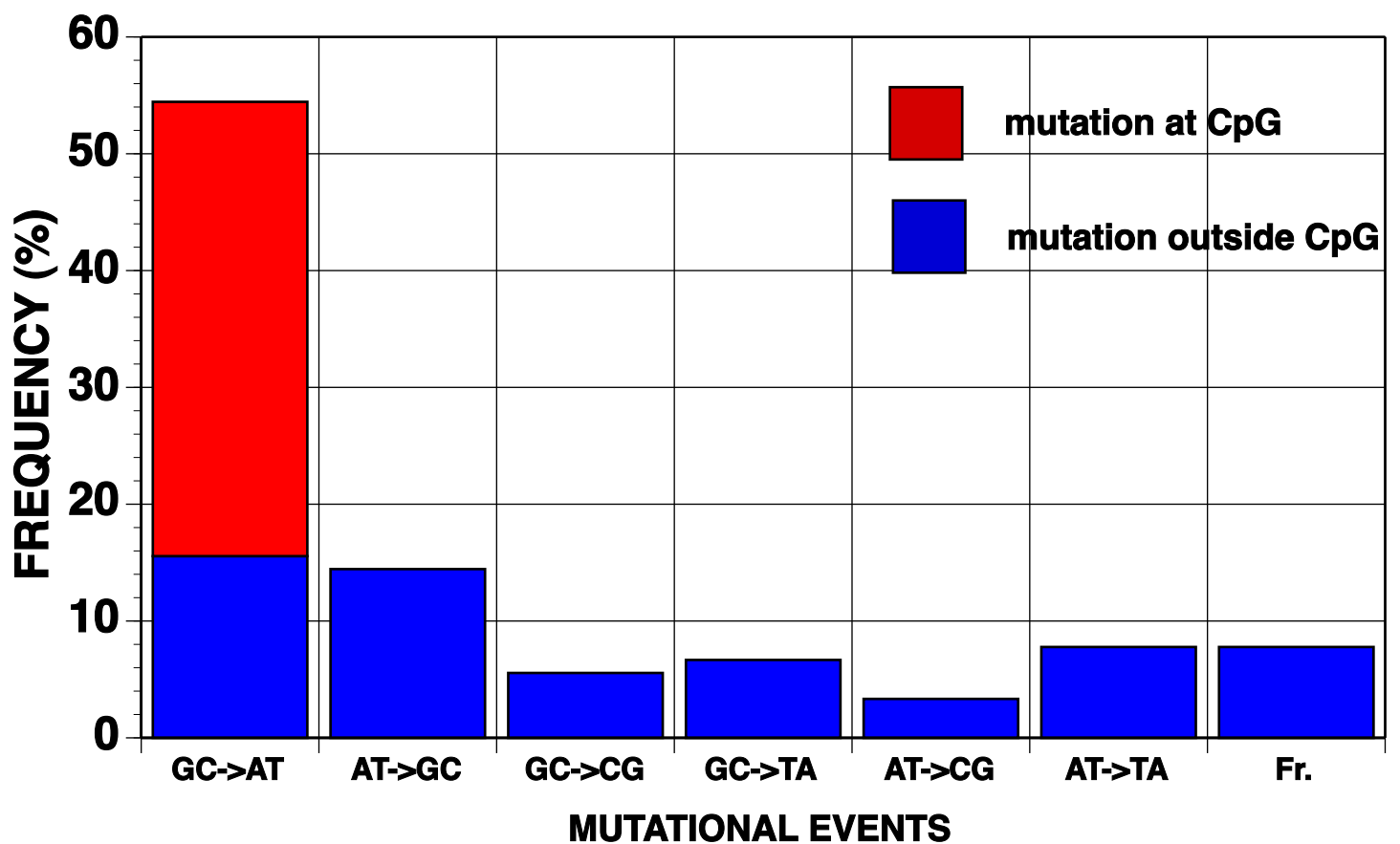
COLORECTAL CARCINOMA

Analysis summary

	178
Number of tumors	3342
Number of mutations	3596
Number of tumors with 1 mutation	3137
Number of tumors with 2 mutations	163
Number of tumors with more than 2 mutations	32
In studies	173
Out studies 95	2
Out studies 99	3

Strategy of analysis

I   II   III   IV   V

Exon 2   Exon 3   Exon 4   Exon 5   Exon 6   Exon 7   Exon 8   Exon 9   Exon 10   Exon 11

Exon 5-8
◄──────────────►
48 studies

Exon 4-9
◄──────────────►
18 studies

Exon 2-11
◄──────────────────────────►
38 studies

Other
- -
100 studies

Prescreening

Studies with prescreening	**120**		**Studies without prescreening**	**84**

SSCP	68	IHC	7
DGGE/CDGE	28	dHPLC	1
Yeast Assay	6	Other	13

COLORECTAL CARCINOMA

p53 mutation frequency

Number of missense mutations	2916	81%
Number of nonsense mutations	314	9%
Number of frameshift mutations	354	10%
Total number of mutations	3584	100%
Number of polymorphisms	88	2%

p53 mutant frequency

Number of missense mutants	569	72%
Number of nonsense mutants	49	6%
Number of frameshift mutants	171	22%
Total number of mutants	789	100%
Number of polymorphisms	61	8%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
175	CGC	CAC	Arg	His	Ts	Yes	357
248	CGG	CAG	Arg	Gln	Ts	Yes	210
248	CGG	TGG	Arg	Trp	Ts	Yes	187
273	CGT	CAT	Arg	His	Ts	Yes	182
282	CGG	TGG	Arg	Trp	Ts	Yes	178
245	GGC	AGC	Gly	Ser	Ts	Yes	134
273	CGT	TGT	Arg	Cys	Ts	Yes	128
213	CGA	TGA	Arg	Stop	Ts	Yes	75
196	CGA	TGA	Arg	Stop	Ts	Yes	70
245	GGC	GAC	Gly	Asp	Ts	No	45

Exon Distribution
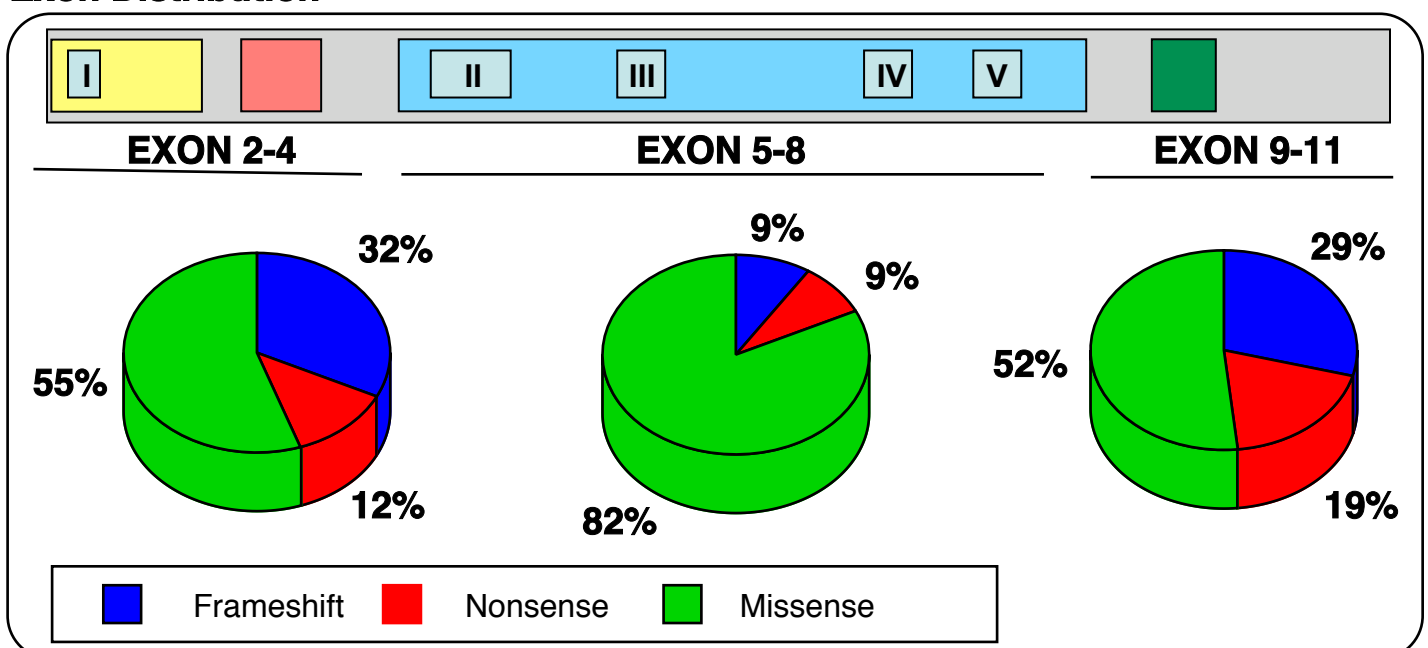
EXON 2-4 — 32%, 55%, 12%

EXON 5-8 — 9%, 9%, 82%

EXON 9-11 — 29%, 52%, 19%

Frameshift | Nonsense | Missense

COLORECTAL CARCINOMA

p53 mutation distribution

p53 CODON

p53 mutational events

MUTATIONAL EVENTS

COLORECTAL CANCER
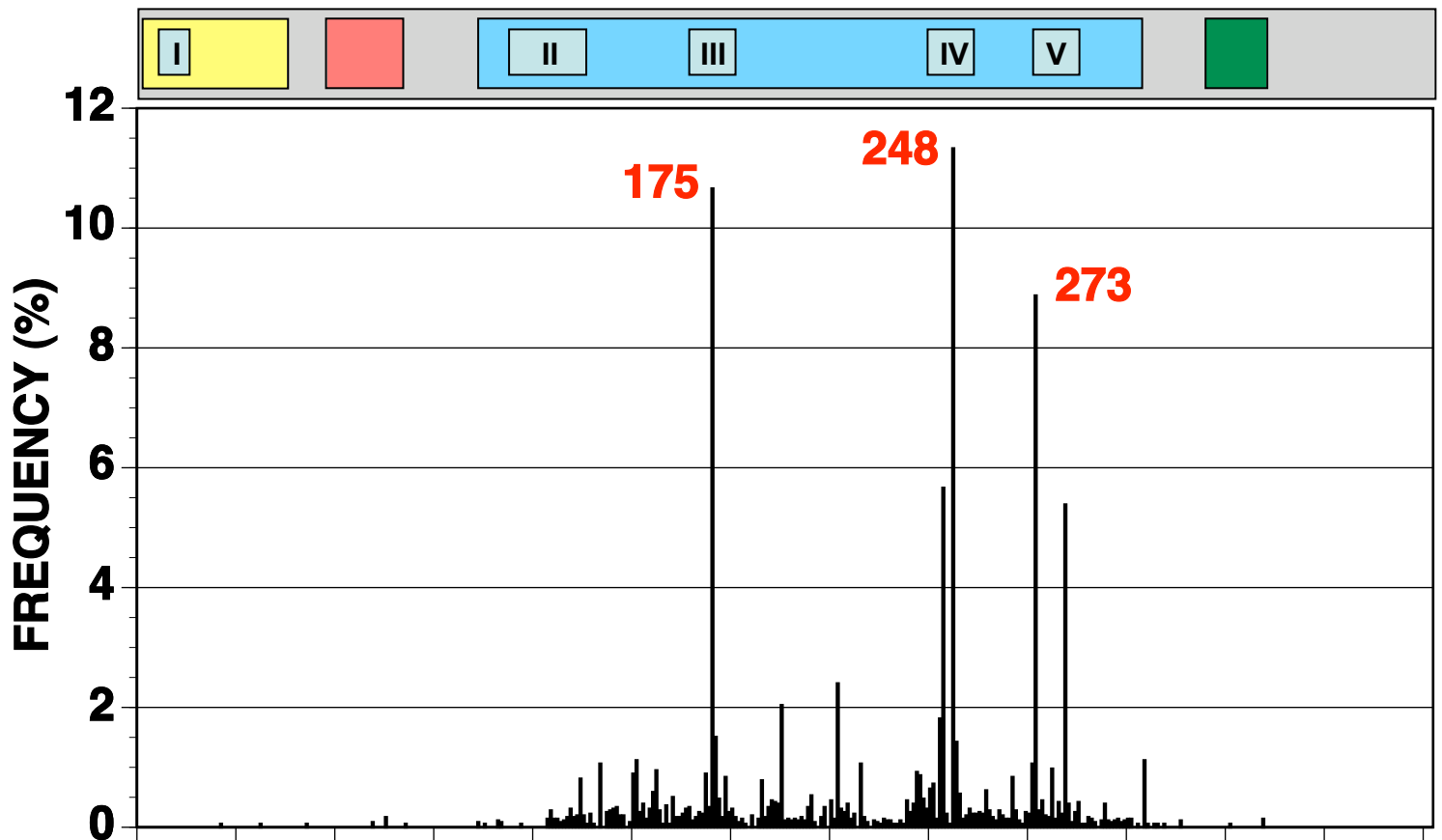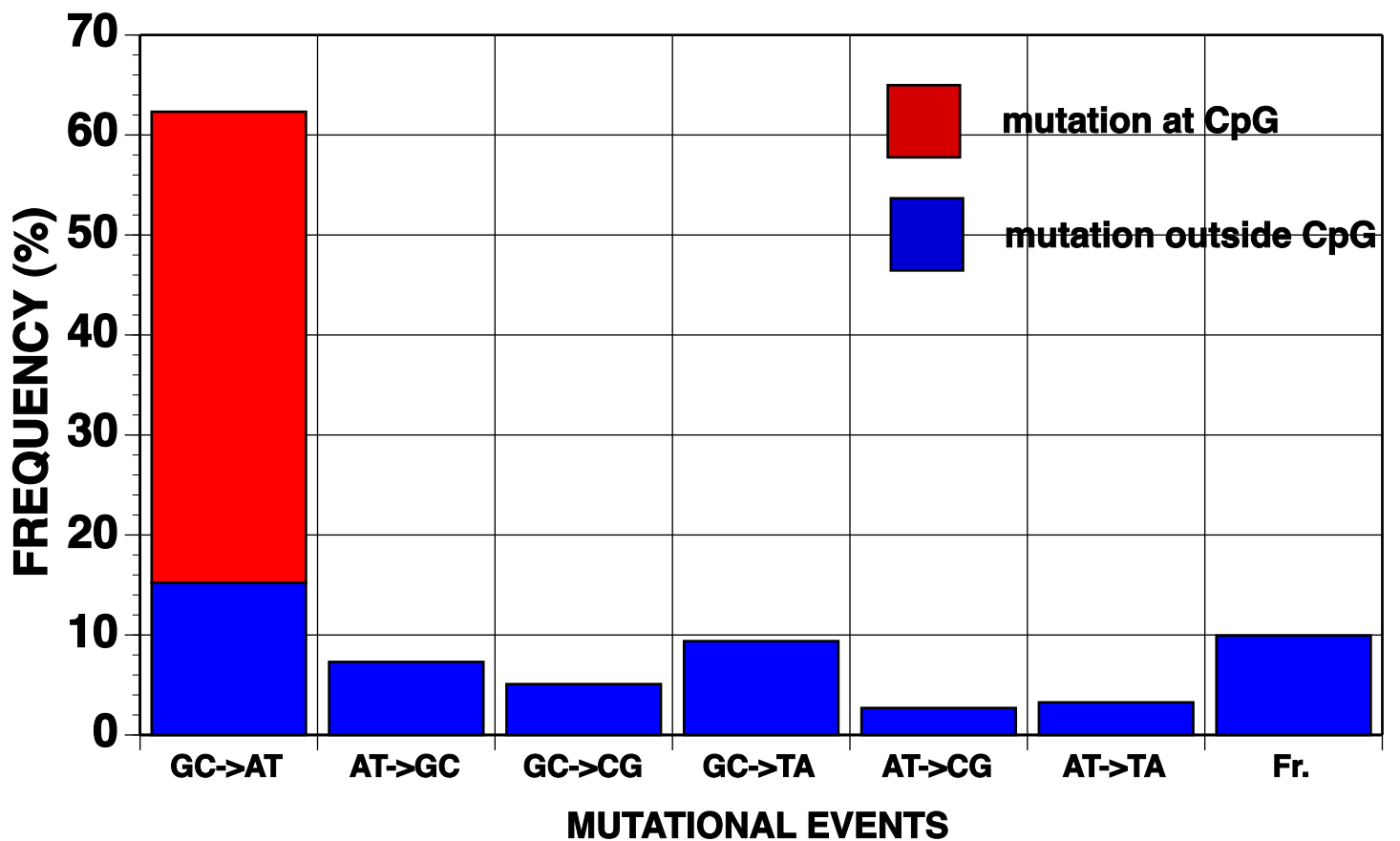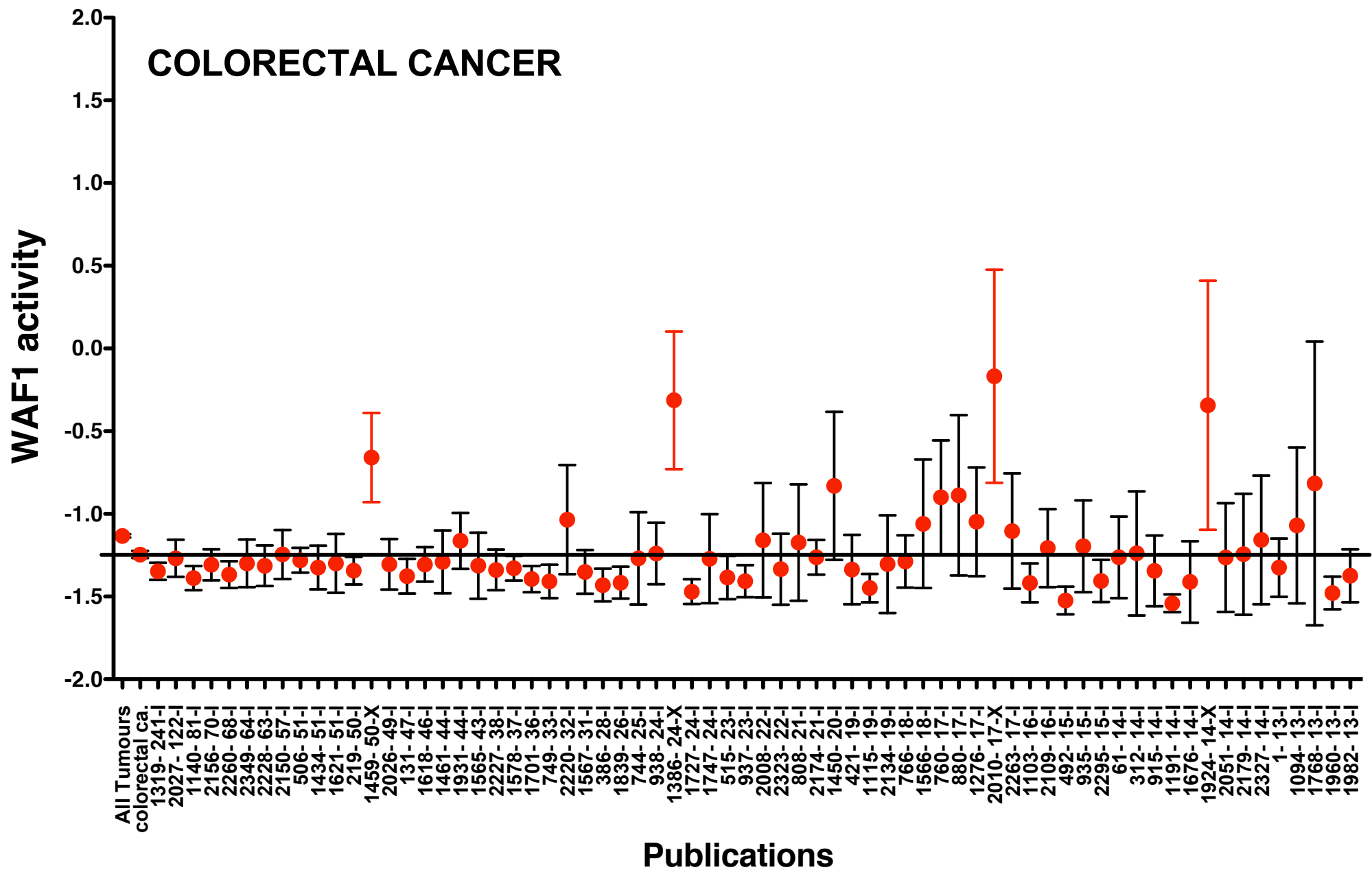
ENDOMETRIAL TUMORS

Analysis summary

Number of studies	33
Number of tumors	222
Number of mutations	236
Number of tumors with 1 mutation	208
Number of tumors with 2 mutations	10
Number of tumors with more than 2 mutations	1
In studies	32
Out studies 95	1
Out studies 99	0

Strategy of analysis

Exon 5-8		
13 studies		
Exon 4-9		
2 studies		
Exon 2-11		
4 studies		
Other		
14 studies		
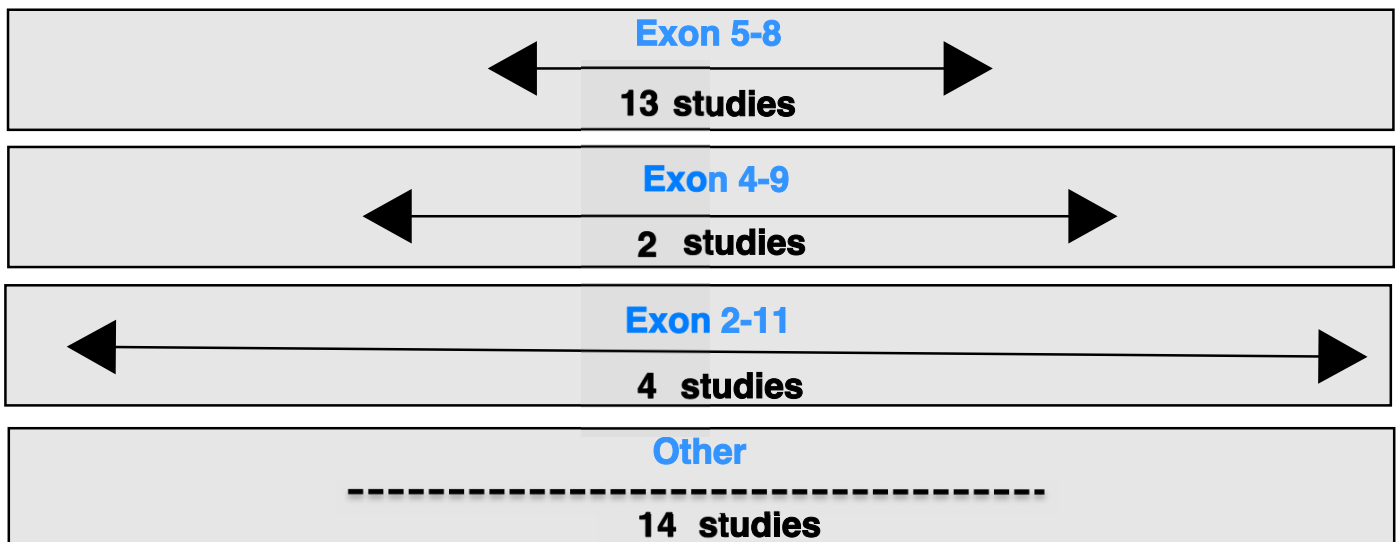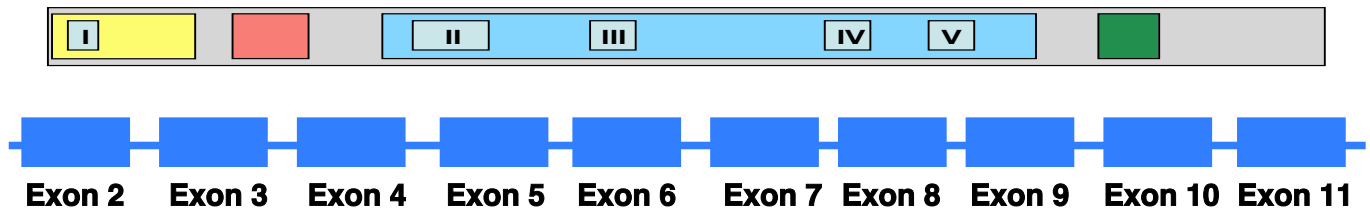
Prescreening

Studies with prescreening 18

SSCP	15	IHC	3
DGGE/CDGE	0	dHPLC	0
Yeast Assay	2	Other	0

Studies without prescreening 15

ENDOMETRIAL TUMORS

p53 mutation frequency

Number of missense mutations	165	81%
Number of nonsense mutations	18	9%
Number of frameshift mutations	22	11%
Total number of mutations	205	100%
Number of polymorphisms	1	1%

p53 mutant frequency

Number of missense mutants	99	78%
Number of nonsense mutants	10	8%
Number of frameshift mutants	18	14%
Total number of mutants	127	100%
Number of polymorphisms	1	1%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
248	CGG	TGG	Arg	Trp	Ts	Yes	17
248	CGG	CAG	Arg	Gln	Ts	Yes	12
175	CGC	CAC	Arg	His	Ts	Yes	7
273	CGT	CAT	Arg	His	Ts	Yes	6
282	CGG	TGG	Arg	Trp	Ts	Yes	5
242	TGC	TTC	Cys	Phe	Tv	No	5
213	CGA	TGA	Arg	Stop	Ts	Yes	5
306	CGA	TGA	Arg	Stop	Ts	Yes	4
245	GGC	AGC	Gly	Ser	Ts	Yes	4
157	GTC	TTC	Val	Phe	Tv	No	3

Exon Distribution

EXON 2-4   EXON 5-8   EXON 9-11

10%
9%
82%
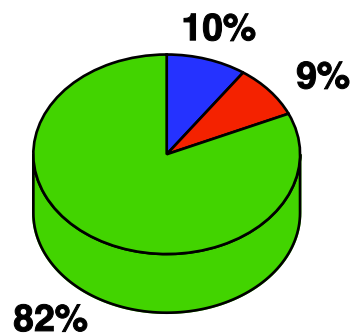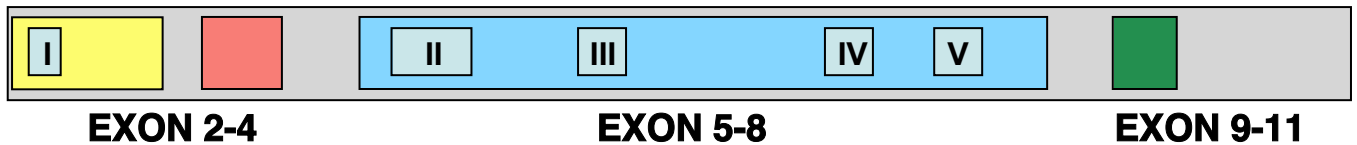
Frameshift   Nonsense   Missense

ENDOMETRIAL TUMORS

p53 mutation distribution

p53 CODON

p53 mutational events

mutation at CpG

mutation outside CpG
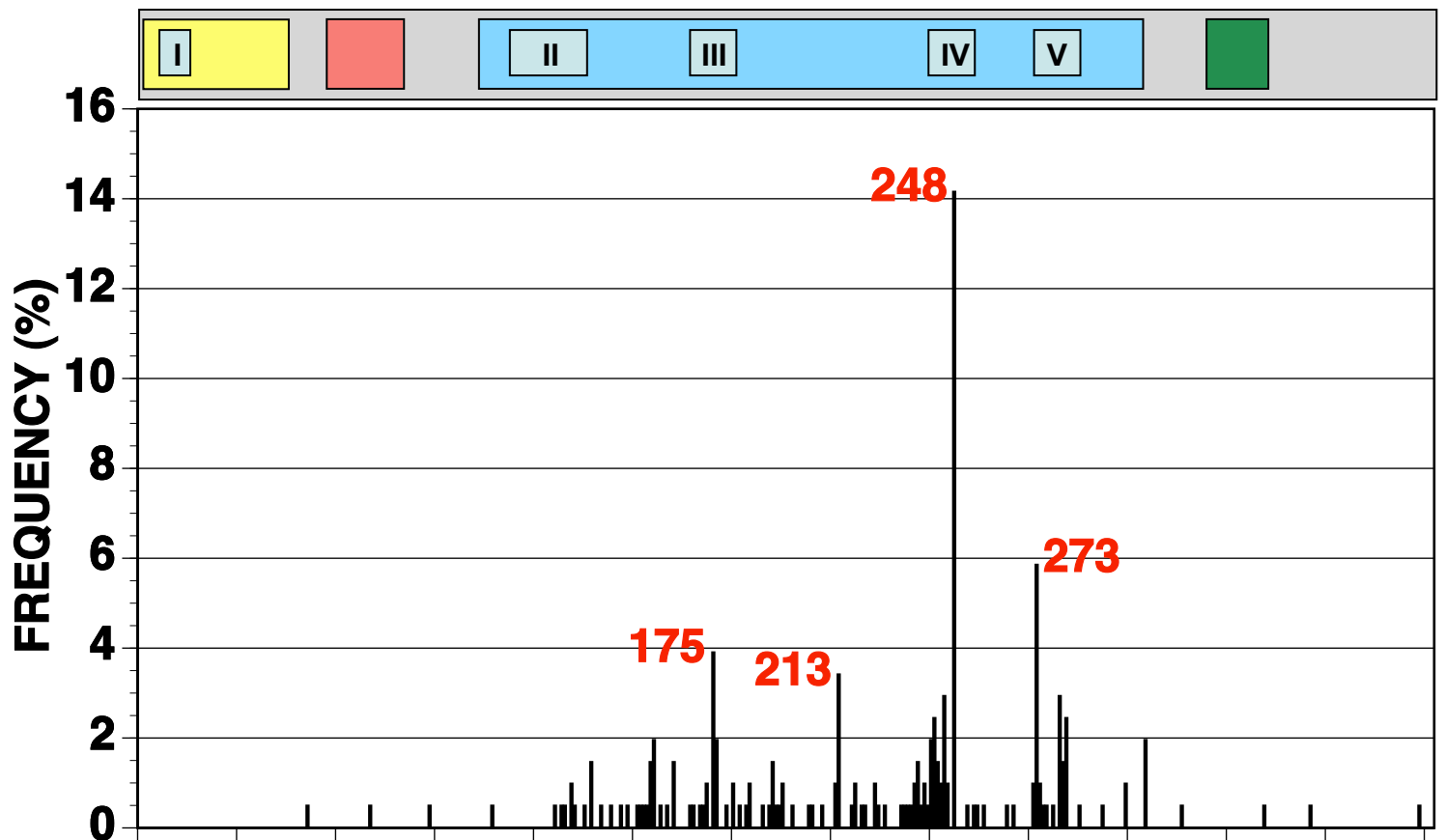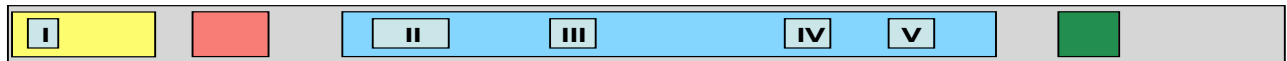
MUTATIONAL EVENTS
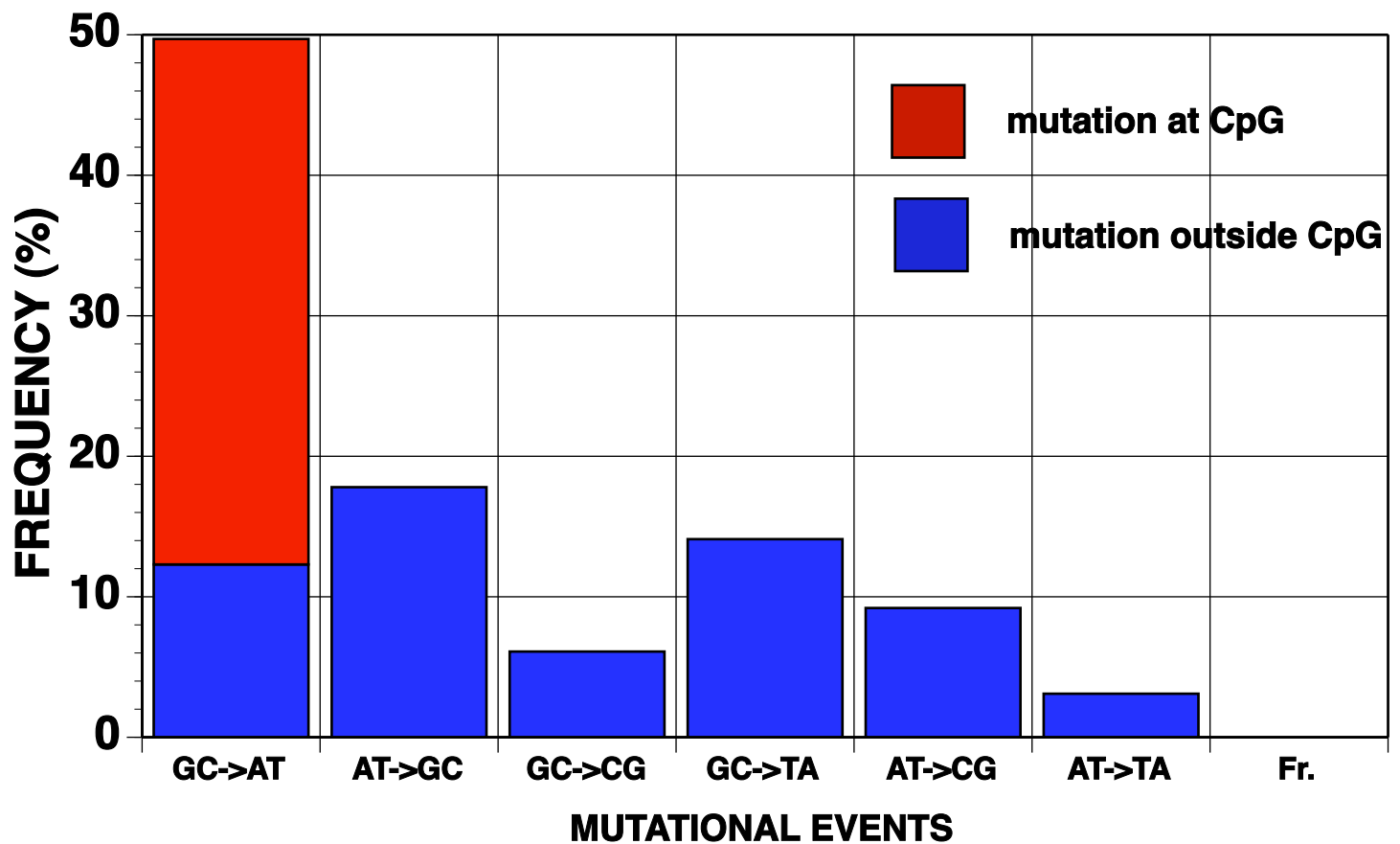
ESOPHAGEAL ADC

Analysis summary

Number of studies	34
Number of tumors	314
Number of mutations	337
Number of tumors with 1 mutation	294
Number of tumors with 2 mutations	17
Number of tumors with more than 2 mutations	3
In studies	33
Out studies 95	0
Out studies 99	1

Strategy of analysis

Exon 2 Exon 3 Exon 4 Exon 5 Exon 6 Exon 7 Exon 8 Exon 9 Exon 10 Exon 11

Exon 5-8
18 studies

Exon 4-9
3 studies

Exon 2-11
0 studies

Other
13 studies

Prescreening
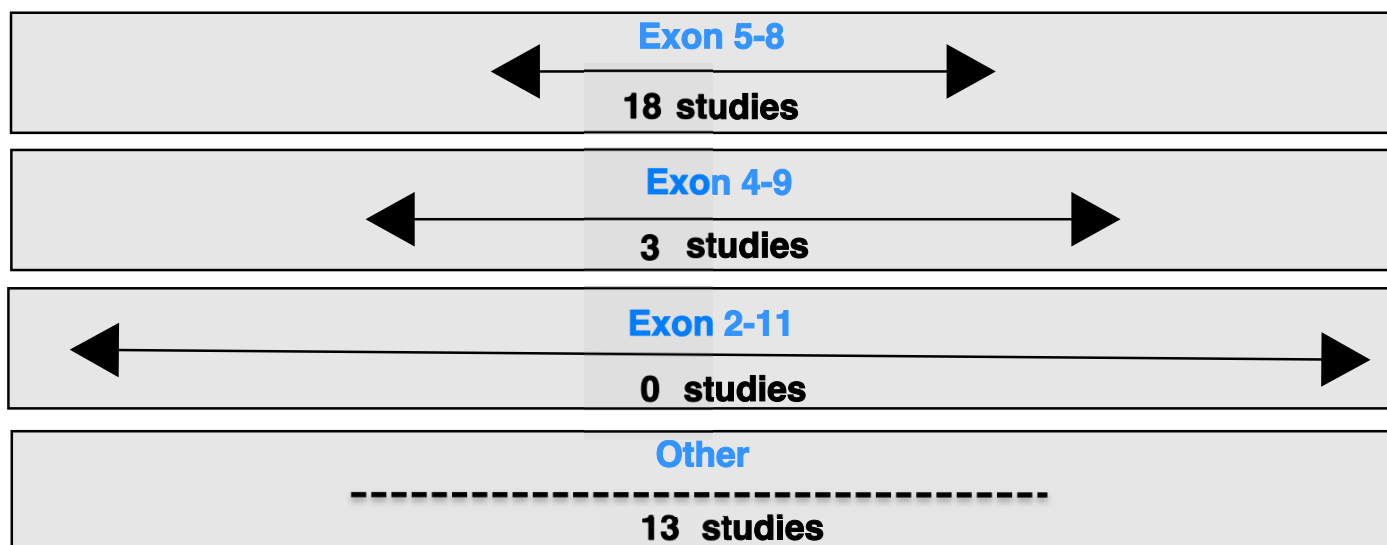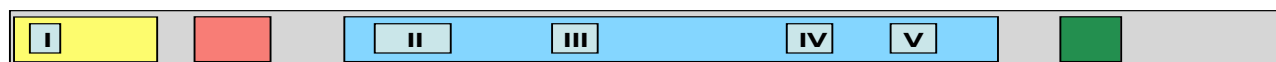
Studies with prescreening	**25**		Studies without prescreening	**9**

SSCP	18	IHC	0
DGGE/CDGE	5	dHPLC	1
Yeast Assay	1	Other	1

ESOPHAGEAL ADC

p53 mutation frequency

Number of missense mutations	258	77%
Number of nonsense mutations	27	8%
Number of frameshift mutations	52	15%
Total number of mutations	337	100%
Number of polymorphisms	9	3%

p53 mutant frequency

Number of missense mutants	92	63%
Number of nonsense mutants	13	9%
Number of frameshift mutants	41	28%
Total number of mutants	146	100%
Number of polymorphisms	7	5%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
176	TGC	TTC	Cys	Phe	Tv	No	44
175	CGC	CAC	Arg	His	Ts	Yes	26
248	CGG	TGG	Arg	Trp	Ts	Yes	15
273	CGT	CAT	Arg	His	Ts	Yes	13
245	GGC	AGC	Gly	Ser	Ts	Yes	12
248	CGG	CAG	Arg	Gln	Ts	Yes	8
282	CGG	TGG	Arg	Trp	Ts	Yes	8
273	CGT	TGT	Arg	Cys	Ts	Yes	8
213	CGA	TGA	Arg	Stop	Ts	Yes	7
245	GGC	CTC	Gly	Leu	Tv	No	6

Exon Distribution

EXON 2-4   EXON 5-8   EXON 9-11
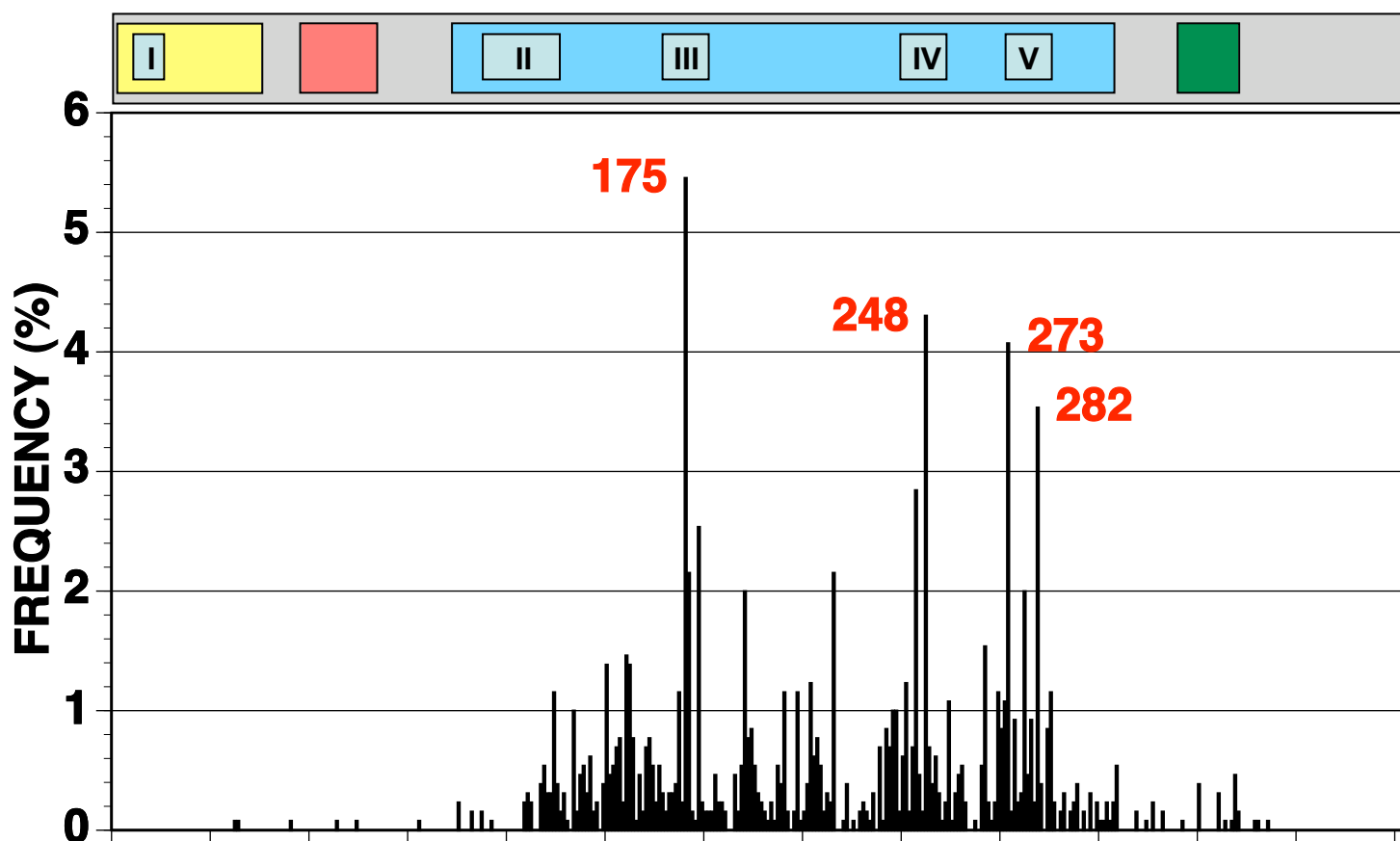
EXON 5-8: 15% / 8% / 78%

EXON 9-11: 50% / 33% / 17%
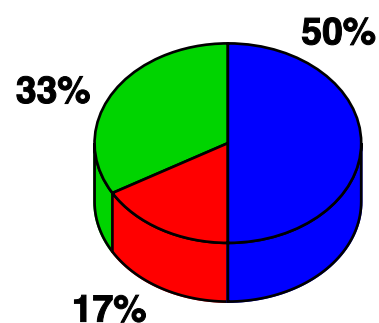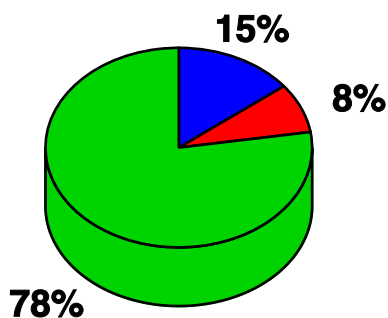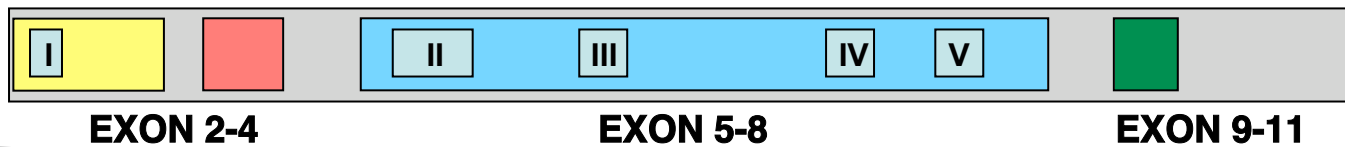
Frameshift   Nonsense   Missense

ESOPHAGEAL ADC

p53 mutation distribution
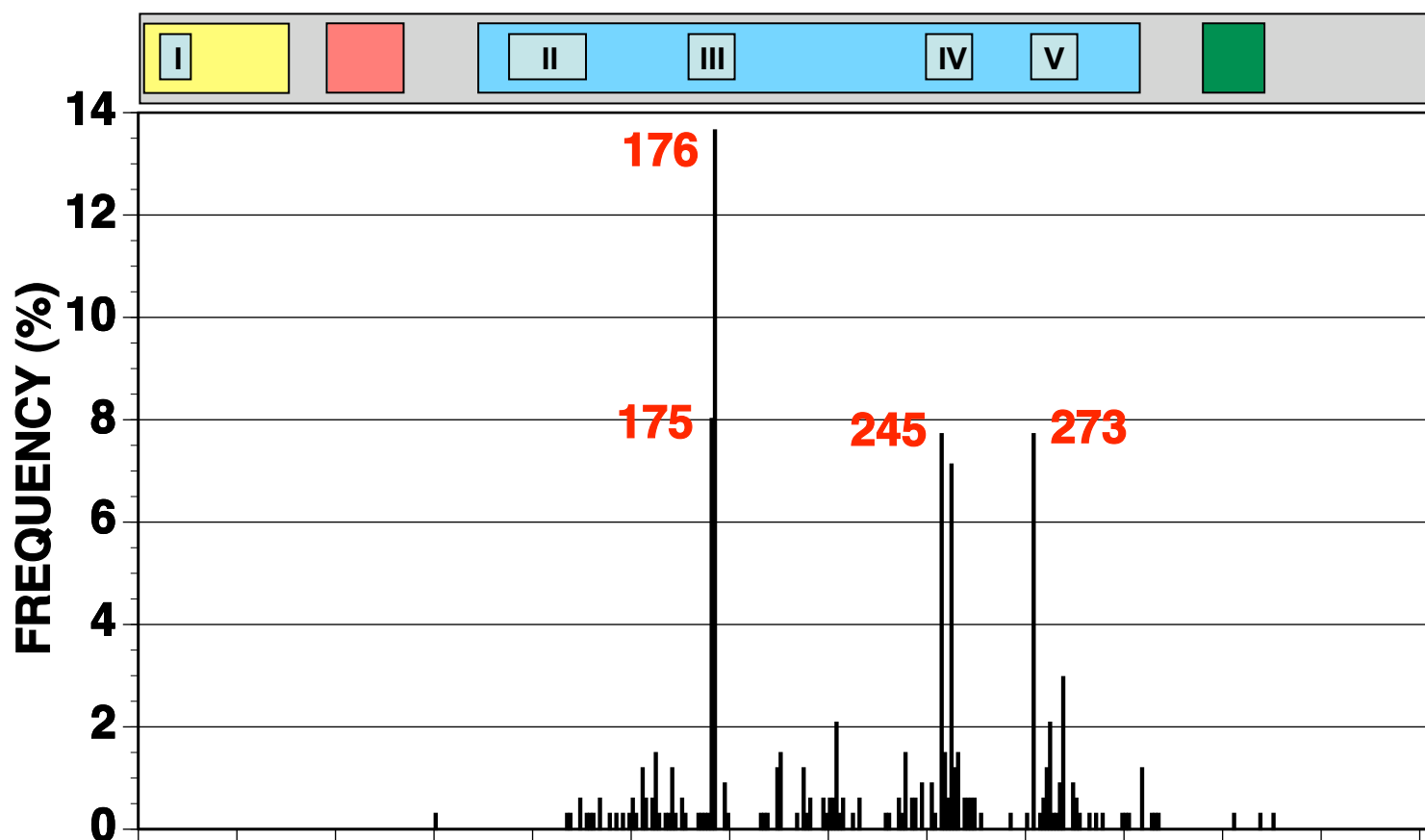
p53 mutational events
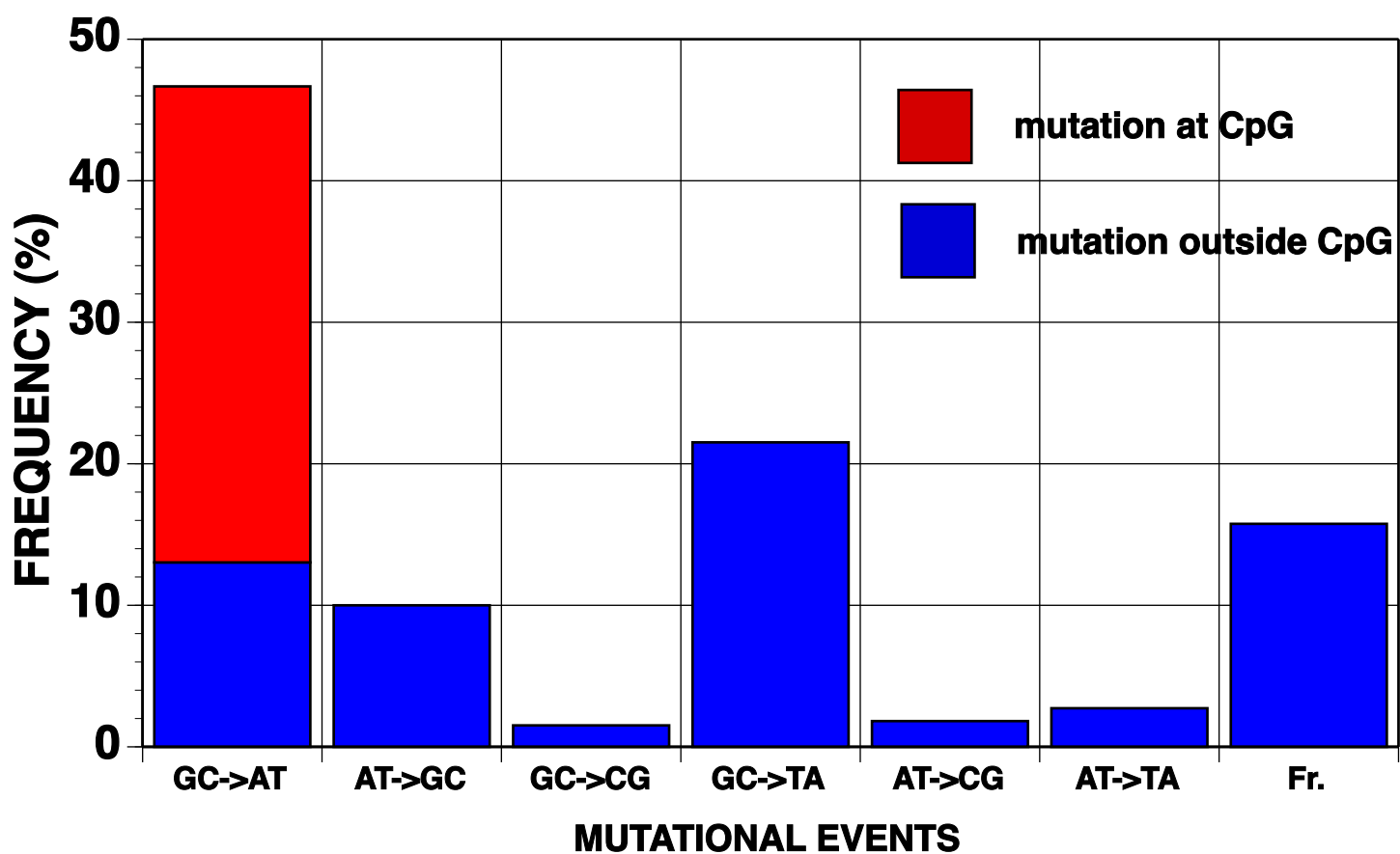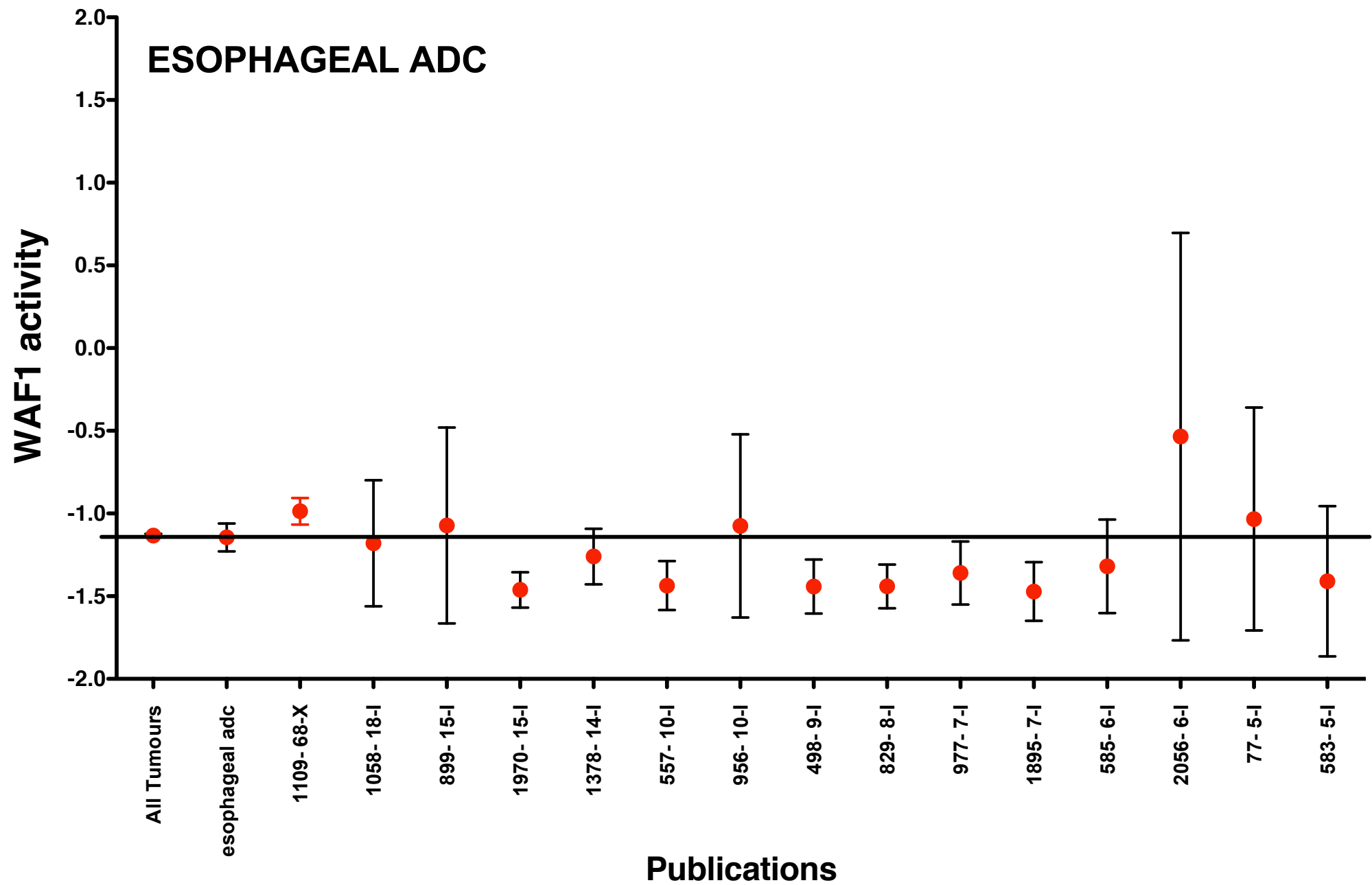
ESOPHAGEAL SCC

Analysis summary

Number of studies	73
Number of tumors	1214
Number of mutations	1306
Number of tumors with 1 mutation	1127
Number of tumors with 2 mutations	78
Number of tumors with more than 2 mutations	7
In studies	71
Out studies 95	2
Out studies 99	0

Strategy of analysis

Exon 2 Exon 3 Exon 4 Exon 5 Exon 6 Exon 7 Exon 8 Exon 9 Exon 10 Exon 11

Exon 5-8
◄———————►
40 studies

Exon 4-9
◄———————————►
7 studies

Exon 2-11
◄———————————————————►
5 studies
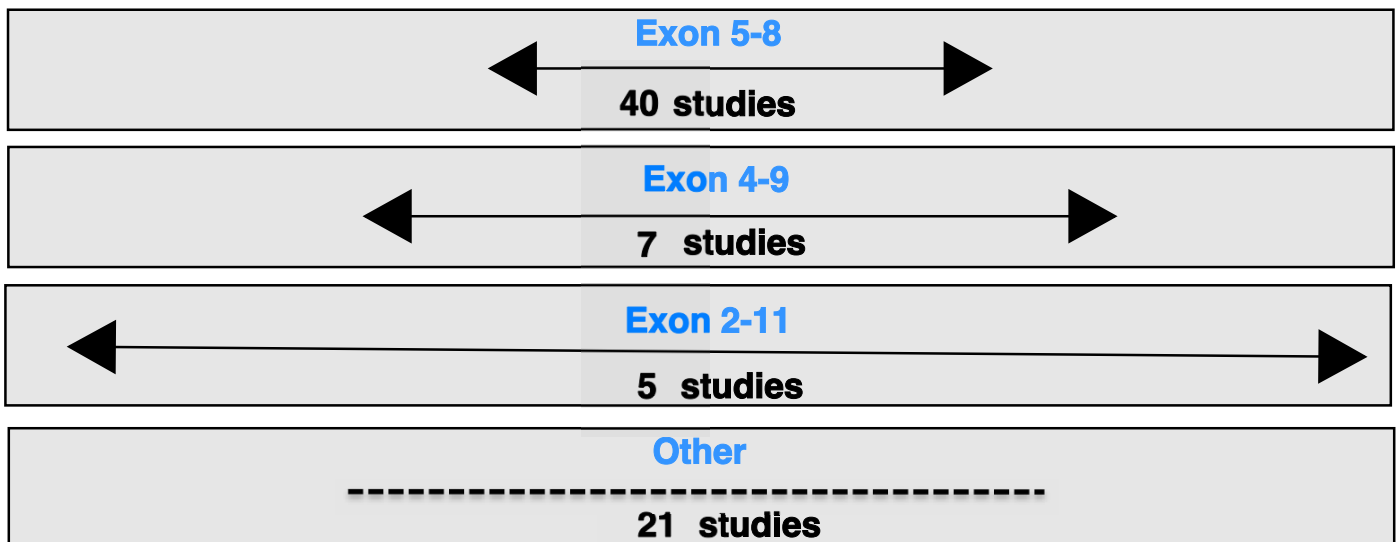
Other
----
21 studies

Prescreening

Studies with prescreening		46
SSCP	30	
DGGE/CDGE	10	
Yeast Assay	3	
IHC	2	
dHPLC	3	
Other	0	

Studies without prescreening 27

ESOPHAGEAL SCC

p53 mutation frequency

Number of missense mutations	994	76%
Number of nonsense mutations	137	11%
Number of frameshift mutations	171	13%
Total number of mutations	1302	100%
Number of polymorphisms	44	3%

p53 mutant frequency

Number of missense mutants	319	66%
Number of nonsense mutants	49	10%
Number of frameshift mutants	115	24%
Total number of mutants	483	100%
Number of polymorphisms	33	7%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
175	CGC	CAC	Arg	His	Ts	Yes	70
282	CGG	TGG	Arg	Trp	Ts	Yes	43
220	TAT	TGT	Tyr	Cys	Ts	No	26
273	CGT	CAT	Arg	His	Ts	Yes	26
248	CGG	TGG	Arg	Trp	Ts	Yes	25
248	CGG	CAG	Arg	Gln	Ts	Yes	24
179	CAT	CGT	His	Arg	Ts	No	19
273	CGT	TGT	Arg	Cys	Ts	Yes	18
176	TGC	TTC	Cys	Phe	Tv	No	14
157	GTC	TTC	Val	Phe	Tv	No	13

Exon Distribution

EXON 2-4: 43%, 43%, 14%

EXON 5-8: 13%, 10%, 78%

EXON 9-11: 23%, 45%, 32%

Legend: Frameshift (blue), Nonsense (red), Missense (green)

ESOPHAGEAL SCC

p53 mutation distribution

p53 CODON

p53 mutational events

MUTATIONAL EVENTS

ESOPHAGEAL SCC

GASTRIC CARCINOMA

Analysis summary

Number of studies	92
Number of tumors	831
Number of mutations	894
Number of tumors with 1 mutation	768
Number of tumors with 2 mutations	53
Number of tumors with more than 2 mutations	5
In studies	89
Out studies 95	3
Out studies 99	0

Strategy of analysis

Exon 2 Exon 3 Exon 4 Exon 5 Exon 6 Exon 7 Exon 8 Exon 9 Exon 10 Exon 11

Exon 5-8

48 studies

Exon 4-9

2 studies

Exon 2-11

9 studies
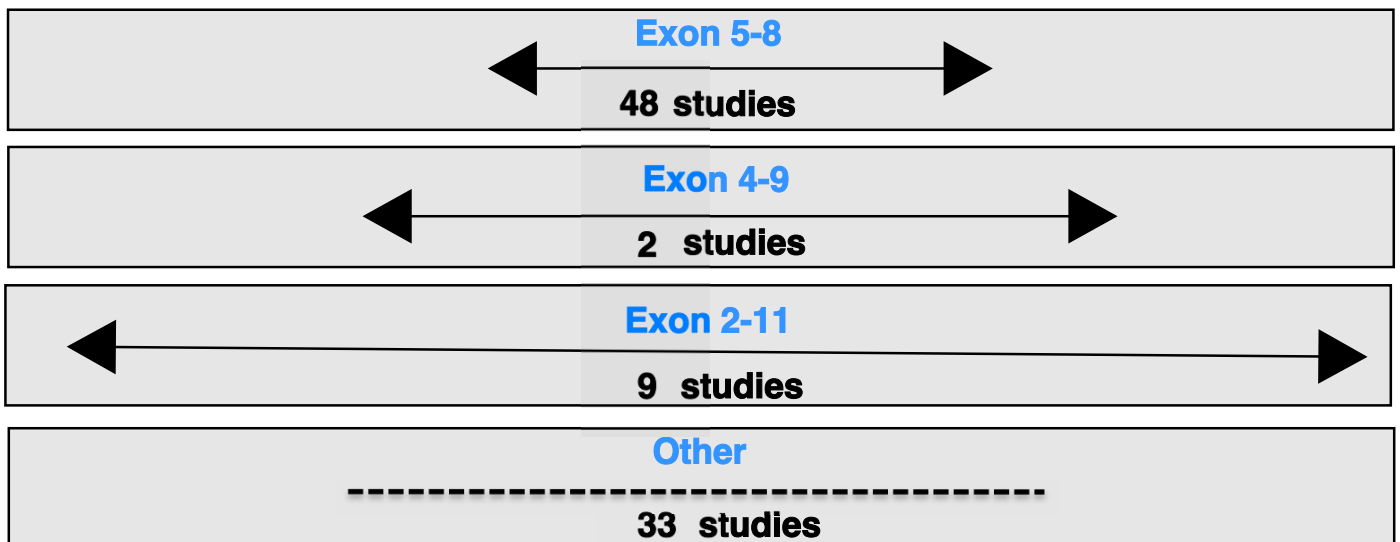
Other

33 studies

Prescreening

Studies with prescreening 58

Studies without prescreening 34

SSCP	46	**IHC**	1	
DGGE/CDGE	6	**dHPLC**	2	
Yeast Assay	1	**Other**	3	

GASTRIC CARCINOMA

p53 mutation frequency

Number of missense mutations	746	84%
Number of nonsense mutations	63	7%
Number of frameshift mutations	80	9%
Total number of mutations	889	100%
Number of polymorphisms	53	6%

p53 mutant frequency

Number of missense mutants	286	77%
Number of nonsense mutants	23	6%
Number of frameshift mutants	62	17%
Total number of mutants	371	100%
Number of polymorphisms	37	10%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
175	CGC	CAC	Arg	His	Ts	Yes	64
282	CGG	TGG	Arg	Trp	Ts	Yes	46
248	CGG	CAG	Arg	Gln	Ts	Yes	32
273	CGT	CAT	Arg	His	Ts	Yes	32
248	CGG	TGG	Arg	Trp	Ts	Yes	31
245	GGC	AGC	Gly	Ser	Ts	Yes	30
273	CGT	TGT	Arg	Cys	Ts	Yes	25
213	CGA	TGA	Arg	Stop	Ts	Yes	13
196	CGA	TGA	Arg	Stop	Ts	Yes	13
220	TAT	TGT	Tyr	Cys	Ts	No	11

Exon Distribution
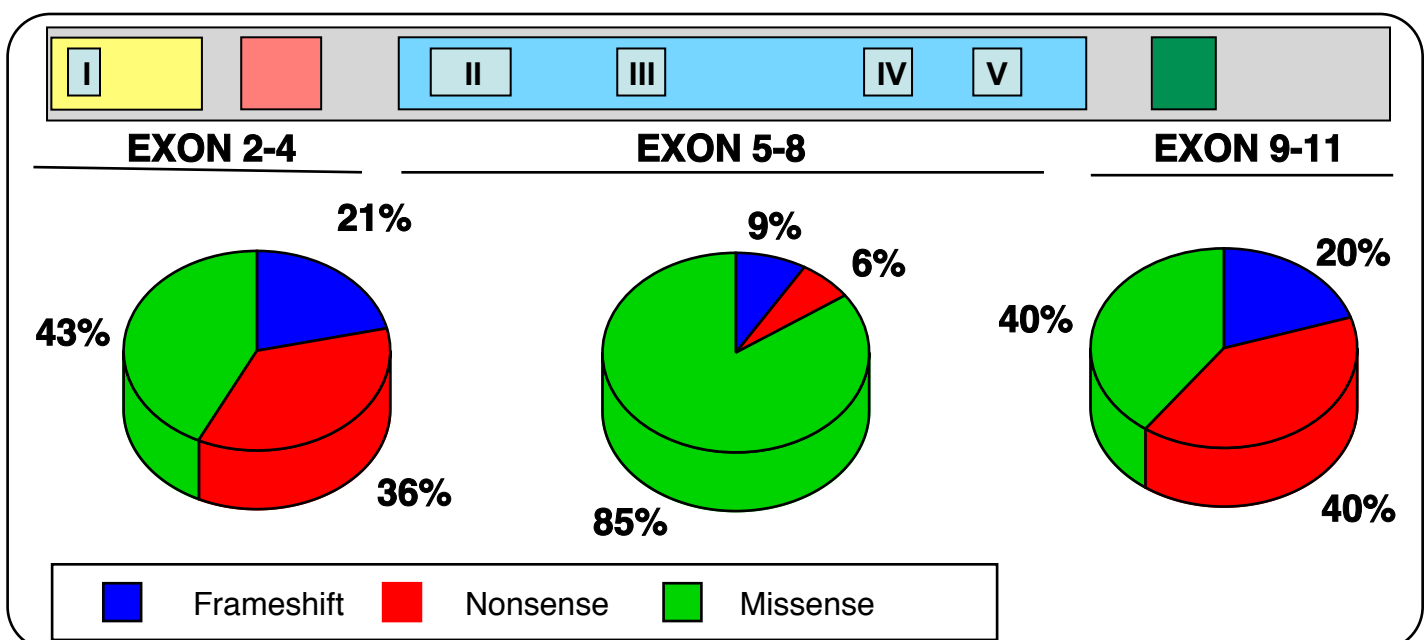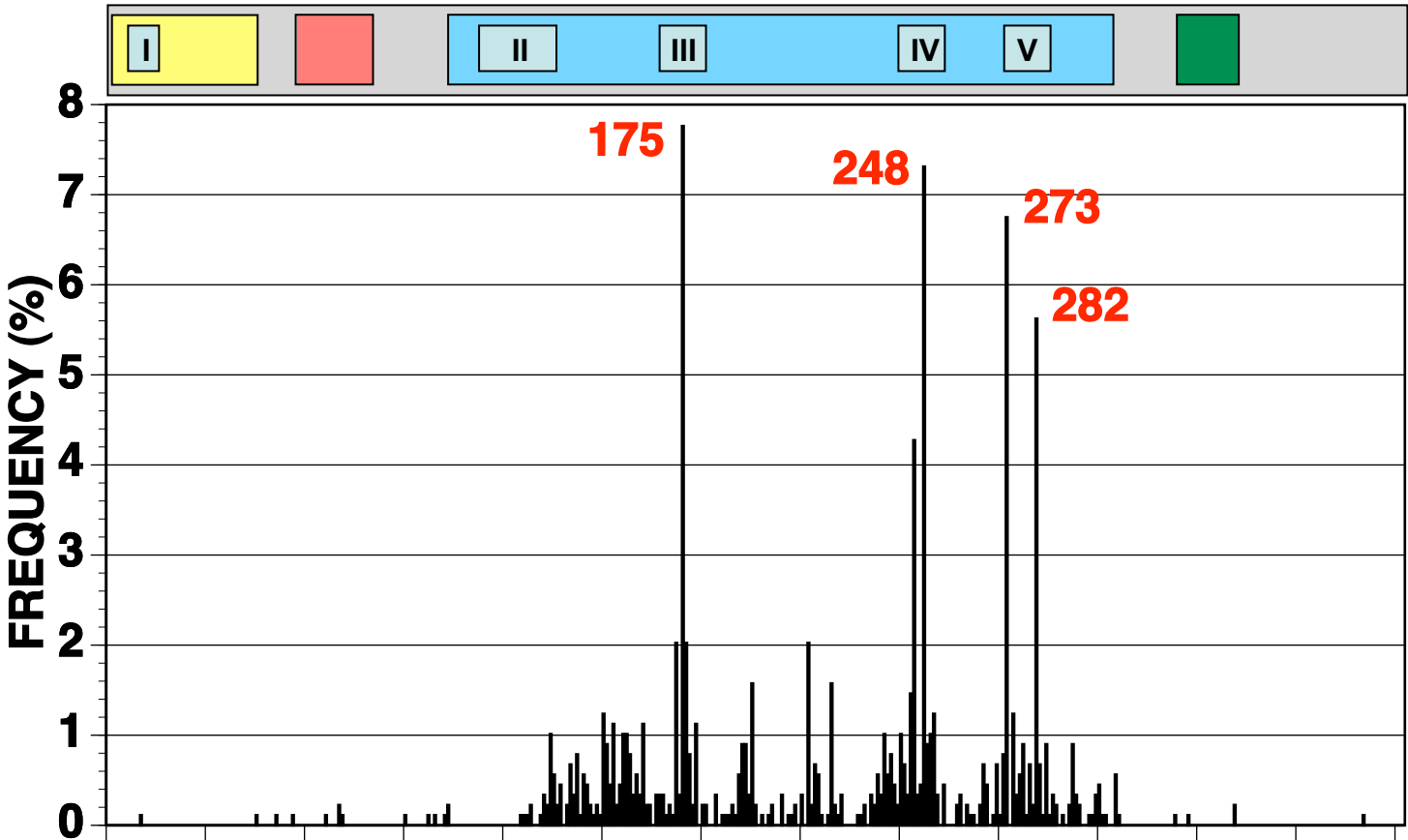
EXON 2-4

EXON 5-8

EXON 9-11

EXON 2-4: 21%, 43%, 36%

EXON 5-8: 9%, 6%, 85%

EXON 9-11: 20%, 40%, 40%

Frameshift   Nonsense   Missense

GASTRIC CARCINOMA

p53 mutation distribution

p53 CODON

p53 mutational events

FREQUENCY (%)

MUTATIONAL EVENTS

mutation at CpG

mutation outside CpG
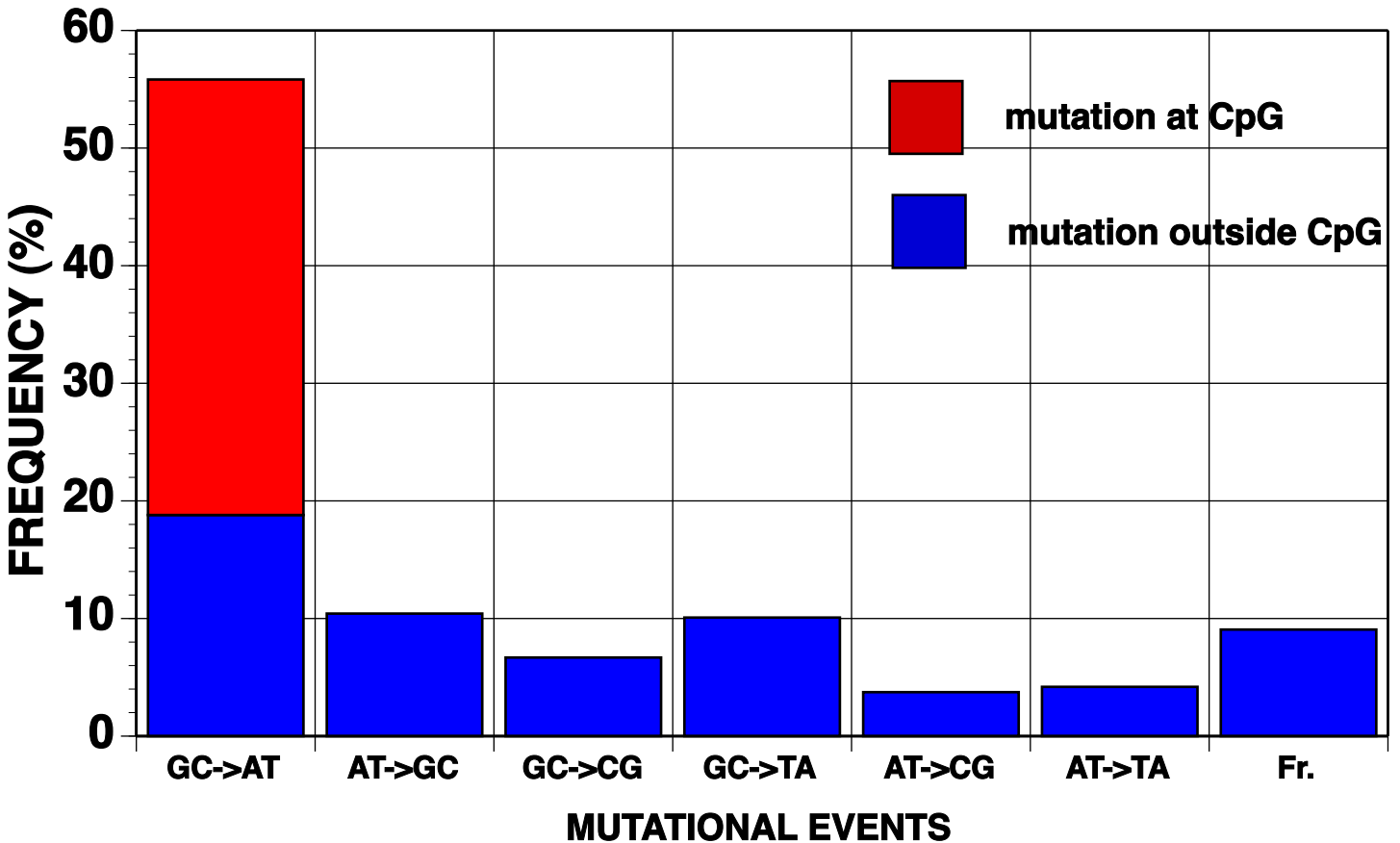
GASTRIC CARCINOMA
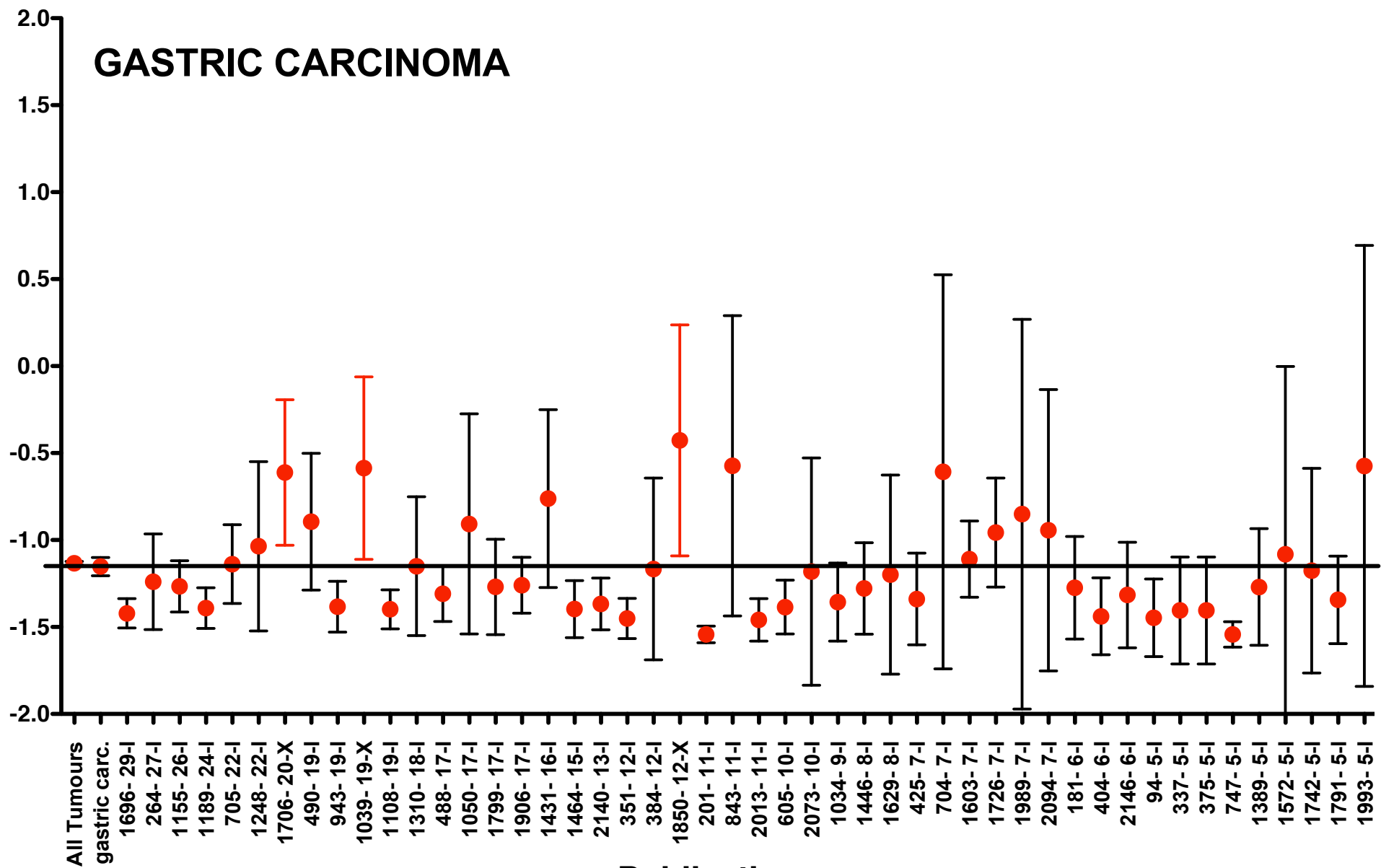
GLIOBLASTOMA

Analysis summary

Number of studies	90
Number of tumors	645
Number of mutations	720
Number of tumors with 1 mutation	545
Number of tumors with 2 mutations	50
Number of tumors with more than 2 mutations	10
In studies	90
Out studies 95	0
Out studies 99	0

Strategy of analysis

Exon 2 Exon 3 Exon 4 Exon 5 Exon 6 Exon 7 Exon 8 Exon 9 Exon 10 Exon 11

Exon 5-8
37 studies

Exon 4-9
5 studies

Exon 2-11
10 studies
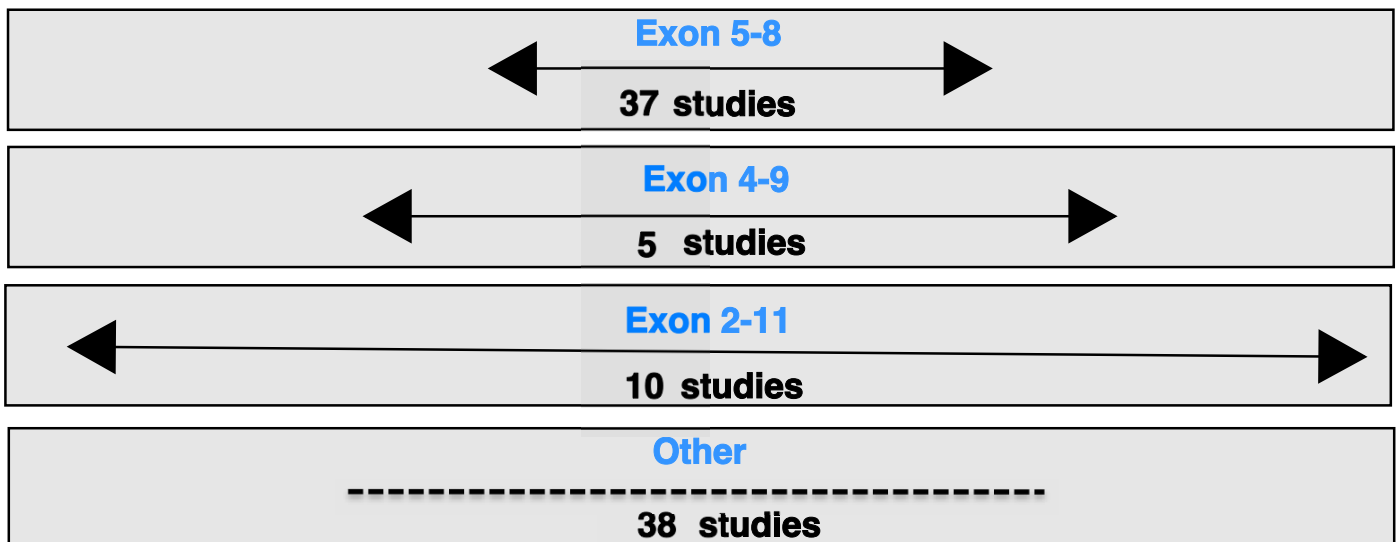
Other
38 studies

Prescreening

Studies with prescreening 49

SSCP	39	IHC	0
DGGE/CDGE	4	dHPLC	0
Yeast Assay	4	Other	3

Studies without prescreening 41

GLIOBLASTOMA

p53 mutation frequency

Number of missense mutations	603	89%
Number of nonsense mutations	22	3%
Number of frameshift mutations	50	7%
Total number of mutations	675	100%
Number of polymorphisms	7	1%

p53 mutant frequency

Number of missense mutants	221	81%
Number of nonsense mutants	10	4%
Number of frameshift mutants	41	15%
Total number of mutants	272	100%
Number of polymorphisms	7	3%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
273	CGT	TGT	Arg	Cys	Ts	Yes	63
175	CGC	CAC	Arg	His	Ts	Yes	44
248	CGG	CAG	Arg	Gln	Ts	Yes	28
273	CGT	CAT	Arg	His	Ts	Yes	27
248	CGG	TGG	Arg	Trp	Ts	Yes	24
282	CGG	TGG	Arg	Trp	Ts	Yes	21
245	GGC	AGC	Gly	Ser	Ts	Yes	14
220	TAT	TGT	Tyr	Cys	Ts	No	10
237	ATG	ATA	Met	Ile	Ts	No	9
158	CGC	CAC	Arg	His	Ts	Yes	8

Exon Distribution
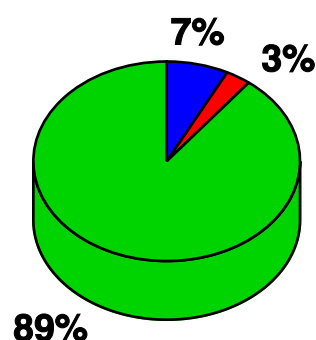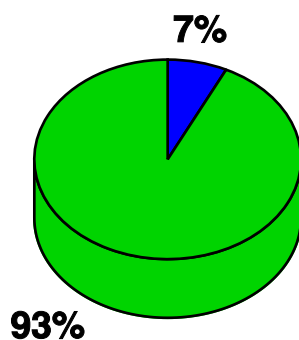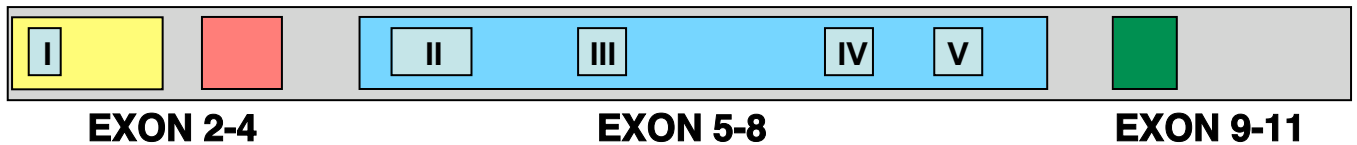
GLIOBLASTOMA

p53 mutation distribution
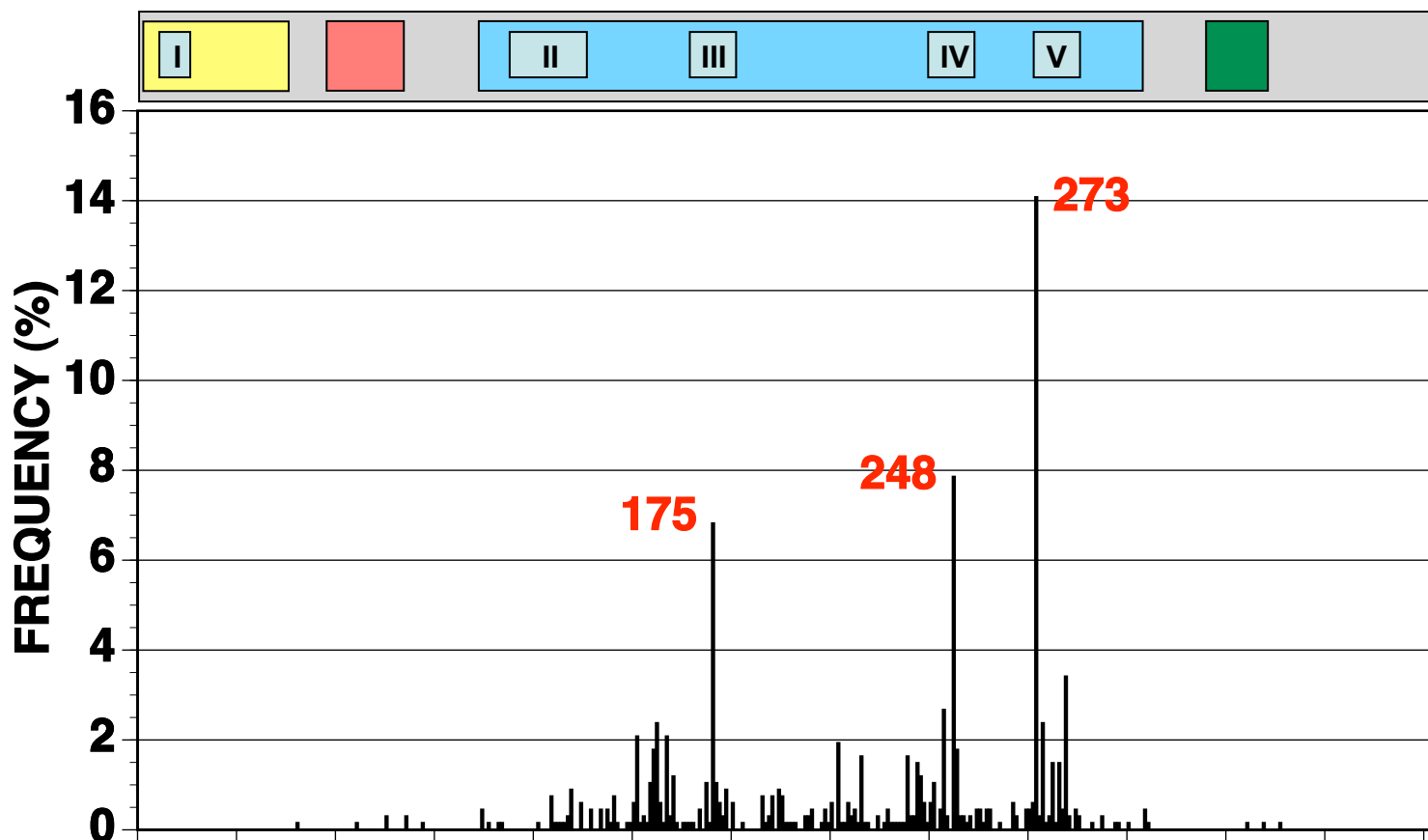
p53 mutational events
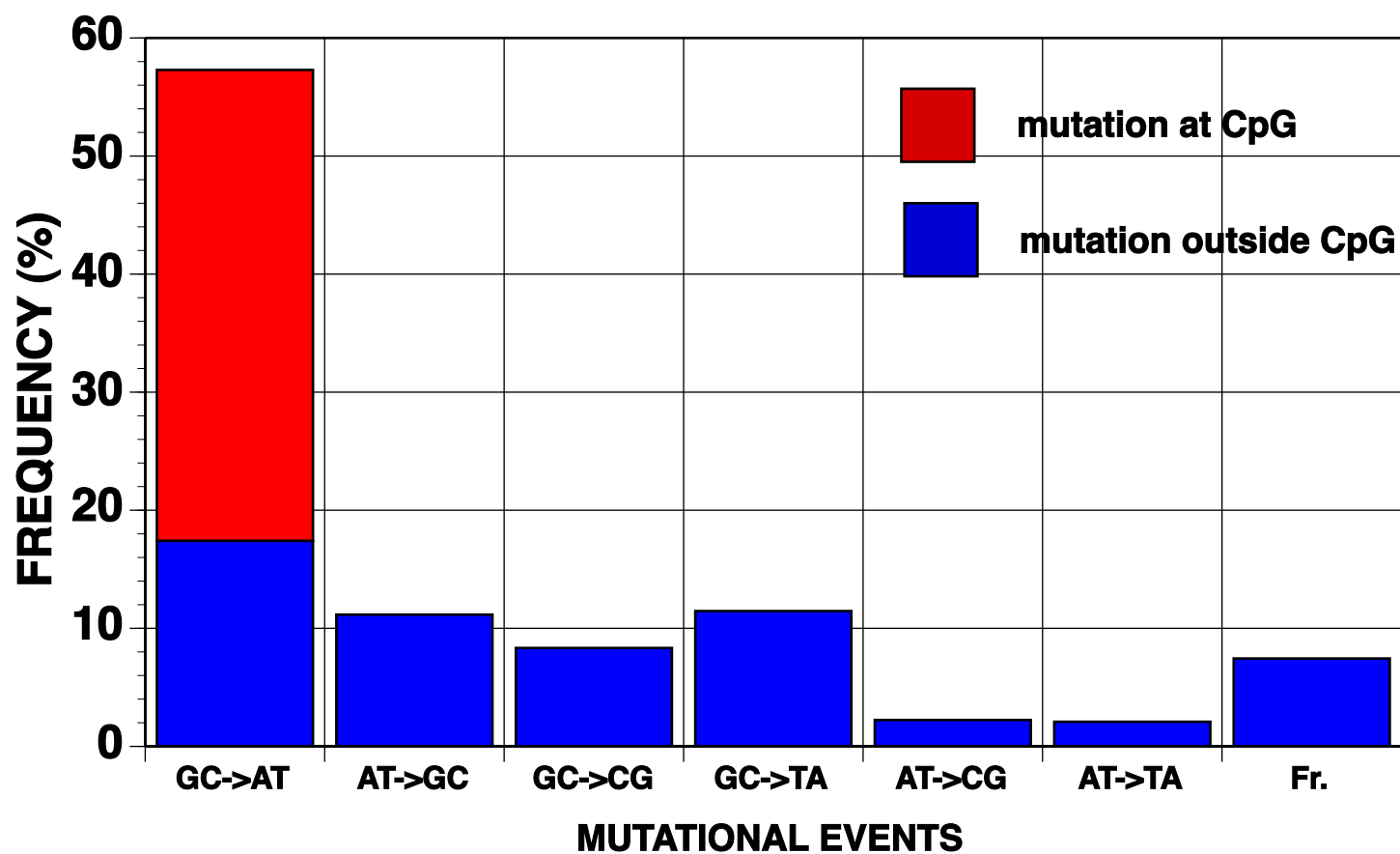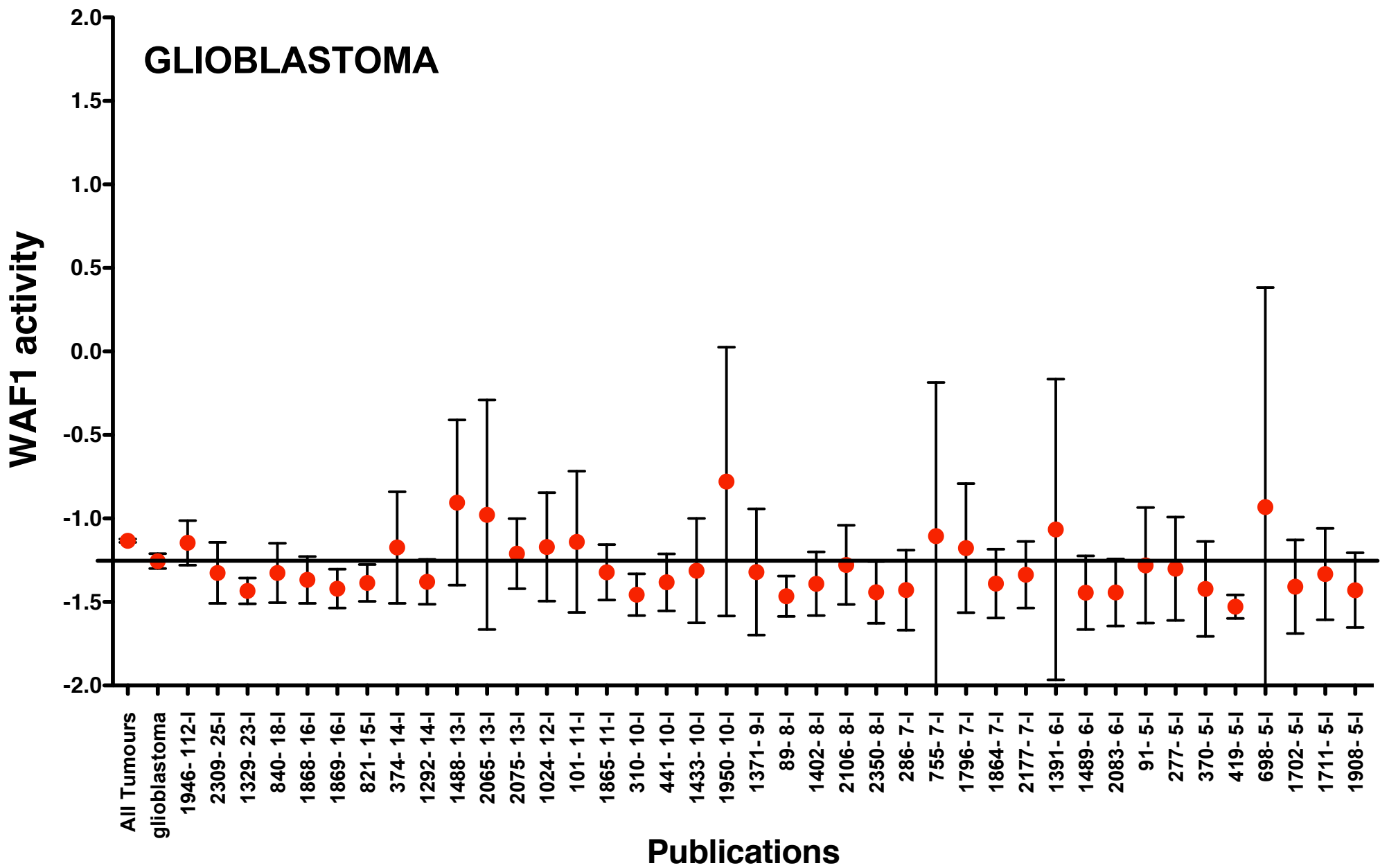
HCC

Analysis summary

Number of studies	102
Number of tumors	987
Number of mutations	1020
Number of tumors with 1 mutation	906
Number of tumors with 2 mutations	21
Number of tumors with more than 2 mutations	5
In studies	100
Out studies 95	1
Out studies 99	1

Strategy of analysis

Exon 2 Exon 3 Exon 4 Exon 5 Exon 6 Exon 7 Exon 8 Exon 9 Exon 10 Exon 11

Exon 5-8
34 studies

Exon 4-9
5 studies

Exon 2-11
14 studies
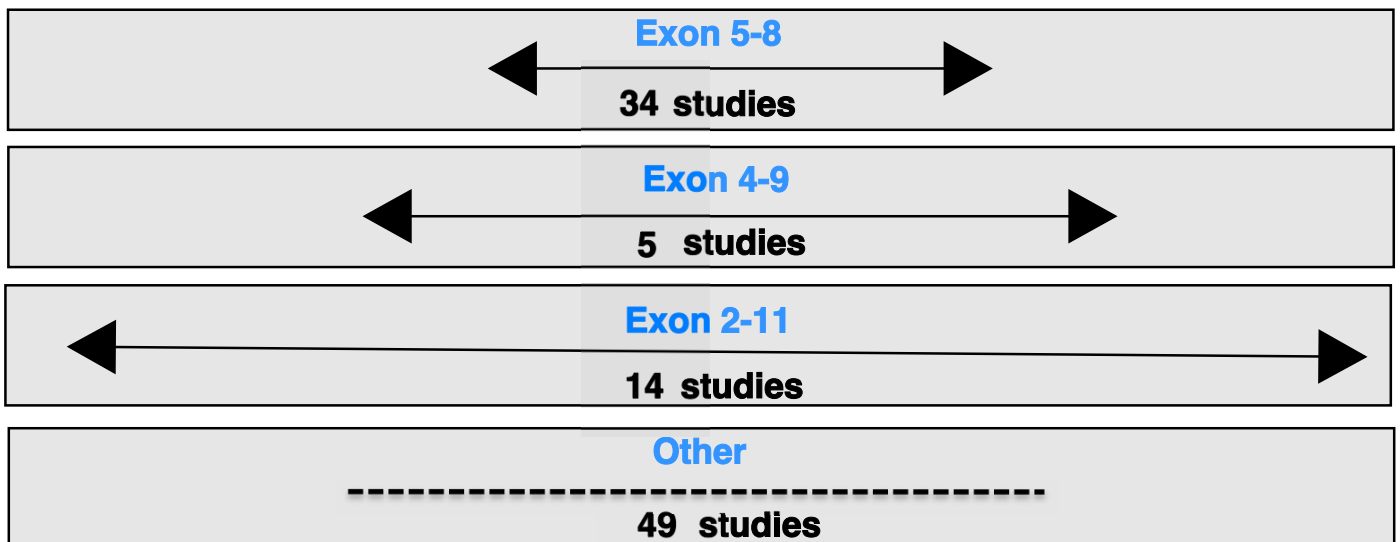
Other
49 studies

Prescreening

Studies with prescreening	50			Studies without prescreening	52
SSCP	41	IHC	0		
DGGE/CDGE	4	dHPLC	0		
Yeast Assay	3	Other	3		

HCC

p53 mutation frequency

Number of missense mutations	859	88%
Number of nonsense mutations	58	6%
Number of frameshift mutations	62	6%
Total number of mutations	979	100%
Number of polymorphisms	27	3%

p53 mutant frequency

Number of missense mutants	286	78%
Number of nonsense mutants	31	8%
Number of frameshift mutants	49	13%
Total number of mutants	366	100%
Number of polymorphisms	23	6%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
249	AGG	AGT	Arg	Ser	Tv	No	286
273	CGT	TGT	Arg	Cys	Ts	Yes	19
157	GTC	TTC	Val	Phe	Tv	No	16
166	TCA	ACA	Ser	Thr	Tv	No	12
251	ATC	AAC	Ile	Asn	Tv	No	12
220	TAT	TGT	Tyr	Cys	Ts	No	10
249	AGG	ATG	Arg	Met	Tv	No	9
243	ATG	AAG	Met	Lys	Tv	No	9
175	CGC	CAC	Arg	His	Ts	Yes	7
159	GCC	CCC	Ala	Pro	Tv	No	7

Exon Distribution

EXON 2-4: 27% Frameshift, 12% Nonsense, 62% Missense

EXON 5-8: 5% Frameshift, 5% Nonsense, 90% Missense

EXON 9-11: 19% Frameshift, 42% Nonsense, 38% Missense

Legend: Frameshift (blue), Nonsense (red), Missense (green)

HCC

p53 mutation distribution

FREQUENCY (%)

249

p53 CODON

p53 mutational events

FREQUENCY (%)

mutation at CpG

mutation outside CpG

GC->AT AT->GC GC->CG GC->TA AT->CG AT->TA Fr.
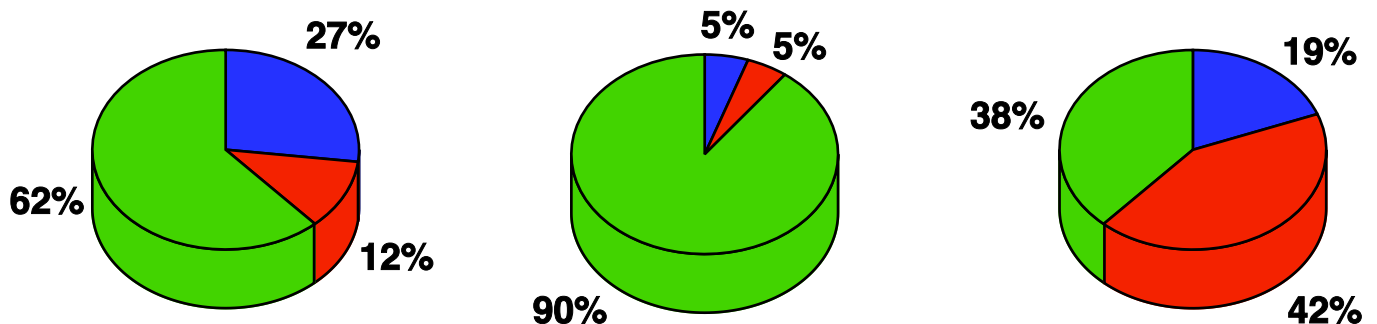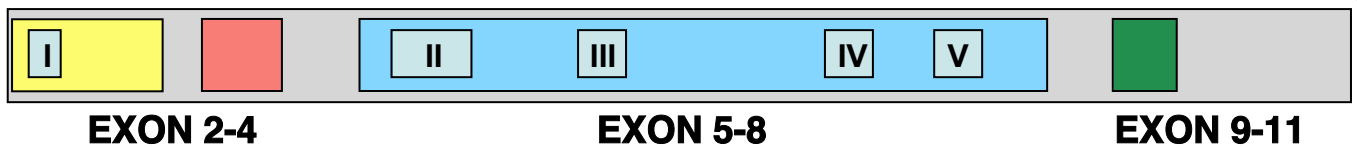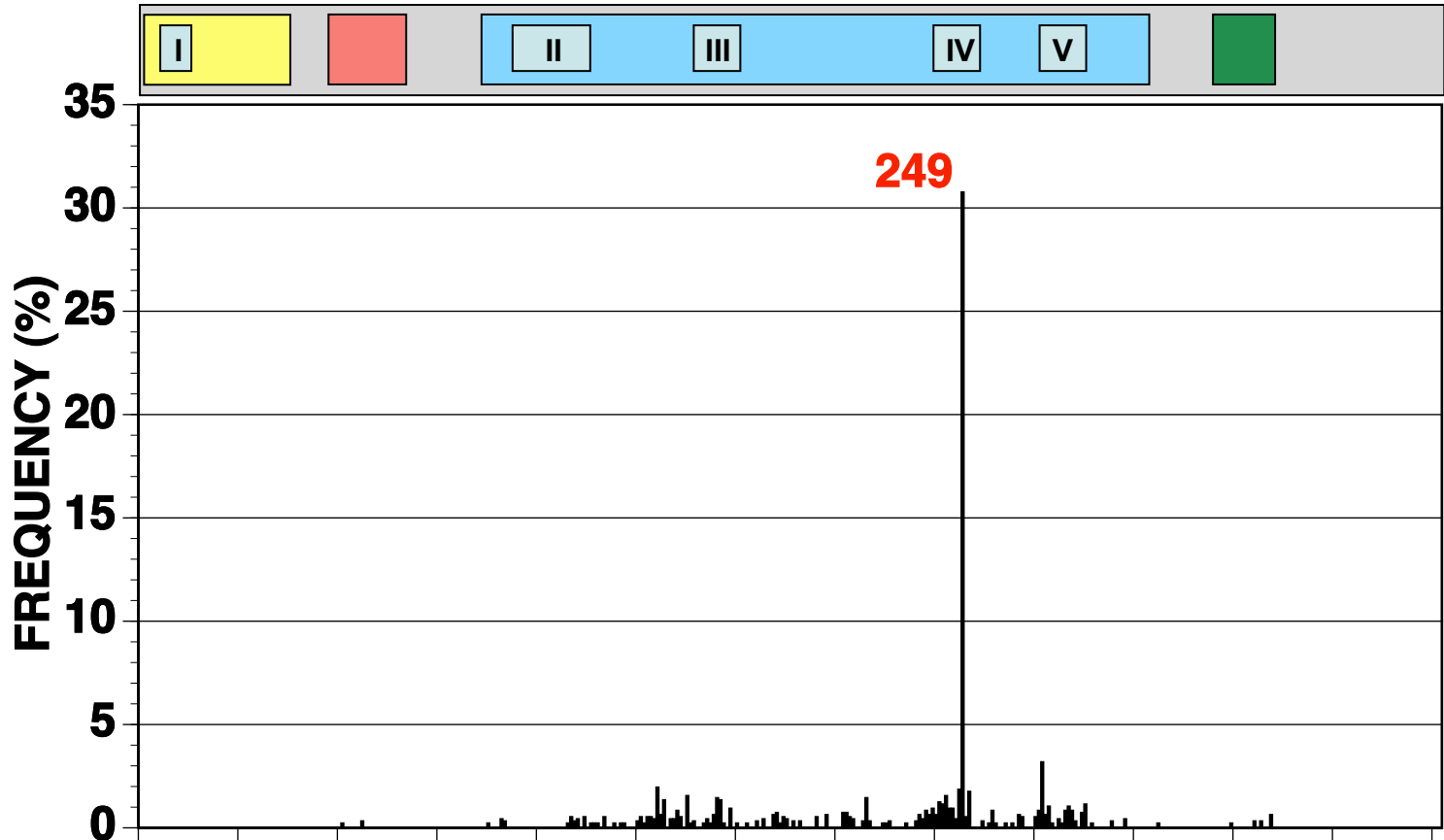
MUTATIONAL EVENTS
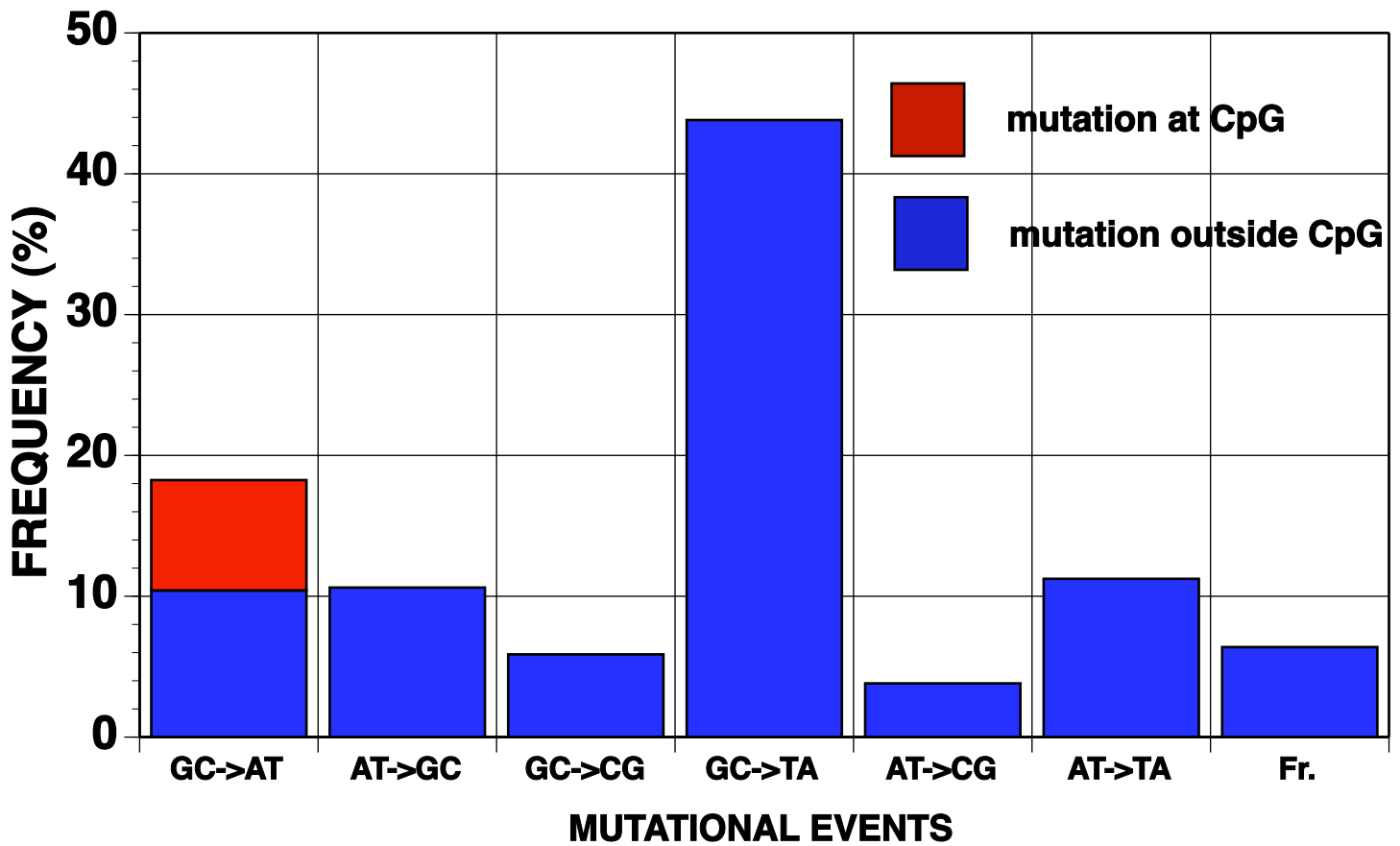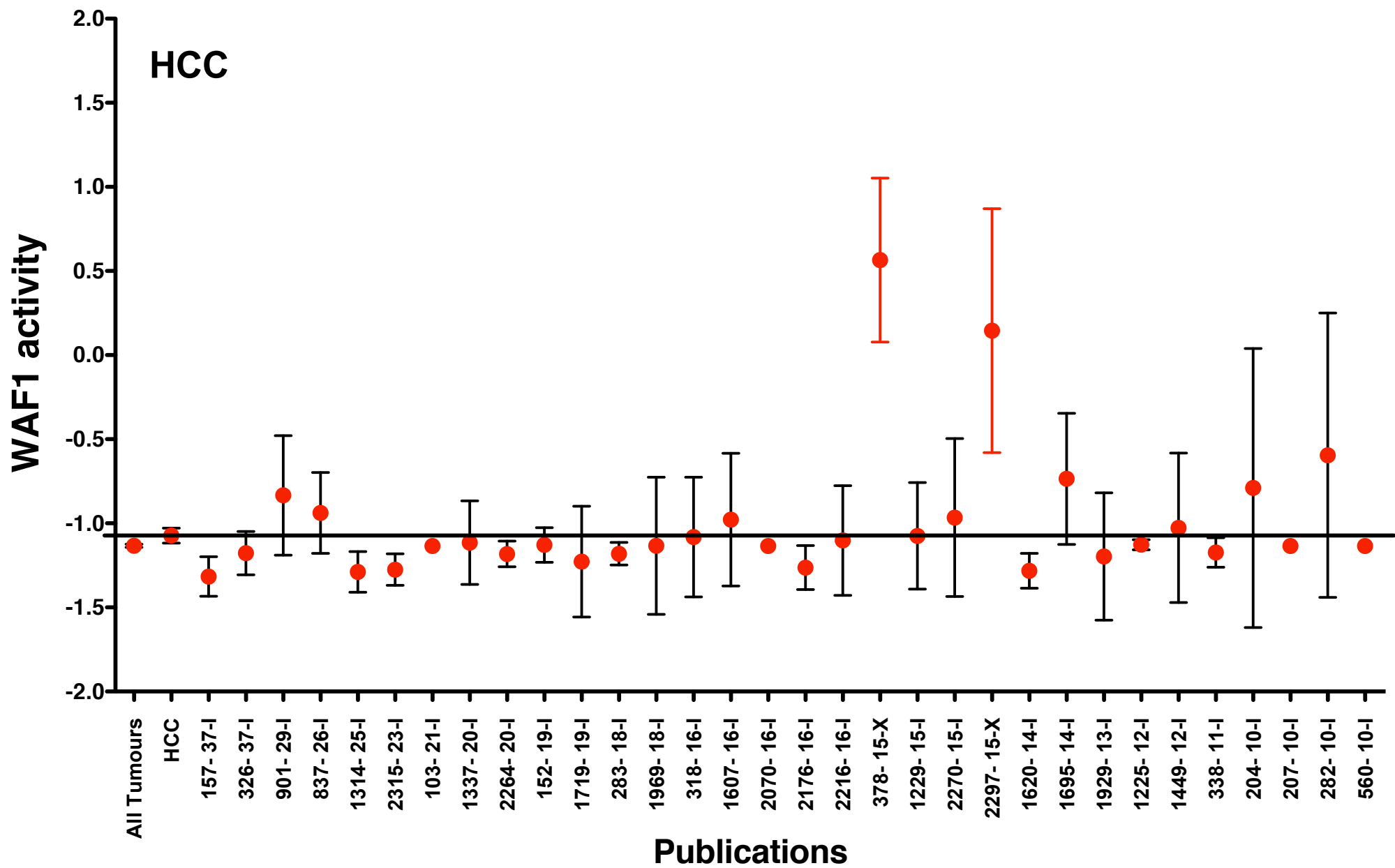
HEAD & NECK SCC

Analysis summary

Number of studies	151
Number of tumors	2331
Number of mutations	2513
Number of tumors with 1 mutation	2110
Number of tumors with 2 mutations	130
Number of tumors with more than 2 mutations	22
In studies	143
Out studies 95	3
Out studies 99	5

Strategy of analysis

I | II | III | IV | V

Exon 2 | Exon 3 | Exon 4 | Exon 5 | Exon 6 | Exon 7 | Exon 8 | Exon 9 | Exon 10 | Exon 11

Exon 5-8
41 studies

Exon 4-9
11 studies

Exon 2-11
23 studies
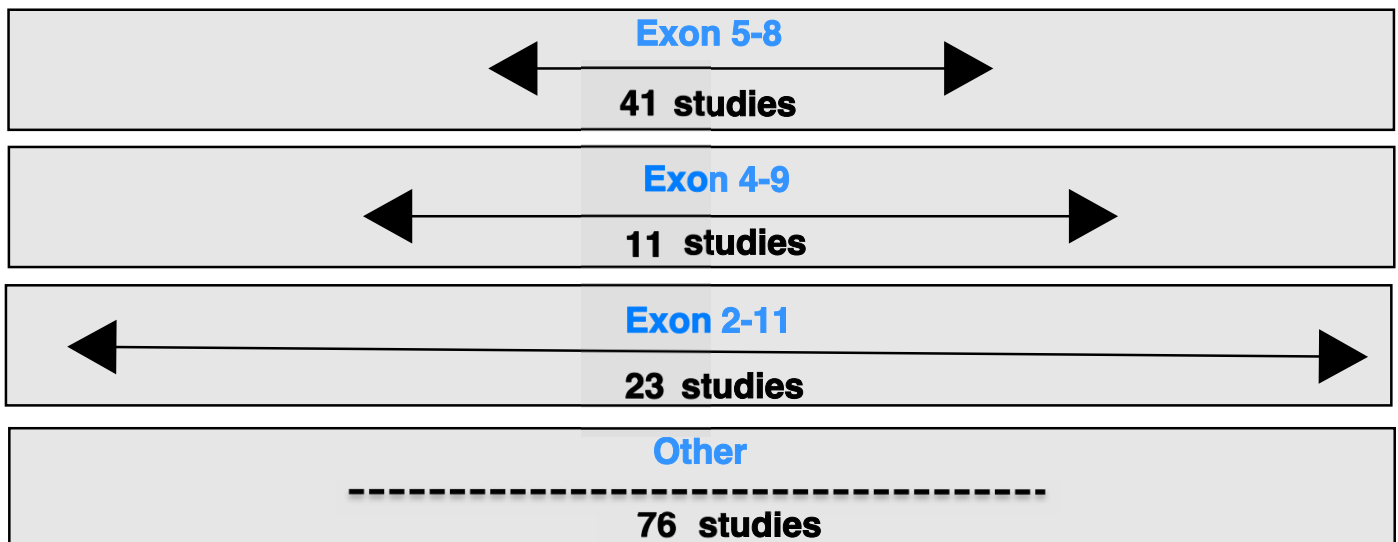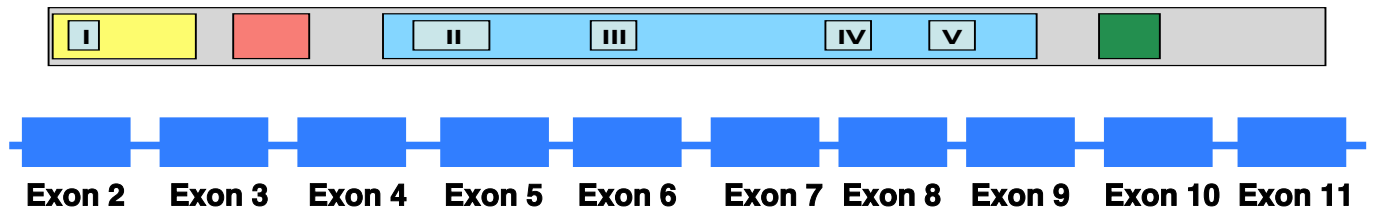
Other
76 studies

Prescreening

Studies with prescreening	81		Studies without prescreening	70

SSCP	59	IHC	5
DGGE/CDGE	8	dHPLC	2
Yeast Assay	8	Other	2

p53 mutation frequency

Number of missense mutations	1858	76%
Number of nonsense mutations	271	11%
Number of frameshift mutations	315	13%
Total number of mutations	2444	100%
Number of polymorphisms	92	4%

p53 mutant frequency

Number of missense mutants	537	69%
Number of nonsense mutants	57	7%
Number of frameshift mutants	186	24%
Total number of mutants	780	100%
Number of polymorphisms	61	8%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
175	CGC	CAC	Arg	His	Ts	Yes	76
248	CGG	CAG	Arg	Gln	Ts	Yes	72
273	CGT	CAT	Arg	His	Ts	Yes	60
282	CGG	TGG	Arg	Trp	Ts	Yes	51
220	TAT	TGT	Tyr	Cys	Ts	No	47
248	CGG	TGG	Arg	Trp	Ts	Yes	46
273	CGT	TGT	Arg	Cys	Ts	Yes	43
205	TAT	TGT	Tyr	Cys	Ts	No	33
176	TGC	TTC	Cys	Phe	Tv	No	32
157	GTC	TTC	Val	Phe	Tv	No	26

Exon Distribution

EXON 2-4 — 31%, 45%, 24%

EXON 5-8 — 12%, 10%, 78%

EXON 9-11 — 23%, 41%, 36%

Frameshift   Nonsense   Missense
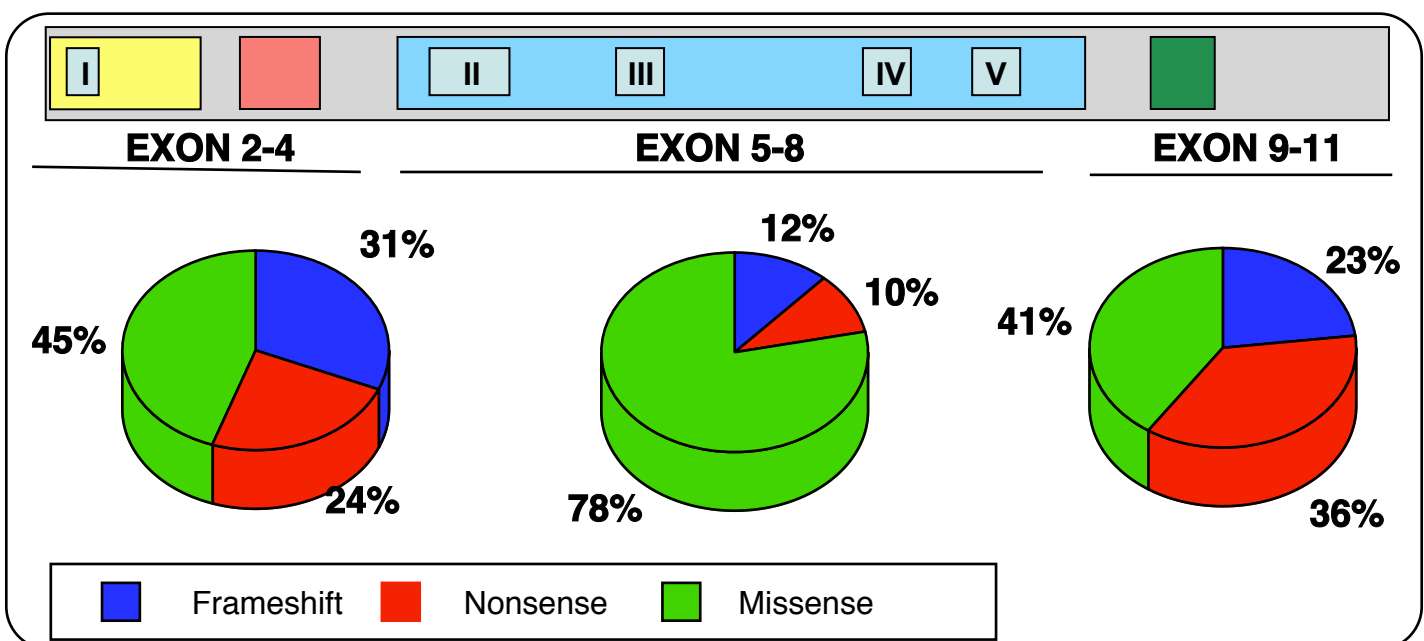
HEAD & NECK SCC

p53 mutation distribution

p53 CODON
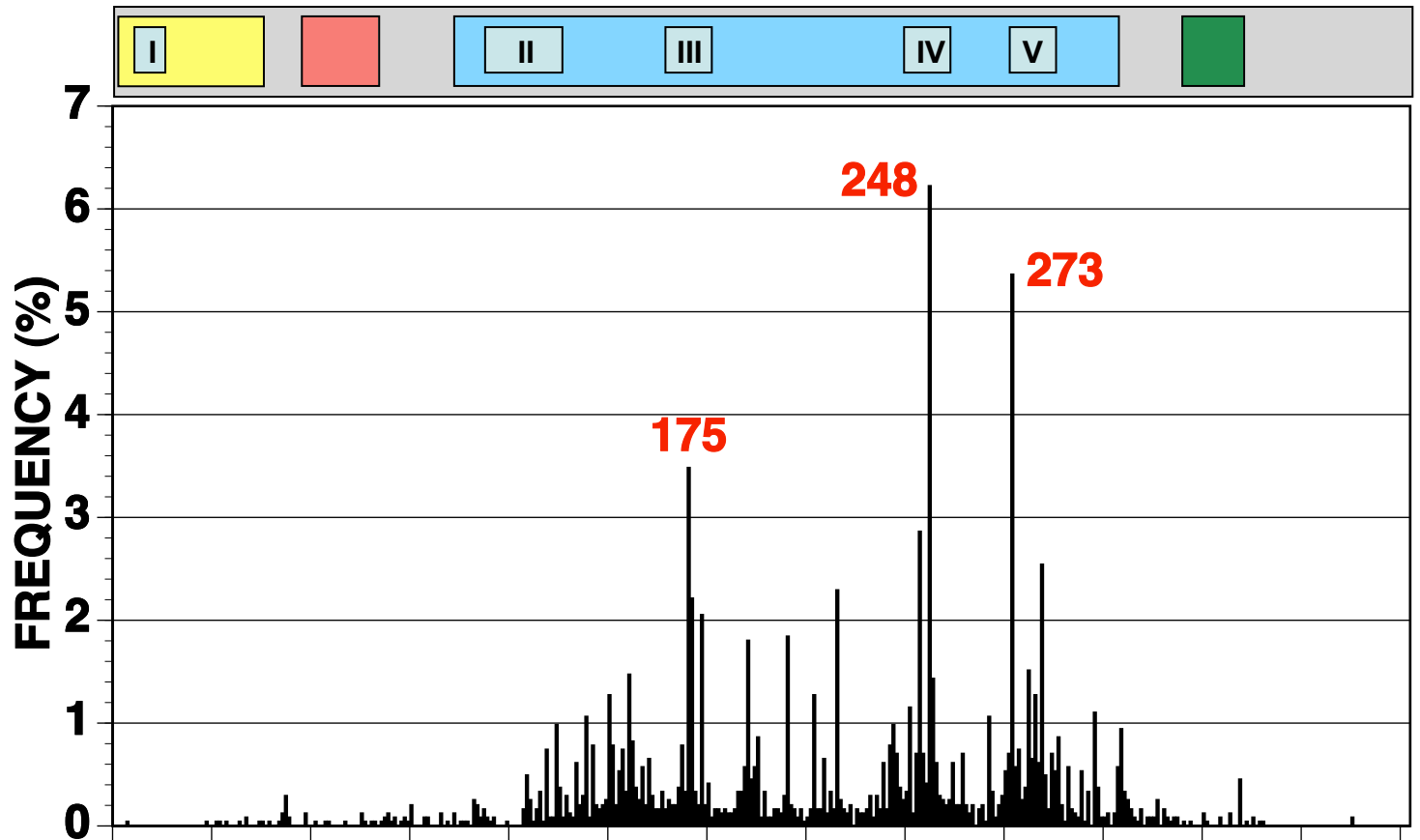
p53 mutational events
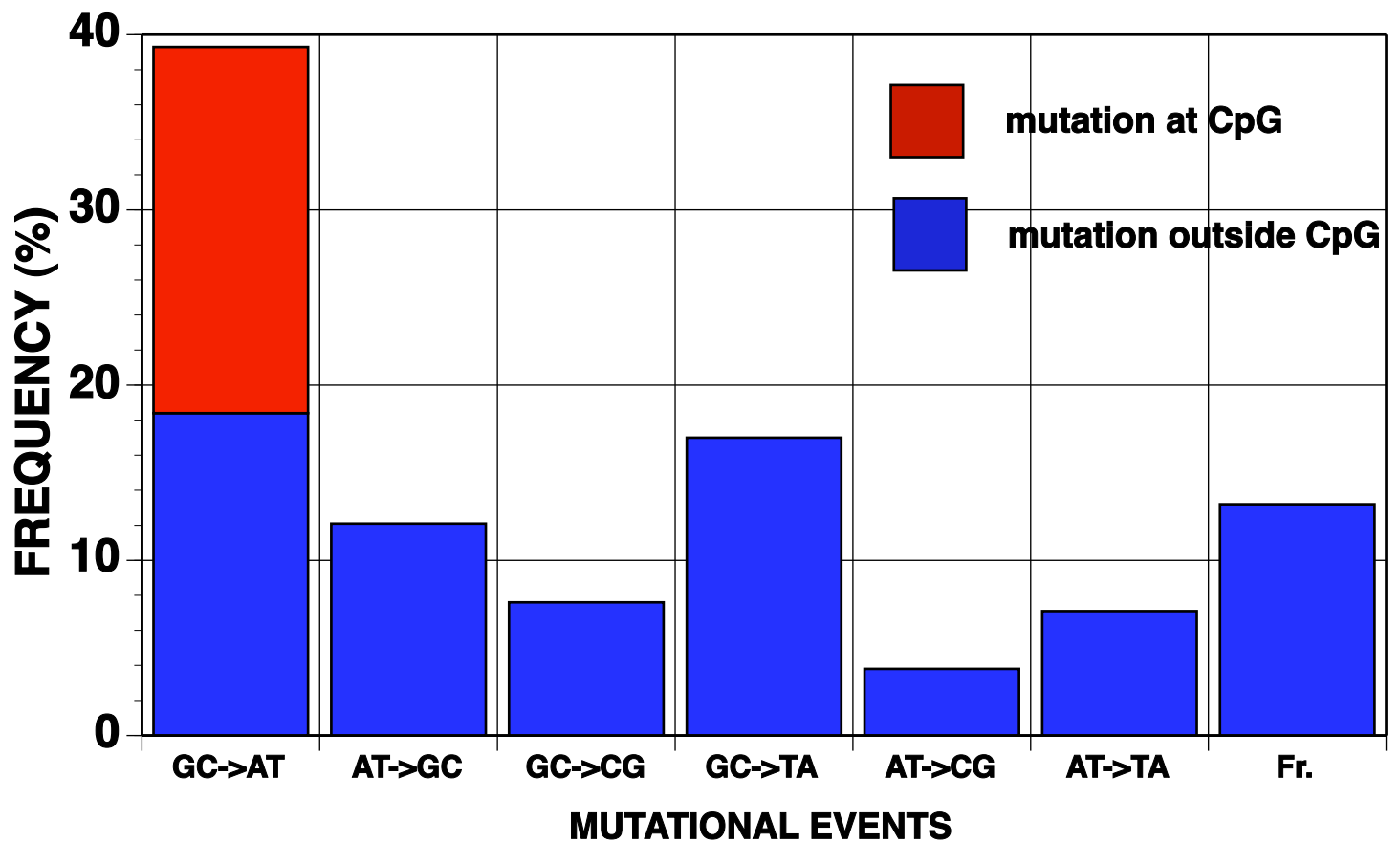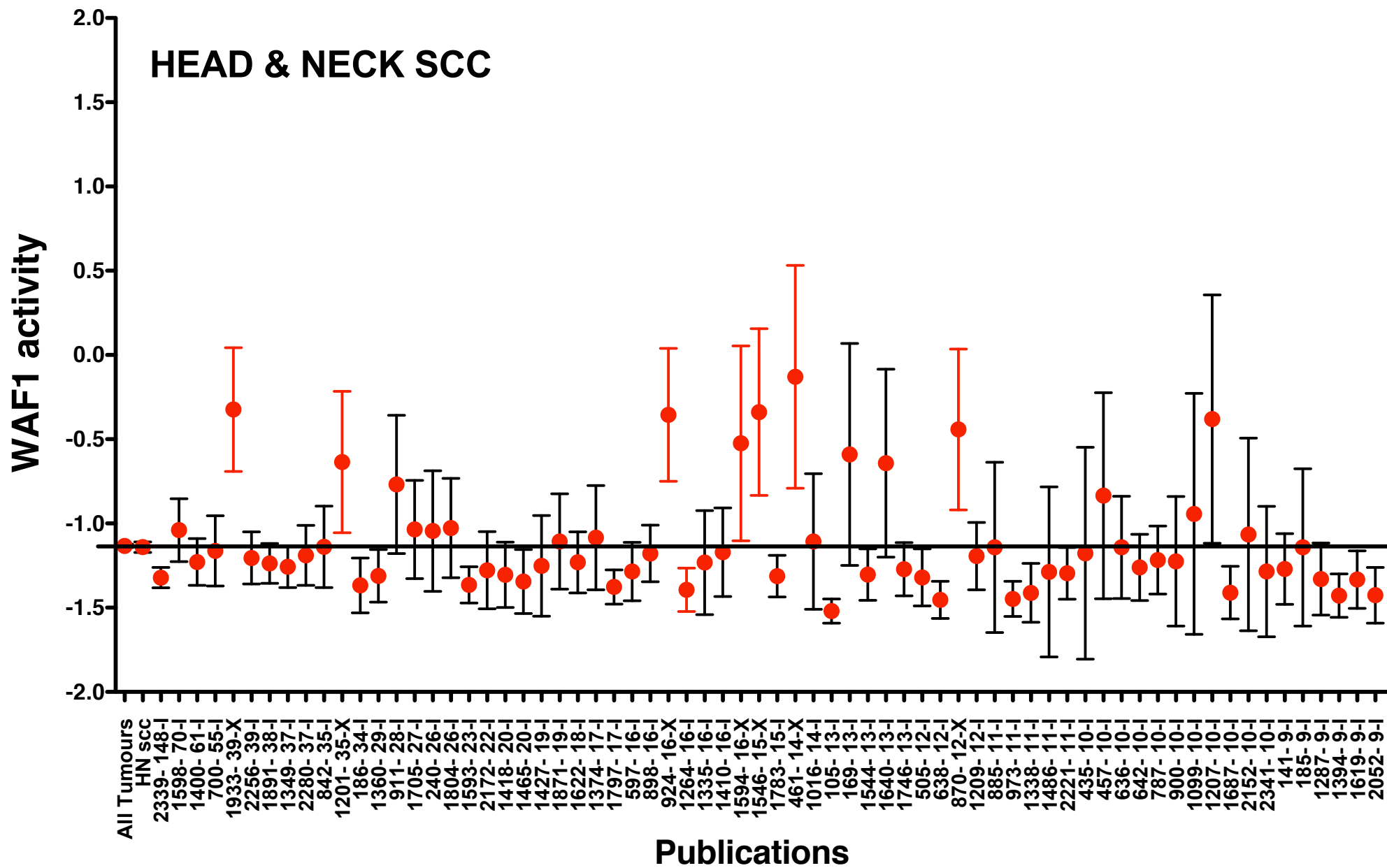
LI-FRAUMENI SYNDROME

Analysis summary

Number of studies	81
Number of tumors	180
Number of mutations	184
Number of tumors with 1 mutation	172
Number of tumors with 2 mutations	2
Number of tumors with more than 2 mutations	1
In studies	81
Out studies 95	0
Out studies 99	0

Strategy of analysis

| I | | II | III | IV | V | | |

Exon 2　Exon 3　Exon 4　Exon 5　Exon 6　Exon 7　Exon 8　Exon 9　Exon 10　Exon 11

Exon 5-8
11 studies

Exon 4-9
2 studies

Exon 2-11
17 studies

Other
51 studies

Prescreening
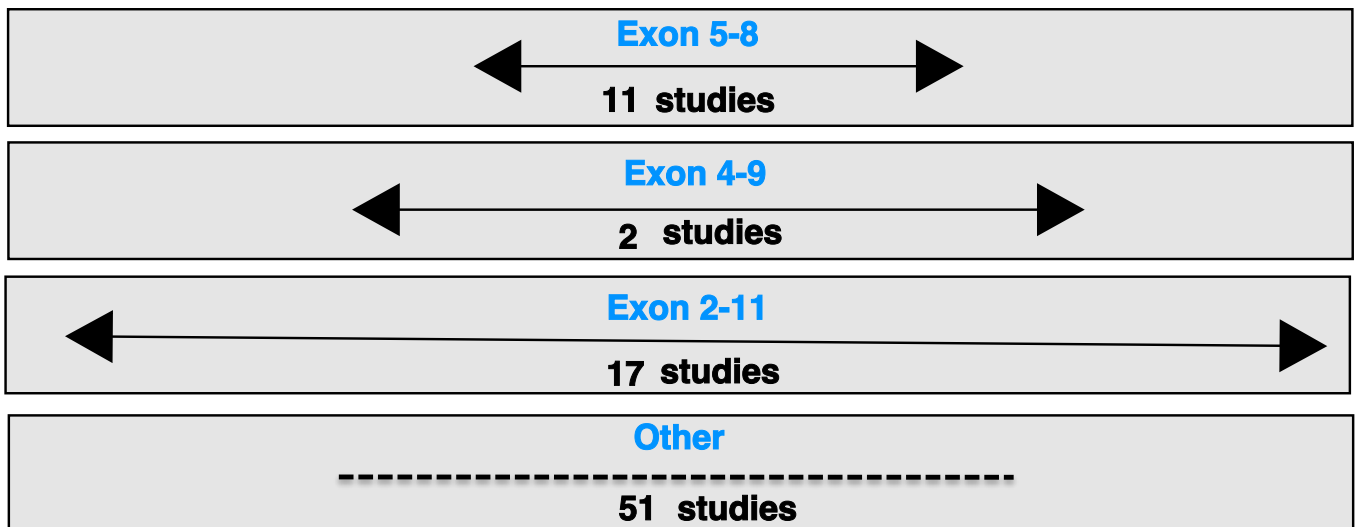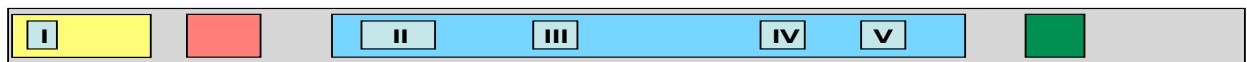
Studies with prescreening	25		Studies without prescreening	56

SSCP	15	IHC	1
DGGE/CDGE	2	dHPLC	0
Yeast Assay	5	Other	2

p53 mutation frequency

Number of missense mutations	143	80%
Number of nonsense mutations	19	11%
Number of frameshift mutations	17	9%
Total number of mutations	179	100%
Number of polymorphisms	0	0%

p53 mutant frequency

Number of missense mutants	49	68%
Number of nonsense mutants	9	13%
Number of frameshift mutants	14	19%
Total number of mutants	72	100%
Number of polymorphisms	0	0%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
248	CGG	CAG	Arg	Gln	Ts	Yes	15
175	CGC	CAC	Arg	His	Ts	Yes	15
248	CGG	TGG	Arg	Trp	Ts	Yes	12
245	GGC	AGC	Gly	Ser	Ts	Yes	11
273	CGT	CAT	Arg	His	Ts	Yes	9
273	CGT	TGT	Arg	Cys	Ts	Yes	7
282	CGG	TGG	Arg	Trp	Ts	Yes	6
213	CGA	TGA	Arg	Stop	Ts	Yes	5
290	CGC	CAC	Arg	His	Ts	Yes	5
267	CGG	CAG	Arg	Gln	Ts	Yes	4

Exon Distribution

EXON 2-4   EXON 5-8   EXON 9-11

EXON 2-4: 60%, 40%, 0%
EXON 5-8: 8%, 10%, 82%
EXON 9-11: 40%, 60%

Frameshift | Nonsense | Missense
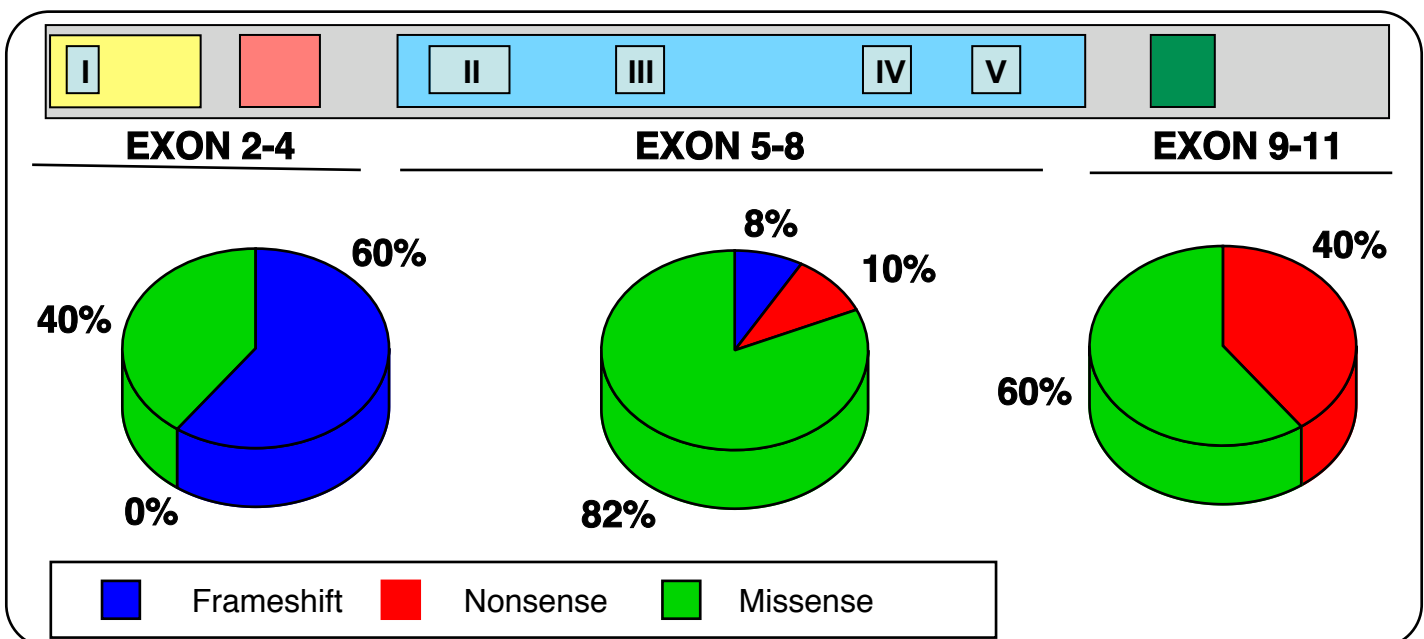
LI-FRAUMENI SYNDROME

p53 mutation distribution
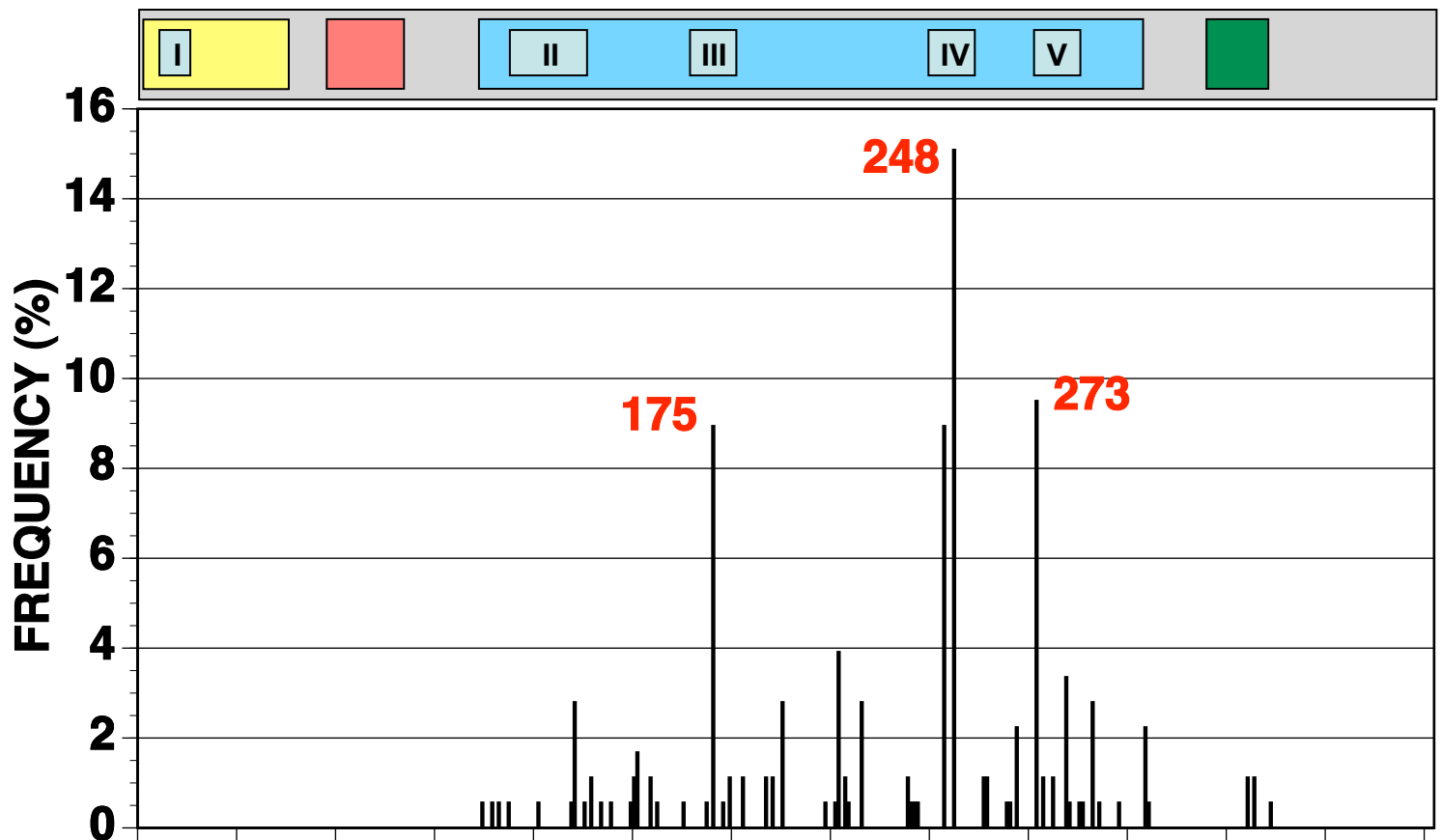
p53 mutational events
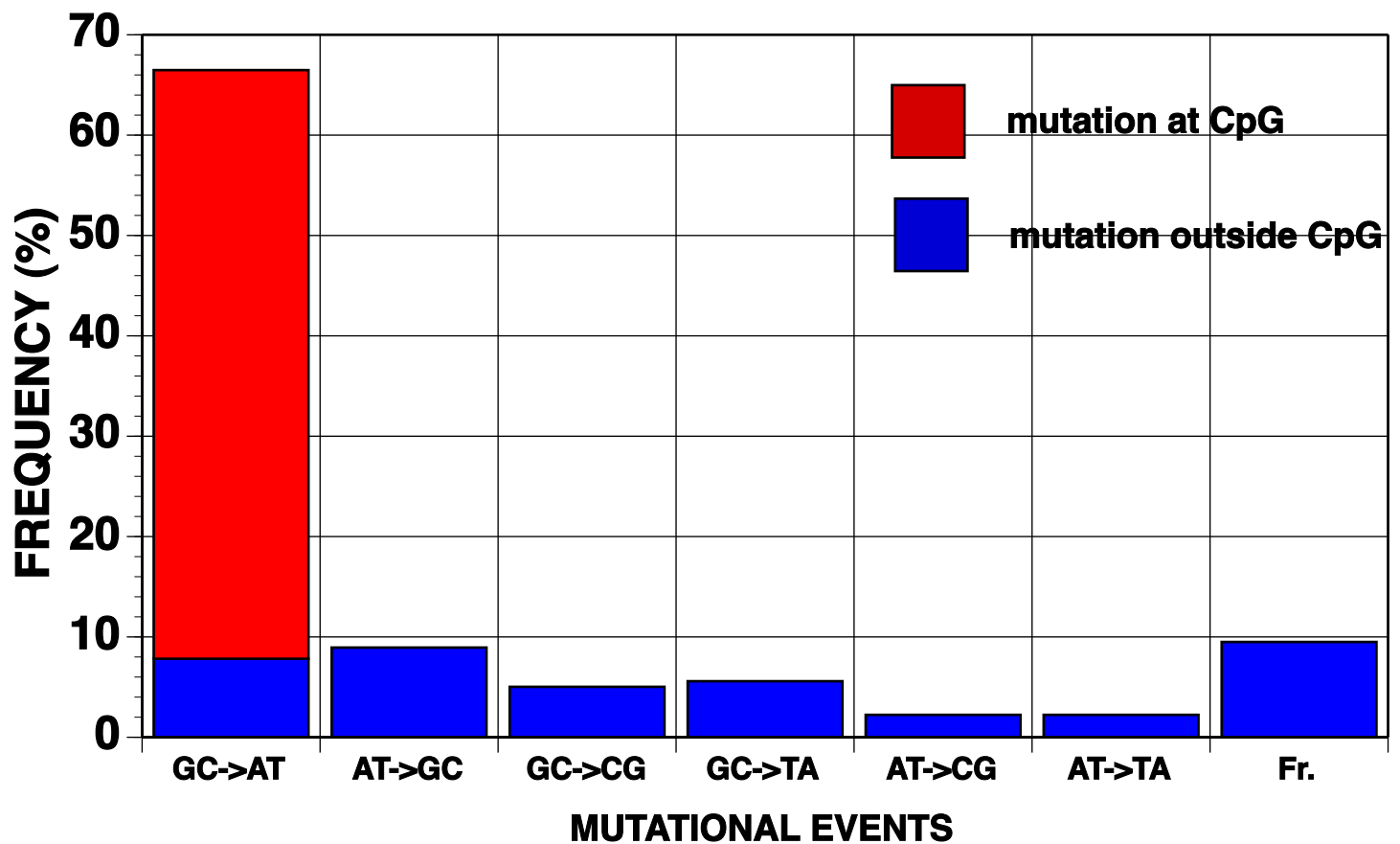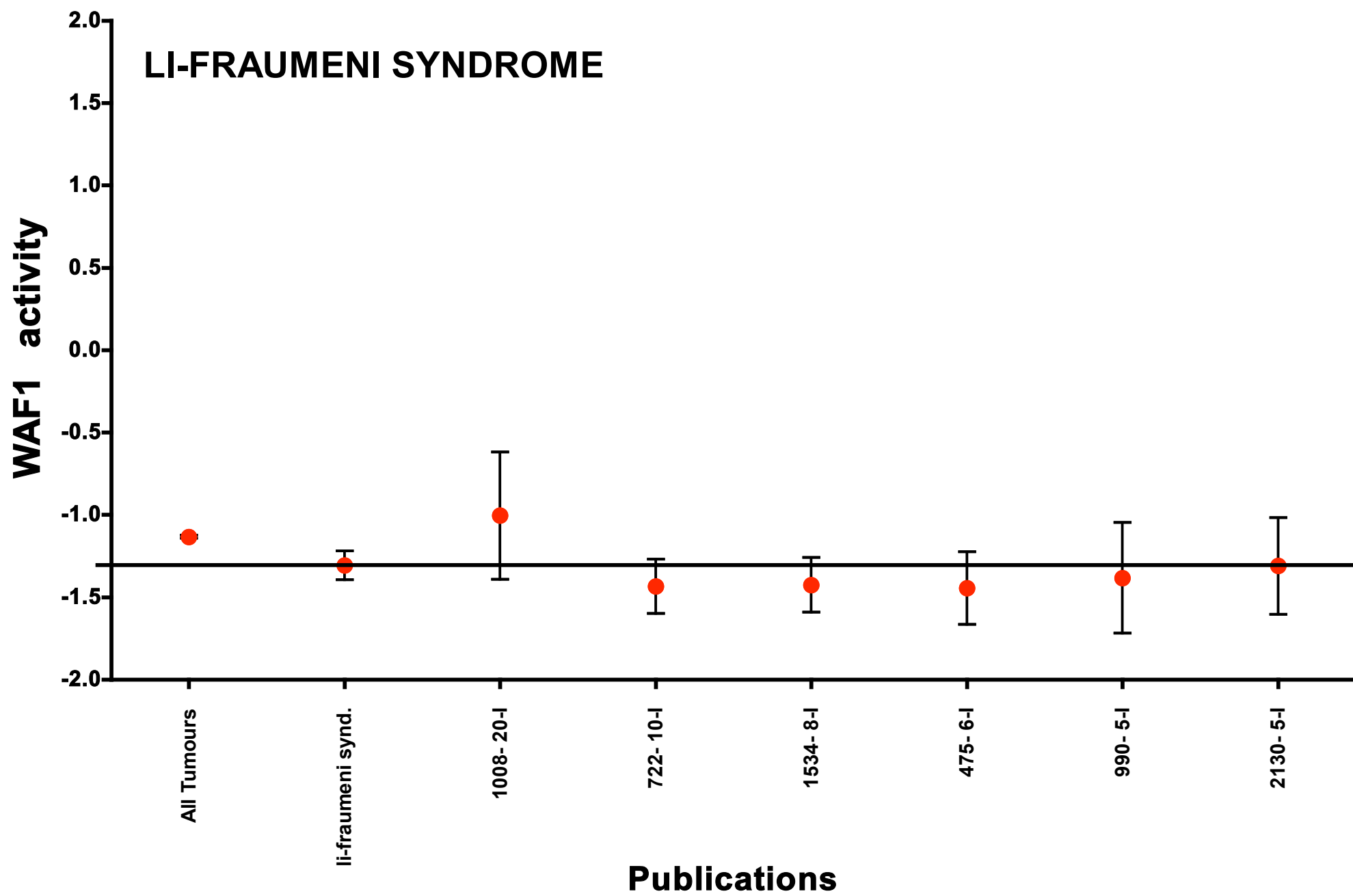
LUNG CANCER (NSCLC)

Analysis summary

Number of studies	167
Number of tumors	2557
Number of mutations	2770
Number of tumors with 1 mutation	2358
Number of tumors with 2 mutations	108
Number of tumors with more than 2 mutations	22
In studies	163
Out studies 95	2
Out studies 99	2

Strategy of analysis

Exon 5-8

62 studies

Exon 4-9

9 studies

Exon 2-11

23 studies

Other

----
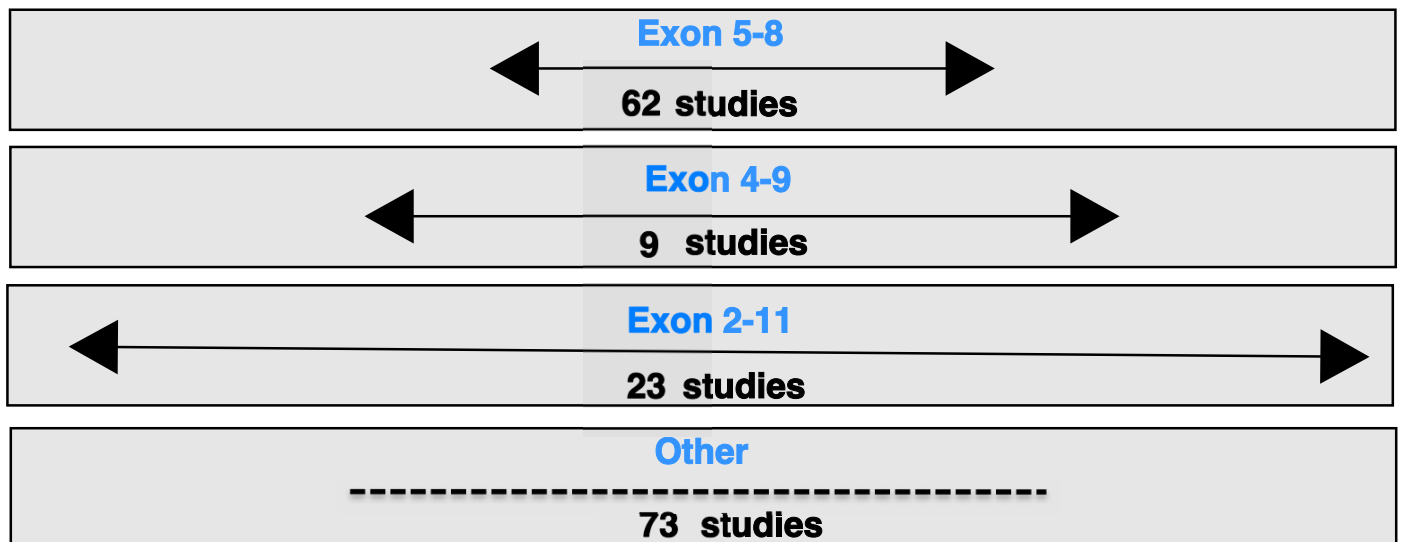
73 studies

Prescreening

Studies with prescreening	**94**		Studies without prescreening	**73**

SSCP	75	IHC	1
DGGE/CDGE	15	dHPLC	1
Yeast Assay	2	Other	1

LUNG CANCER (NSCLC)

p53 mutation frequency

Number of missense mutations	2183	81%
Number of nonsense mutations	241	9%
Number of frameshift mutations	277	10%
Total number of mutations	2701	100%
Number of polymorphisms	109	4%

p53 mutant frequency

Number of missense mutants	565	72%
Number of nonsense mutants	52	7%
Number of frameshift mutants	168	21%
Total number of mutants	785	100%
Number of polymorphisms	63	8%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
249	AGG	AGT	Arg	Ser	Tv	No	59
158	CGC	CTC	Arg	Leu	Tv	No	58
273	CGT	CTT	Arg	Leu	Tv	No	57
248	CGG	CTG	Arg	Leu	Tv	No	57
157	GTC	TTC	Val	Phe	Tv	No	51
220	TAT	TGT	Tyr	Cys	Ts	No	46
248	CGG	TGG	Arg	Trp	Ts	Yes	43
273	CGT	CAT	Arg	His	Ts	Yes	41
175	CGC	CAC	Arg	His	Ts	Yes	40
245	GGC	TGC	Gly	Cys	Tv	No	38

Exon Distribution

| I | | II | III | IV | V | |

EXON 2-4
- 30% Frameshift
- 20% Nonsense
- 50% Missense

EXON 5-8
- 9% Frameshift
- 8% Nonsense
- 82% Missense

EXON 9-11
- 16% Frameshift
- 29% Nonsense
- 55% Missense

Legend: Frameshift (blue), Nonsense (red), Missense (green)
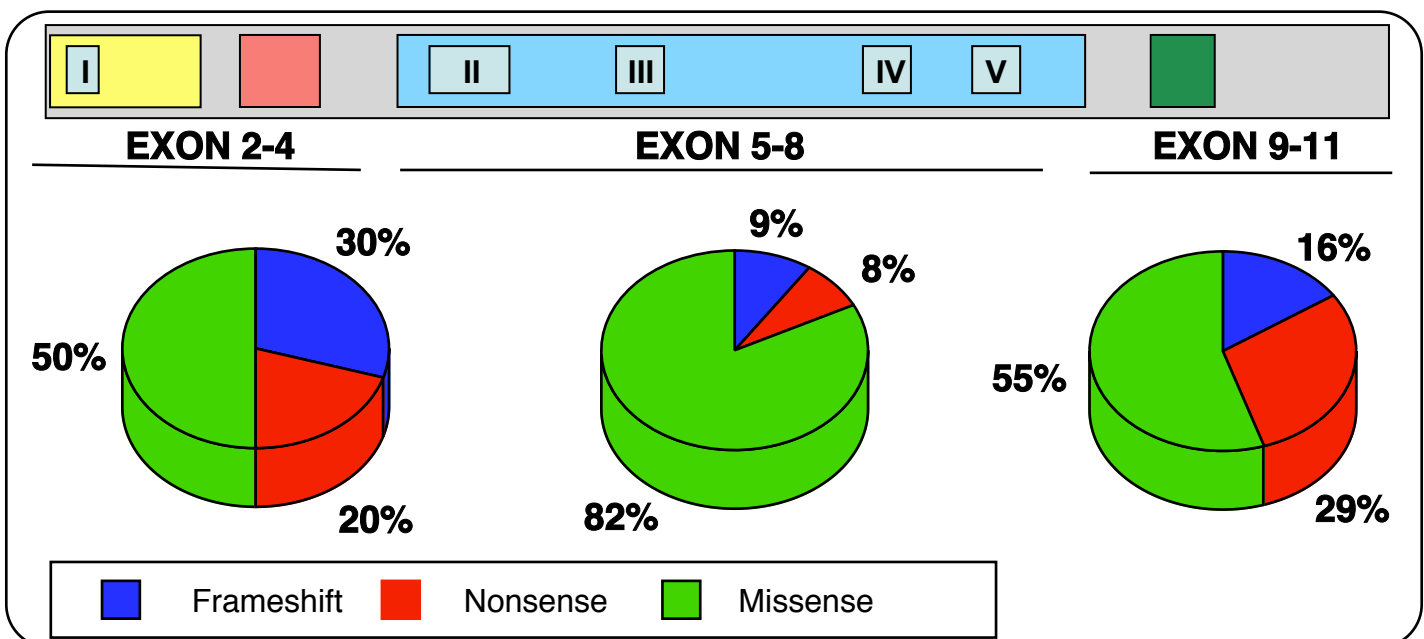
LUNG CANCER (NSCLC)

p53 mutation distribution
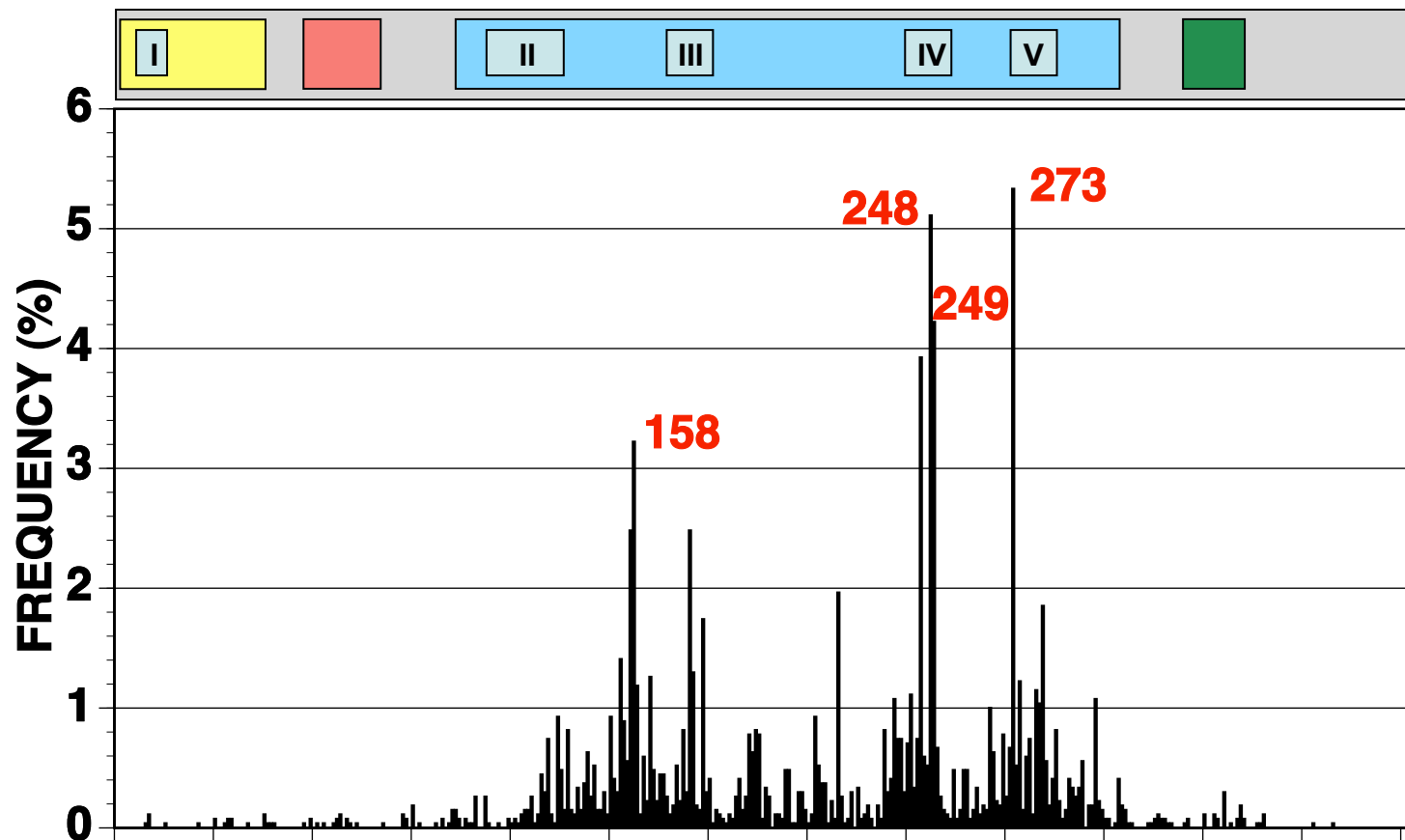
p53 mutational events
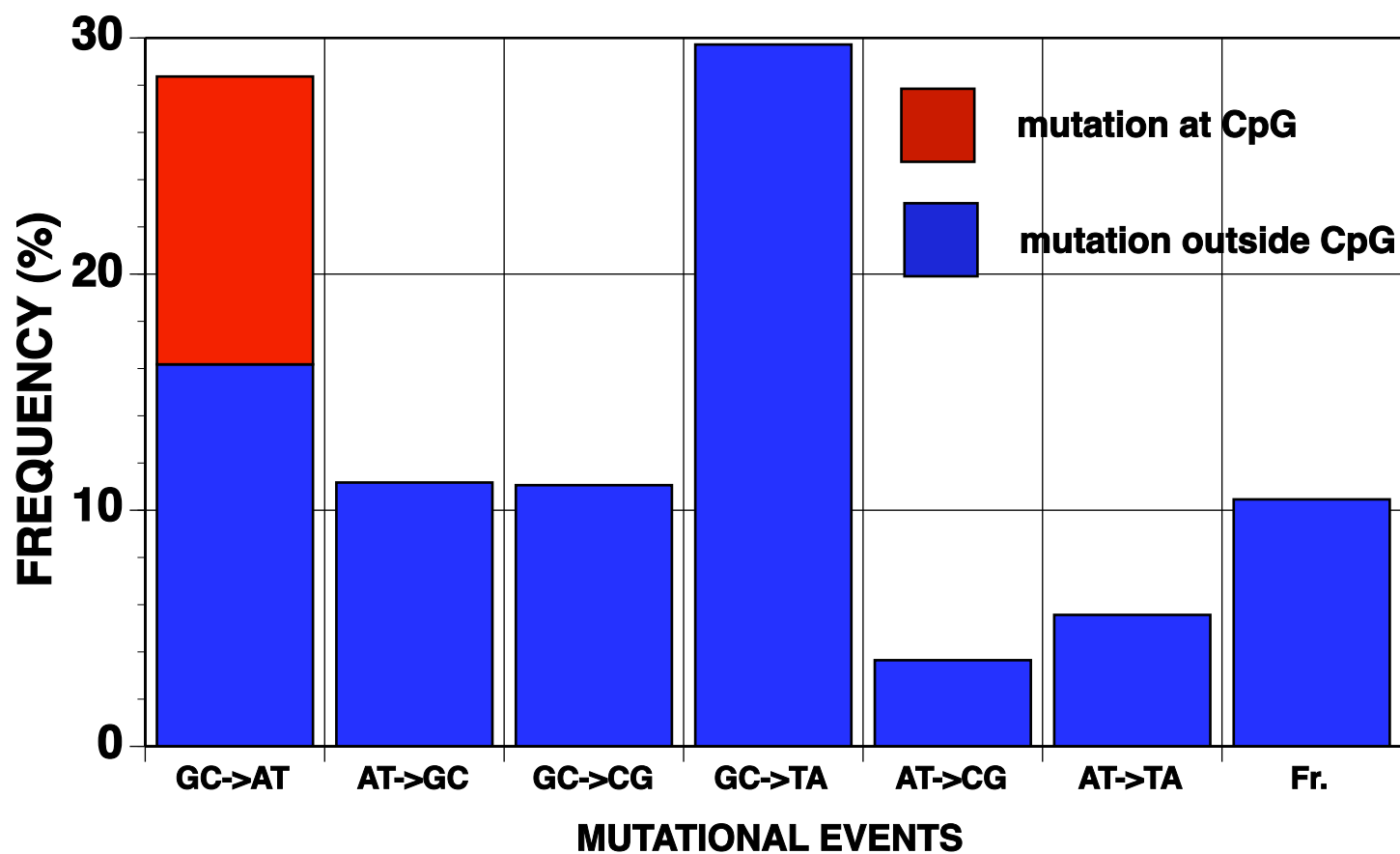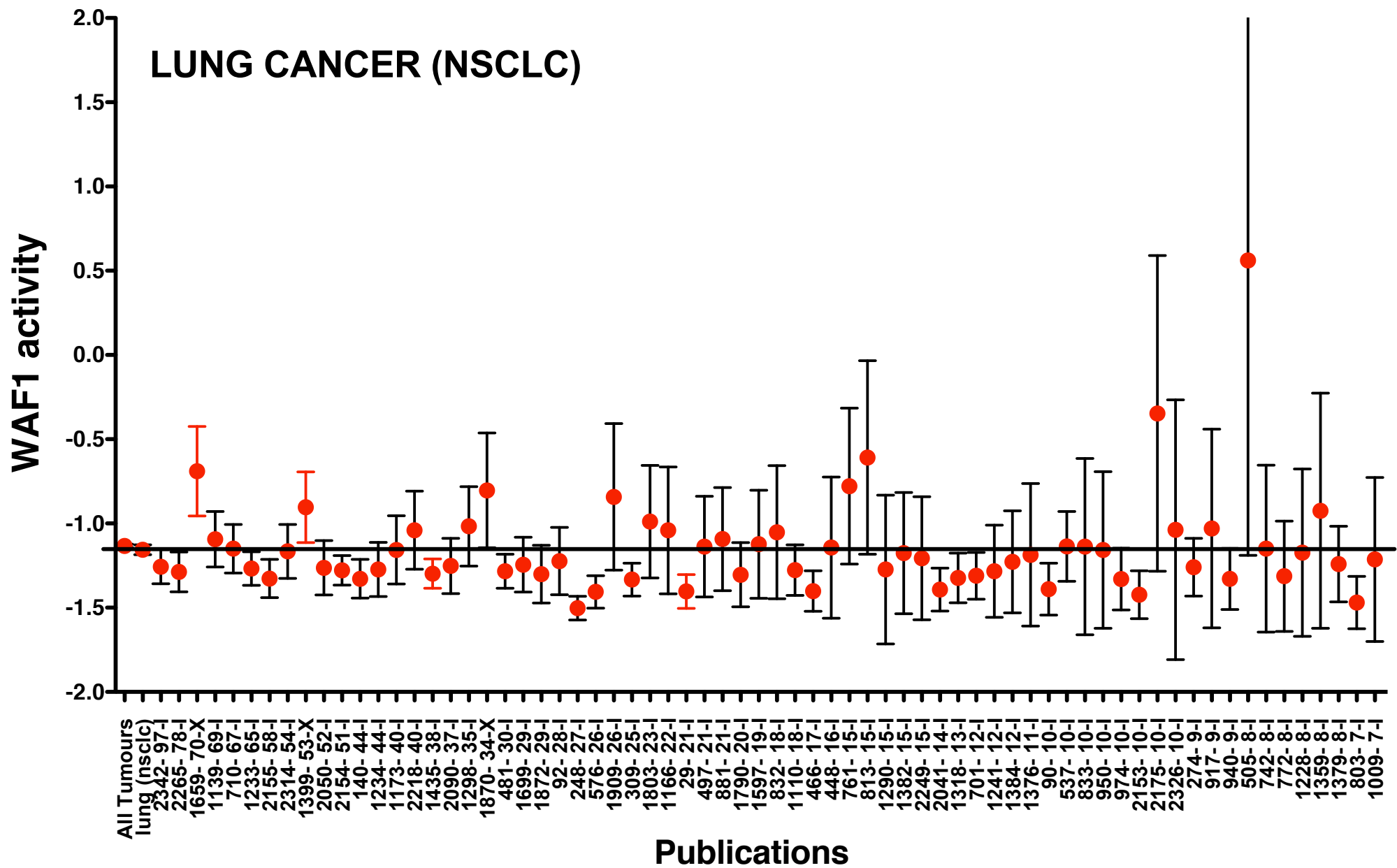
LUNG CANCER (NSCLC)

LUNG CANCER (SCLC)

Analysis summary

Number of studies	48
Number of tumors	255
Number of mutations	266
Number of tumors with 1 mutation	233
Number of tumors with 2 mutations	8
Number of tumors with more than 2 mutations	1
In studies	46
Out studies 95	0
Out studies 99	2

Strategy of analysis

Exon 2   Exon 3   Exon 4   Exon 5   Exon 6   Exon 7   Exon 8   Exon 9   Exon 10   Exon 11

Exon 5-8
16 studies

Exon 4-9
4 studies

Exon 2-11
10 studies

Other
18 studies

Prescreening
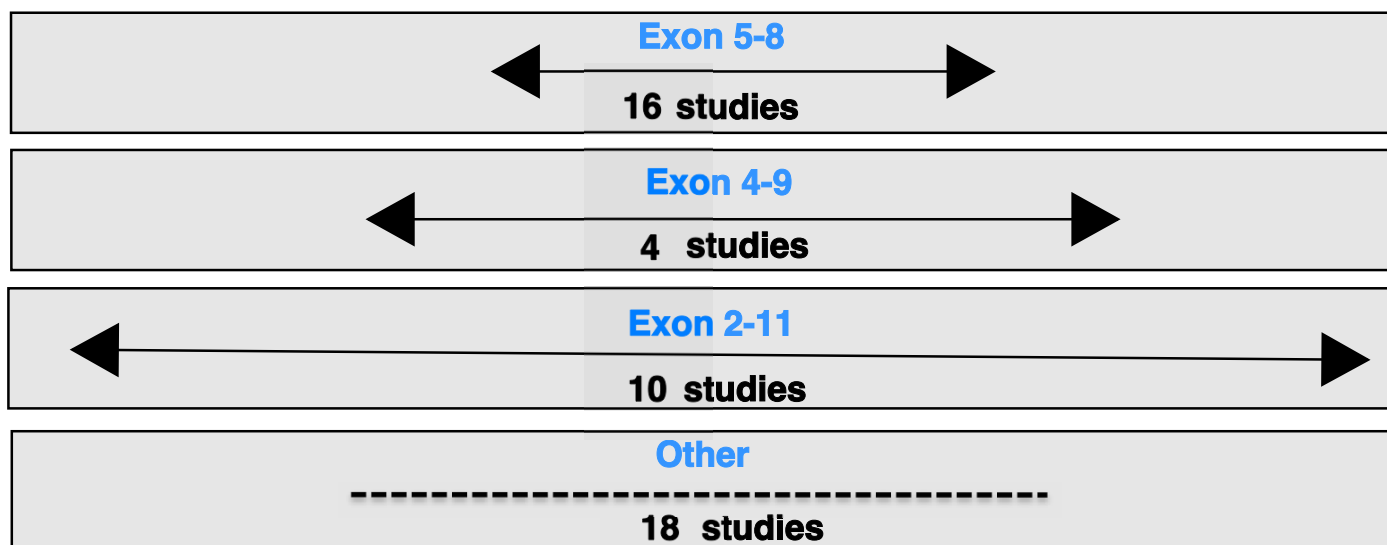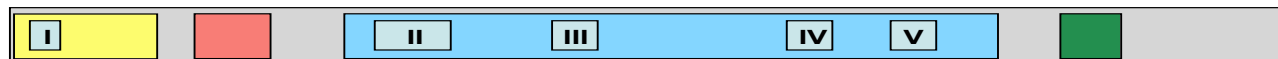
Studies with prescreening	28			Studies without prescreening	20
SSCP	19	IHC	1		
DGGE/CDGE	6	dHPLC	1		
Yeast Assay	1	Other	1		

LUNG CANCER (SCLC)

p53 mutation frequency

Number of missense mutations	201	80%
Number of nonsense mutations	27	11%
Number of frameshift mutations	23	9%
Total number of mutations	251	100%
Number of polymorphisms	9	4%

p53 mutant frequency

Number of missense mutants	111	74%
Number of nonsense mutants	17	11%
Number of frameshift mutants	21	14%
Total number of mutants	149	100%
Number of polymorphisms	8	5%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
248	CGG	CTG	Arg	Leu	Tv	No	12
157	GTC	TTC	Val	Phe	Tv	No	10
249	AGG	AGT	Arg	Ser	Tv	No	7
273	CGT	CTT	Arg	Leu	Tv	No	5
175	CGC	CAC	Arg	His	Ts	Yes	5
158	CGC	CTC	Arg	Leu	Tv	No	5
298	GAG	TAG	Glu	Stop	Tv	No	5
244	GGC	TGC	Gly	Cys	Tv	No	4
278	CCT	CTT	Pro	Leu	Ts	No	4
273	CGT	TGT	Arg	Cys	Ts	Yes	4
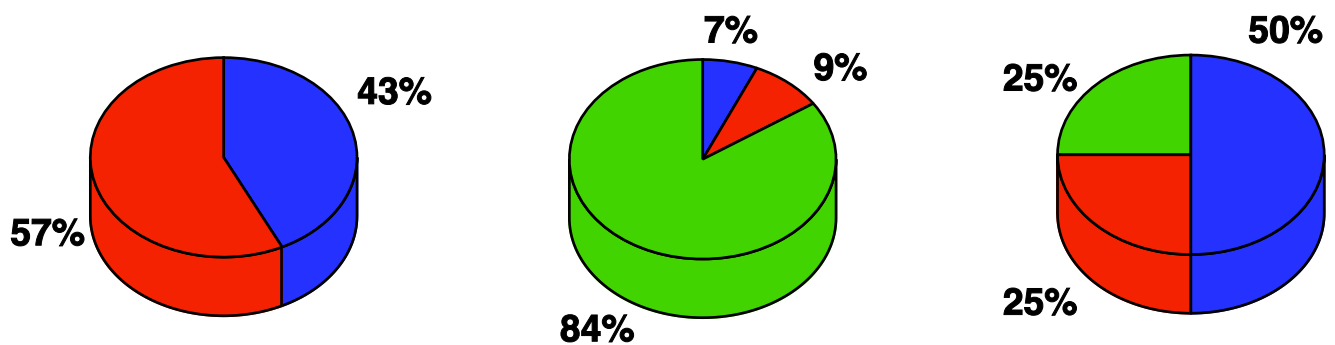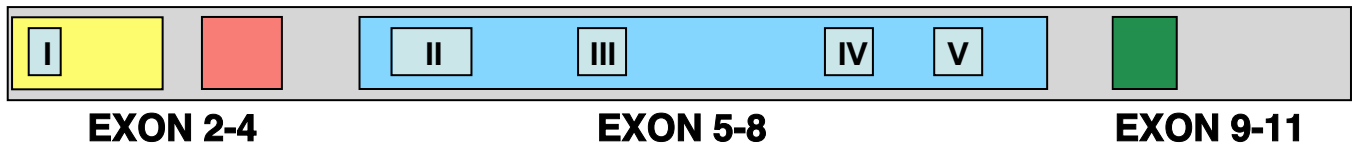
Exon Distribution

EXON 2-4: 43% Frameshift, 57% Nonsense

EXON 5-8: 7% Frameshift, 9% Nonsense, 84% Missense

EXON 9-11: 50% Frameshift, 25% Nonsense, 25% Missense

Legend: Frameshift (blue), Nonsense (red), Missense (green)

LUNG CANCER (SCLC)

p53 mutation distribution

p53 CODON

p53 mutational events

mutation at CpG

mutation outside CpG
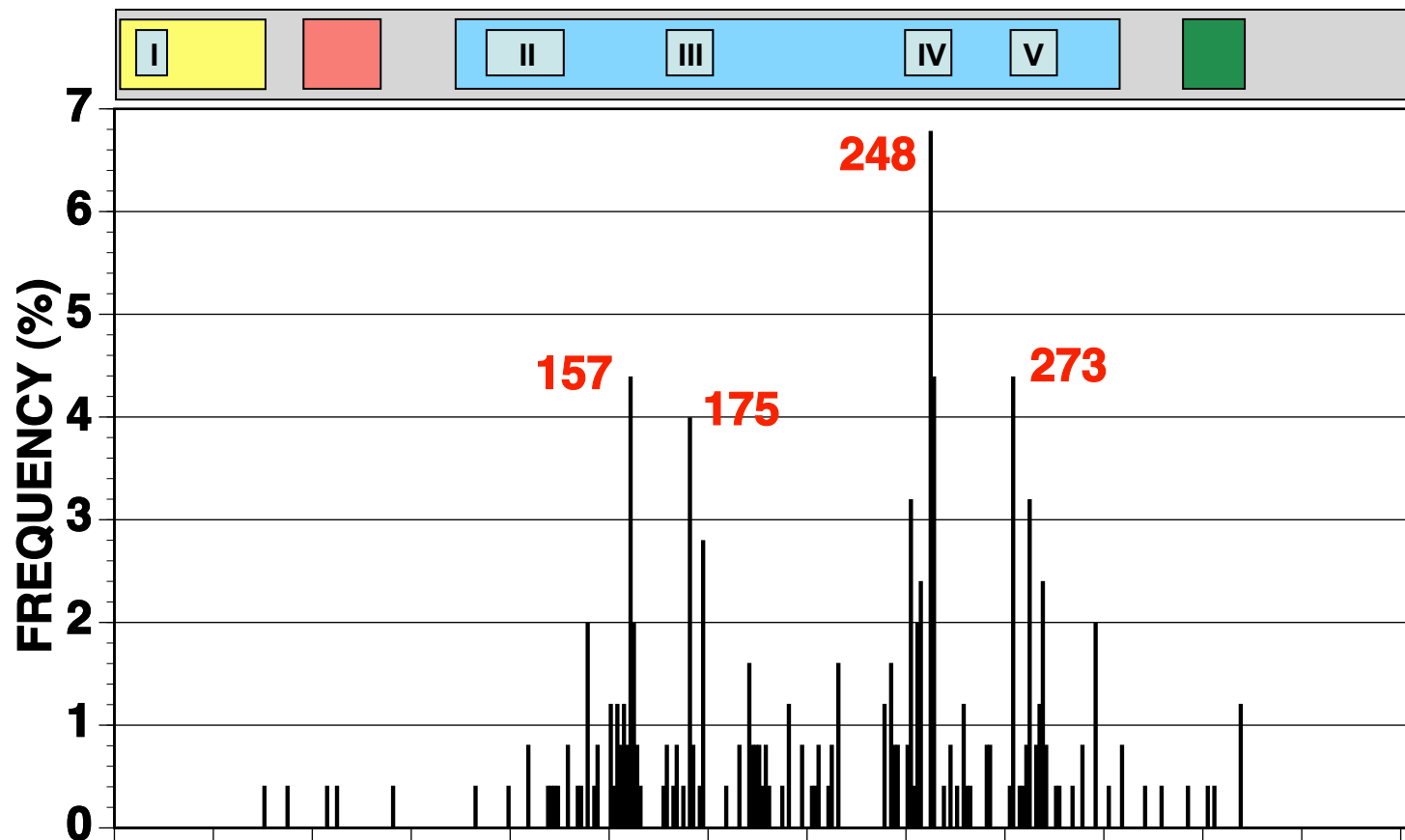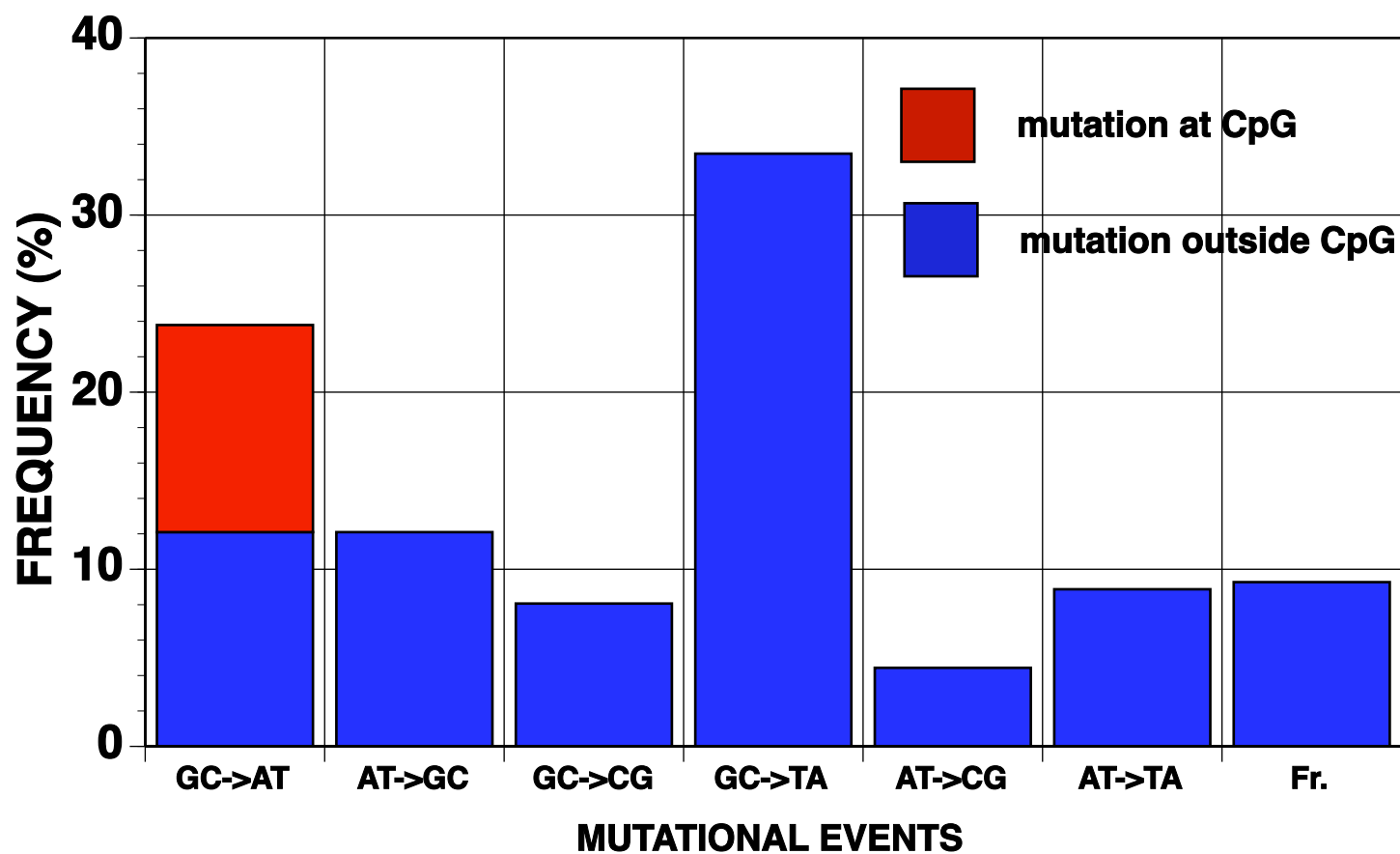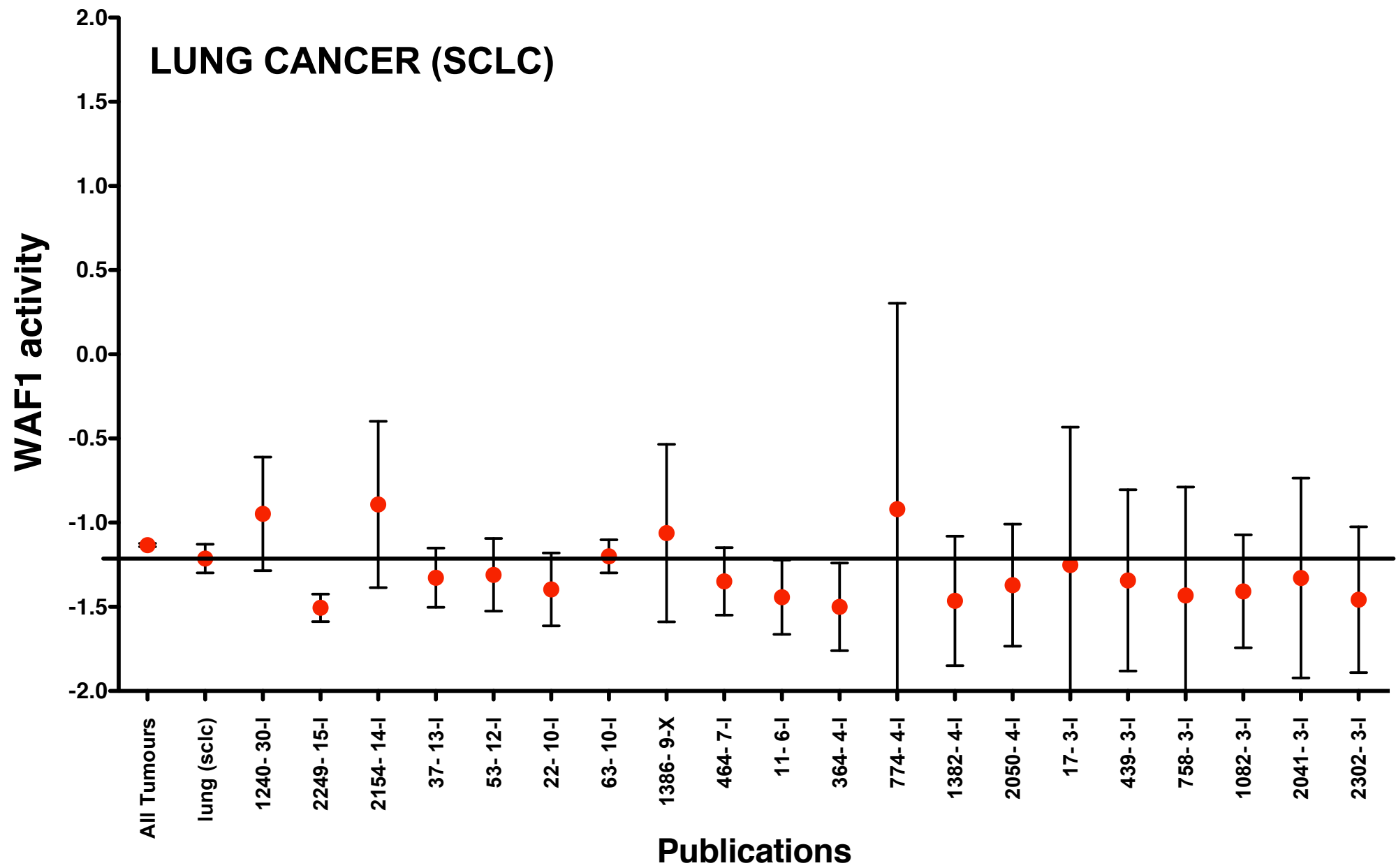
MELANOMA

Analysis summary

Number of studies	26
Number of tumors	106
Number of mutations	128
Number of tumors with 1 mutation	95
Number of tumors with 2 mutations	8
Number of tumors with more than 2 mutations	3
In studies	24
Out studies 95	2
Out studies 99	0

Strategy of analysis

Exon 2 Exon 3 Exon 4 Exon 5 Exon 6 Exon 7 Exon 8 Exon 9 Exon 10 Exon 11

Exon 5-8
3 studies

Exon 4-9
5 studies

Exon 2-11
1 studies

Other
17 studies

Prescreening
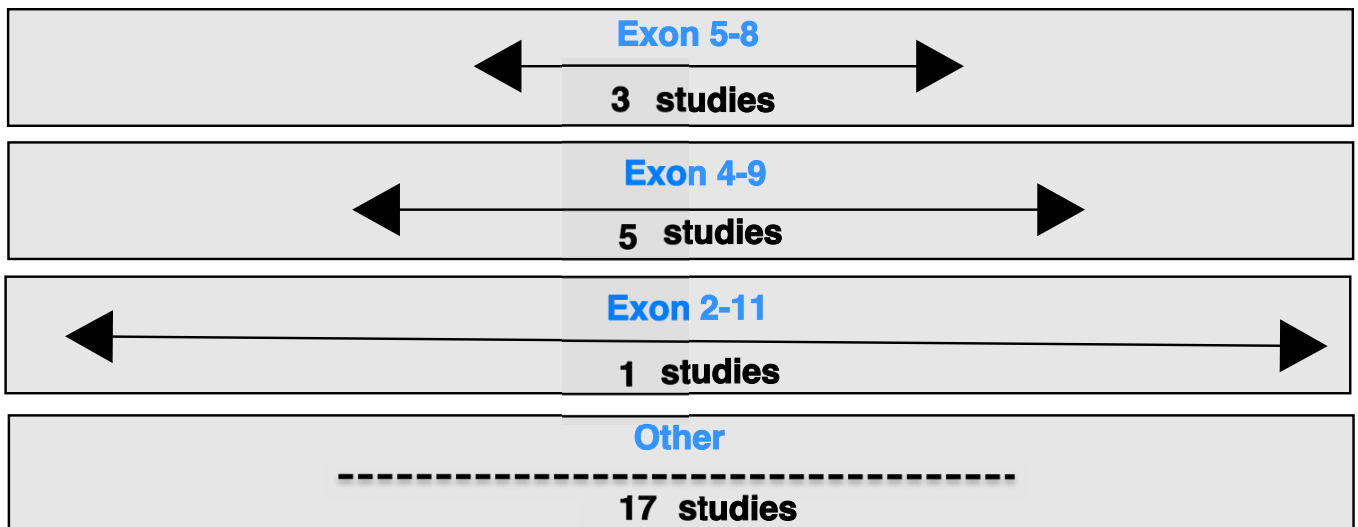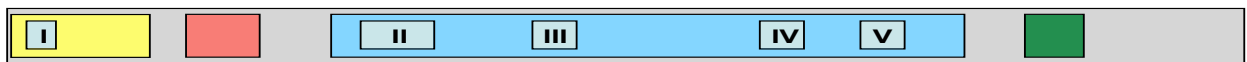
Studies with prescreening	12		Studies without prescreening	14

SSCP	9	IHC	0	
DGGE/CDGE	2	dHPLC	0	
Yeast Assay	0	Other	1	

MELANOMA

p53 mutation frequency

Number of missense mutations	113	88%
Number of nonsense mutations	9	7%
Number of frameshift mutations	7	5%
Total number of mutations	129	100%
Number of polymorphisms	19	15%

p53 mutant frequency

Number of missense mutants	96	86%
Number of nonsense mutants	8	7%
Number of frameshift mutants	7	6%
Total number of mutants	111	100%
Number of polymorphisms	18	16%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
248	CGG	TGG	Arg	Trp	Ts	Yes	5
266	GGA	GAA	Gly	Glu	Ts	No	4
258	GAA	AAA	Glu	Lys	Ts	No	4
290	CGC	CAC	Arg	His	Ts	Yes	3
177	CCC	TCC	Pro	Ser	Ts	No	3
213	CGA	TGA	Arg	Stop	Ts	Yes	2
187	GGT	AGT	Gly	Ser	Ts	No	2
247	AAC	AAT	Asn	Asn	Ts	No	2
127	TCC	TTC	Ser	Phe	Ts	No	2
220	TAT	TGT	Tyr	Cys	Ts	No	1

Exon Distribution

EXON 2-4   EXON 5-8   EXON 9-11

EXON 2-4: 8%, 15%, 77%

EXON 5-8: 4%, 5%, 92%

EXON 9-11: 29%, 29%, 43%

Frameshift | Nonsense | Missense
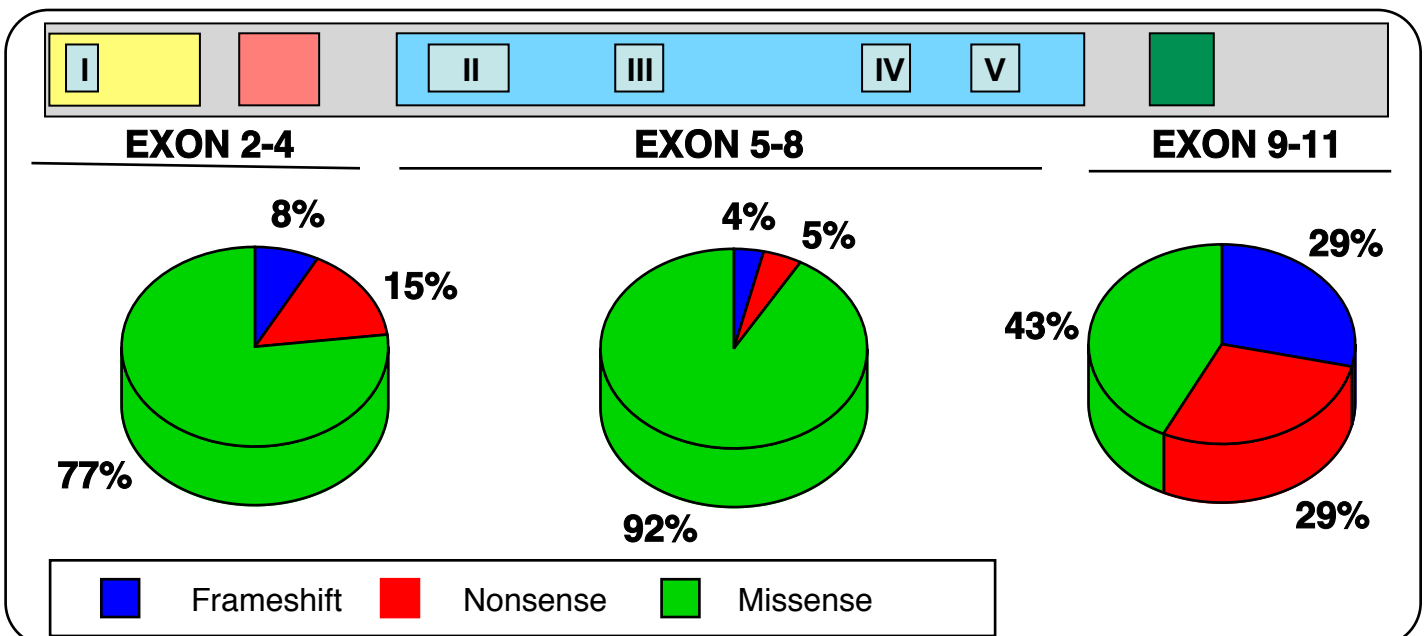
MELANOMA

p53 mutation distribution
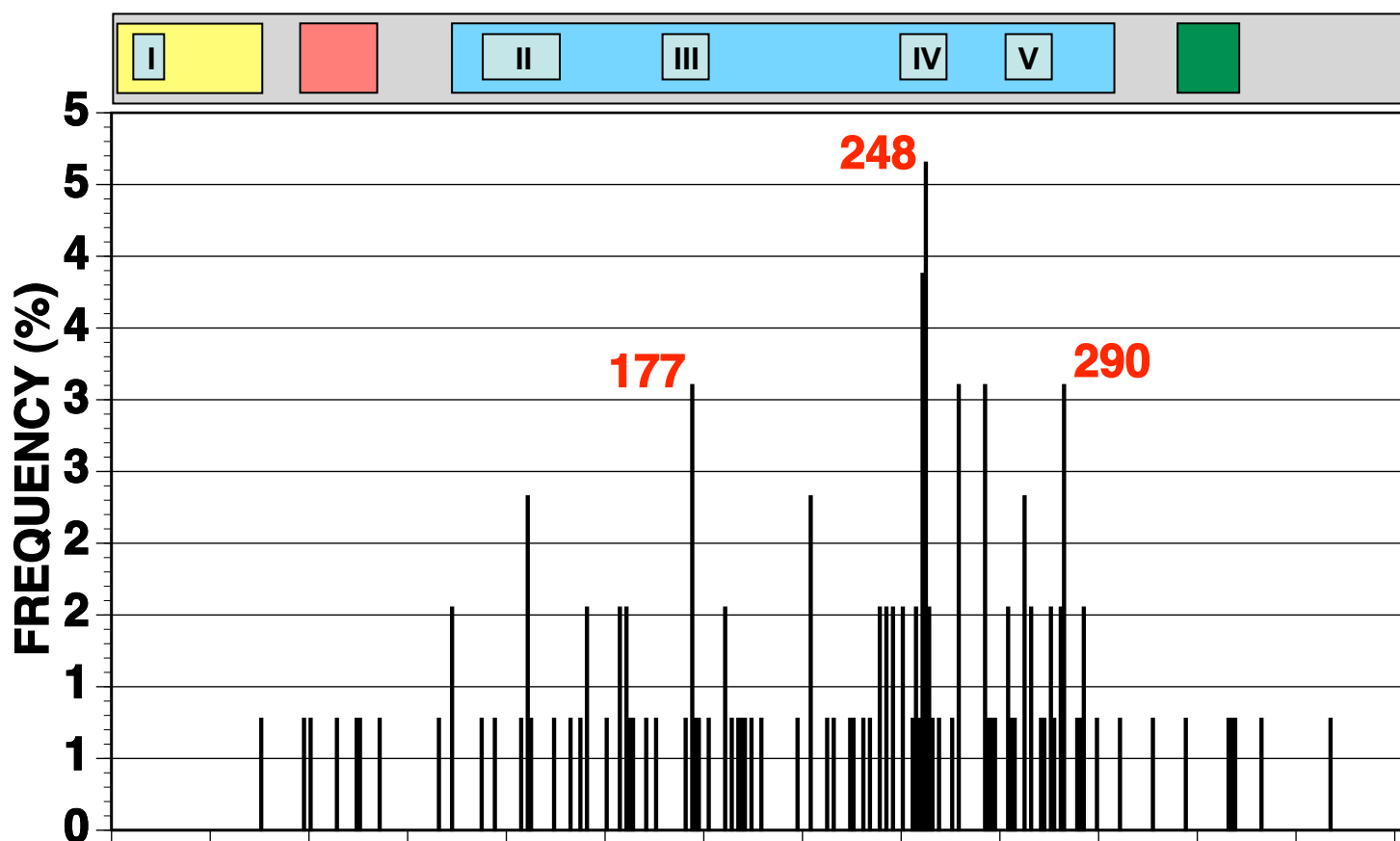
p53 mutational events
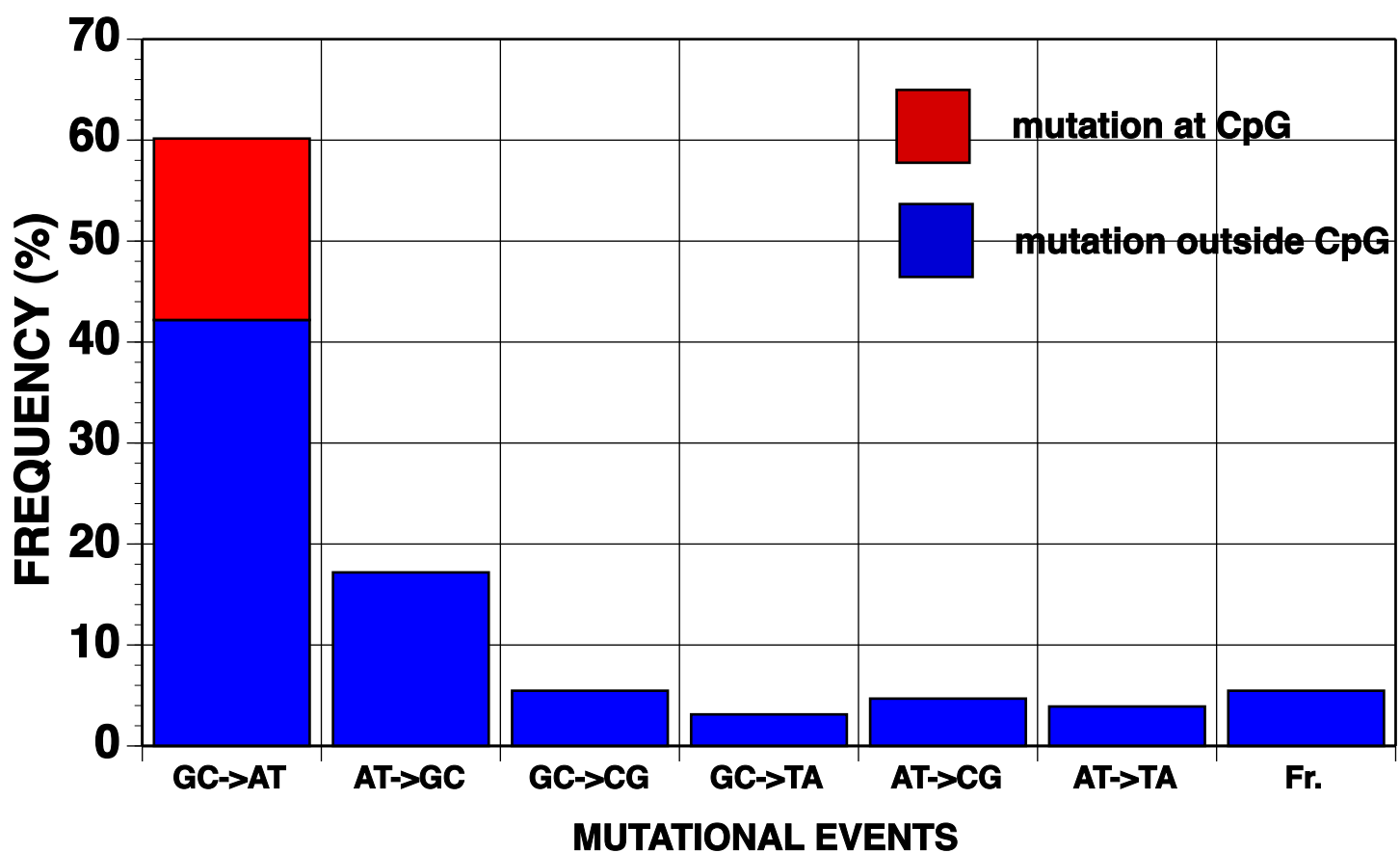
OSTEOSARCOMA

Analysis summary

Number of studies	44
Number of tumors	191
Number of mutations	195
Number of tumors with 1 mutation	187
Number of tumors with 2 mutations	3
Number of tumors with more than 2 mutations	0
In studies	44
Out studies 95	0
Out studies 99	0

Strategy of analysis

Exon 2 Exon 3 Exon 4 Exon 5 Exon 6 Exon 7 Exon 8 Exon 9 Exon 10 Exon 11

Exon 5-8
7 studies

Exon 4-9
1 studies

Exon 2-11
7 studies

Other
----
29 studies

Prescreening
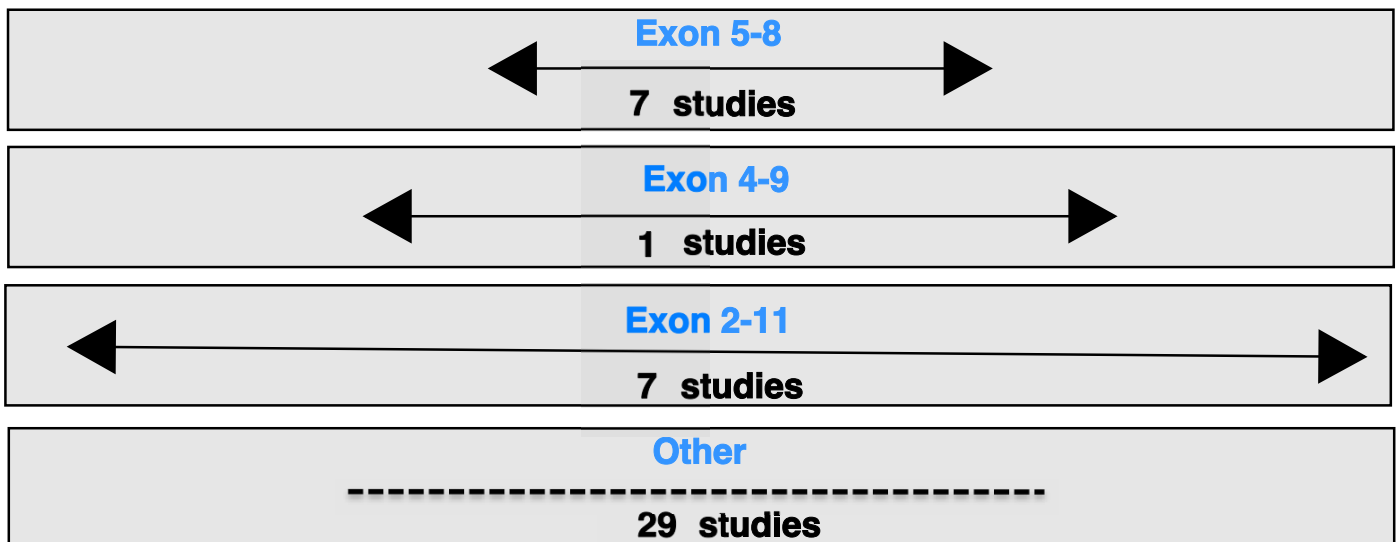
Studies with prescreening	28			Studies without prescreening	16

SSCP	22	IHC	0	
DGGE/CDGE	6	dHPLC	0	
Yeast Assay	0	Other	0	

OSTEOSARCOMA

p53 mutation frequency

Number of missense mutations	140	72%
Number of nonsense mutations	20	10%
Number of frameshift mutations	34	18%
Total number of mutations	194	100%
Number of polymorphisms	2	1%

p53 mutant frequency

Number of missense mutants	72	63%
Number of nonsense mutants	14	12%
Number of frameshift mutants	29	25%
Total number of mutants	115	100%
Number of polymorphisms	2	2%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
248	CGG	CAG	Arg	Gln	Ts	Yes	10
273	CGT	CAT	Arg	His	Ts	Yes	9
175	CGC	CAC	Arg	His	Ts	Yes	8
282	CGG	TGG	Arg	Trp	Ts	Yes	6
237	ATG	ATT	Met	Ile	Tv	No	6
245	GGC	AGC	Gly	Ser	Ts	Yes	4
281	GAC	AAC	Asp	Asn	Ts	No	4
281	GAC	CAC	Asp	His	Tv	No	4
242	TGC	TAC	Cys	Tyr	Ts	No	4
273	CGT	TGT	Arg	Cys	Ts	Yes	4
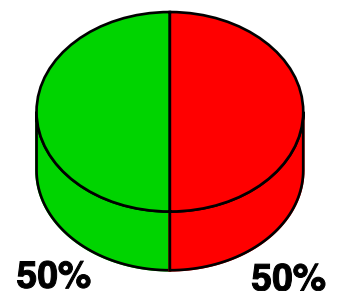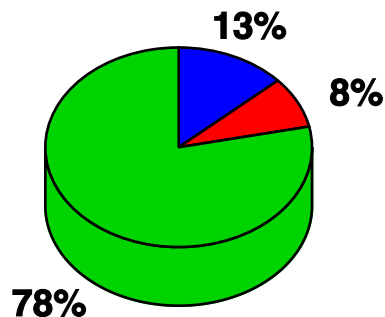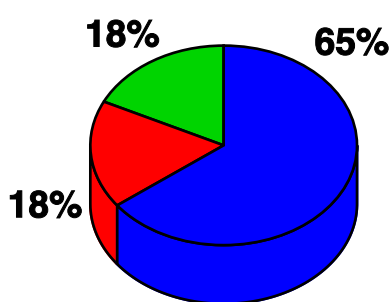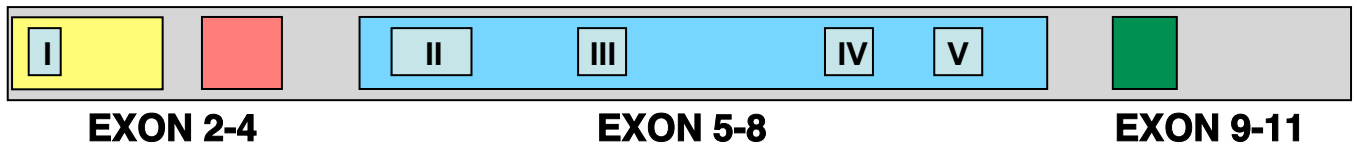
Exon Distribution

EXON 2-4: 65% Frameshift, 18% Nonsense, 18% Missense

EXON 5-8: 13% Frameshift, 8% Nonsense, 78% Missense

EXON 9-11: 50% Nonsense, 50% Missense

Legend: Frameshift (blue), Nonsense (red), Missense (green)

OSTEOSARCOMA

p53 mutation distribution

I   II   III   IV   V

248   273   281   175

FREQUENCY (%)

p53 CODON

p53 mutational events

FREQUENCY (%)

mutation at CpG
mutation outside CpG

GC->AT   AT->GC   GC->CG   GC->TA   AT->CG   AT->TA   Fr.
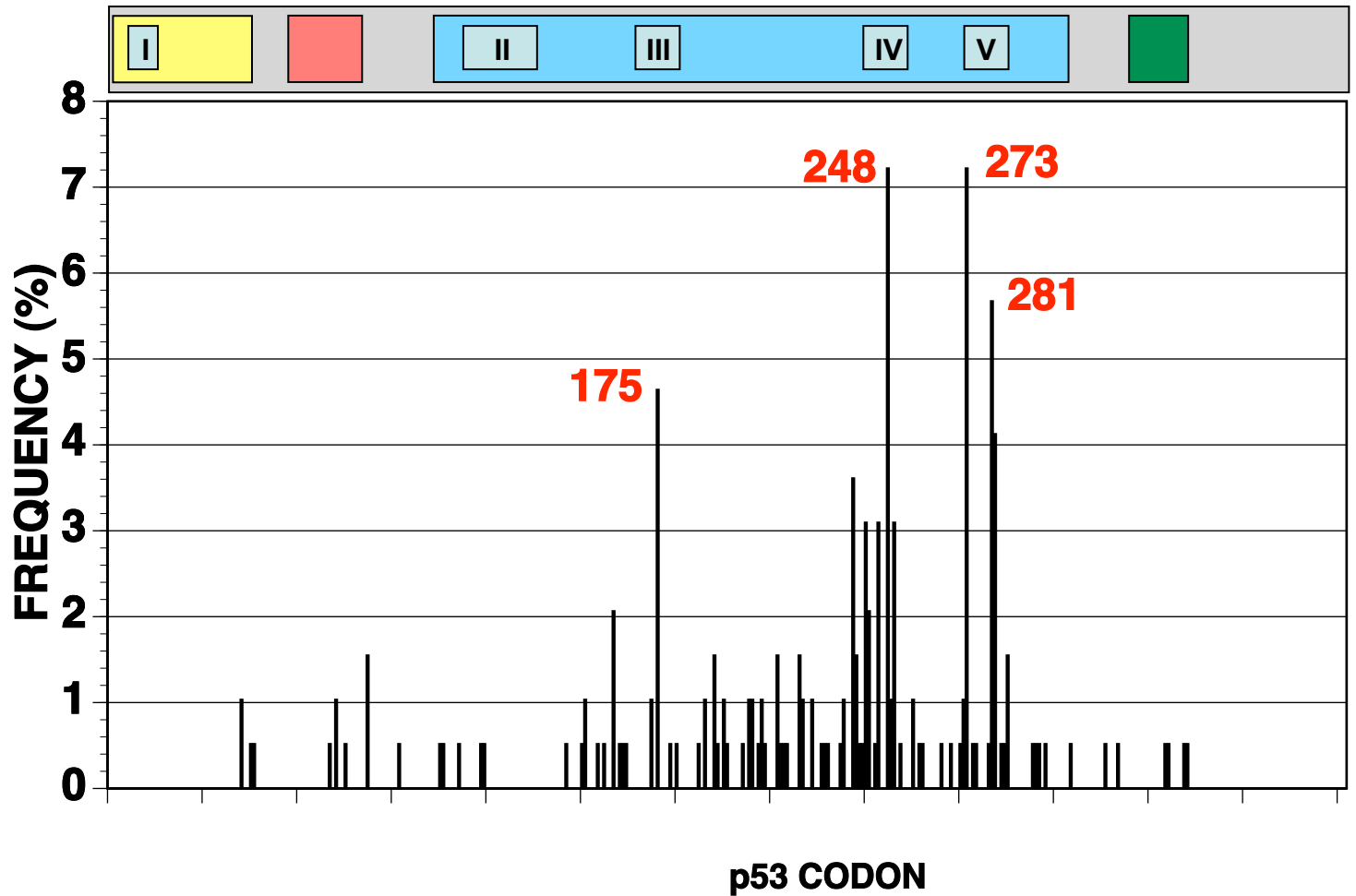
MUTATIONAL EVENTS
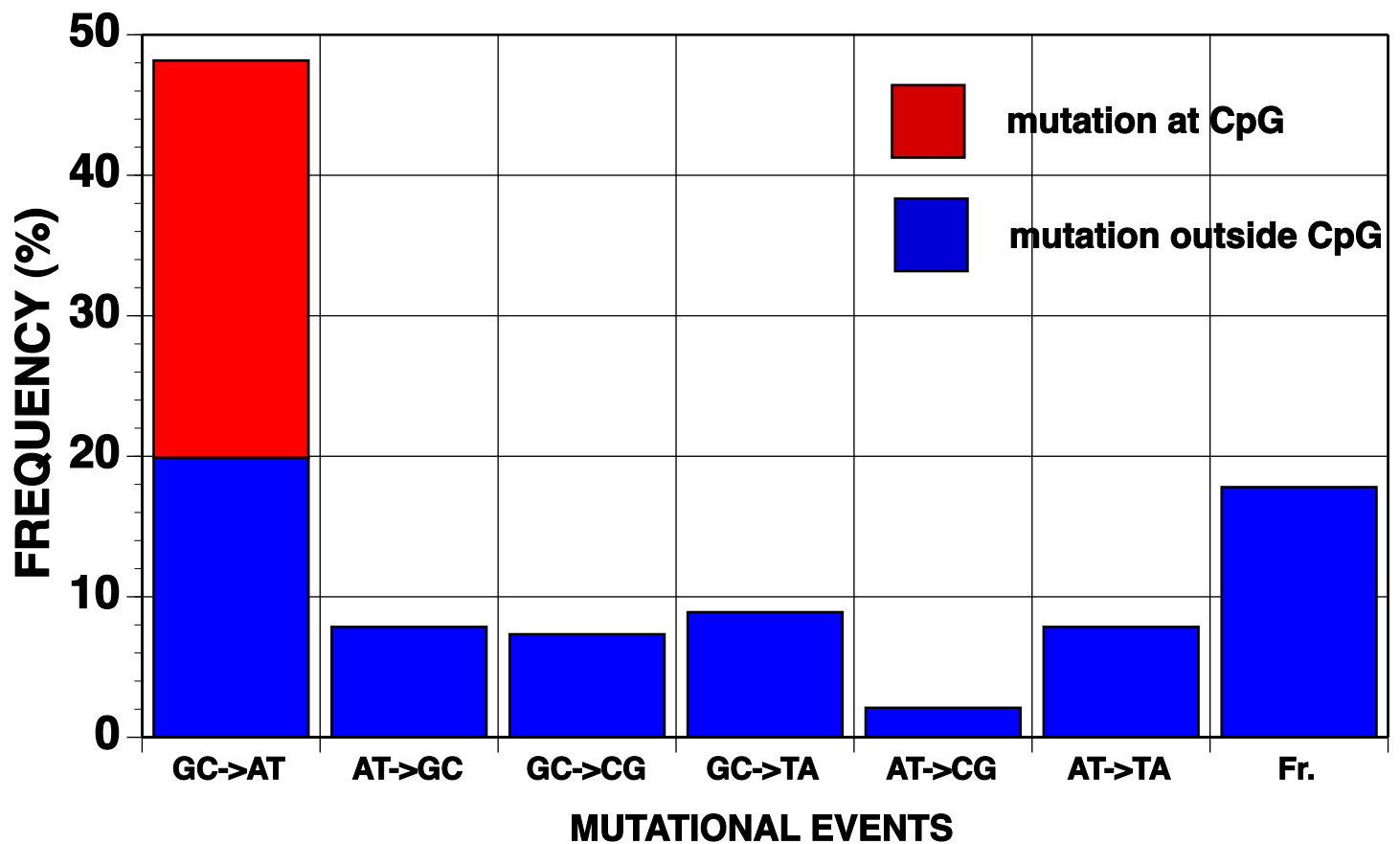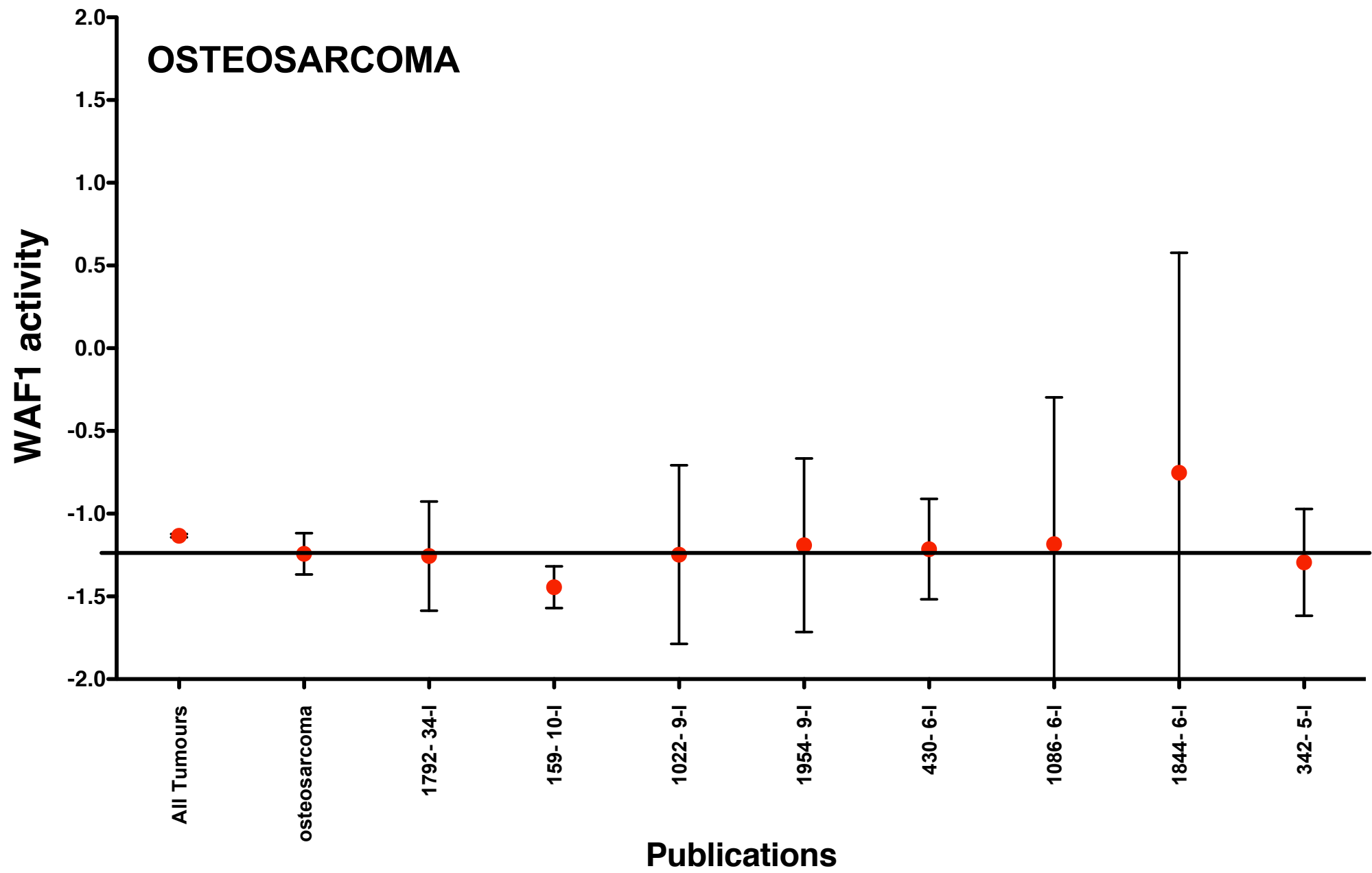
OVARIAN CARCINOMA

Analysis summary

Number of studies	103
Number of tumors	1799
Number of mutations	1875
Number of tumors with 1 mutation	1630
Number of tumors with 2 mutations	65
Number of tumors with more than 2 mutations	6
In studies	100
Out studies 95	1
Out studies 99	2

Strategy of analysis

I			II	III		IV	V			

Exon 2   Exon 3   Exon 4   Exon 5   Exon 6   Exon 7   Exon 8   Exon 9   Exon 10   Exon 11

Exon 5-8
←——————→
24 studies

Exon 4-9
←————————————→
9 studies

Exon 2-11
←——————————————————→
28 studies
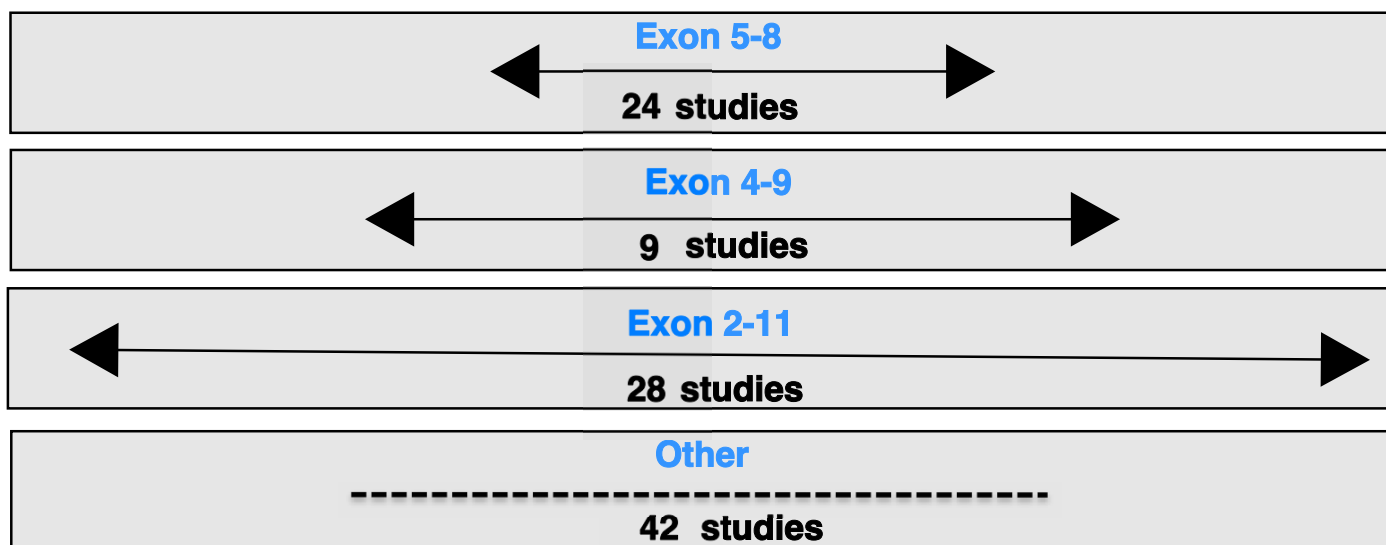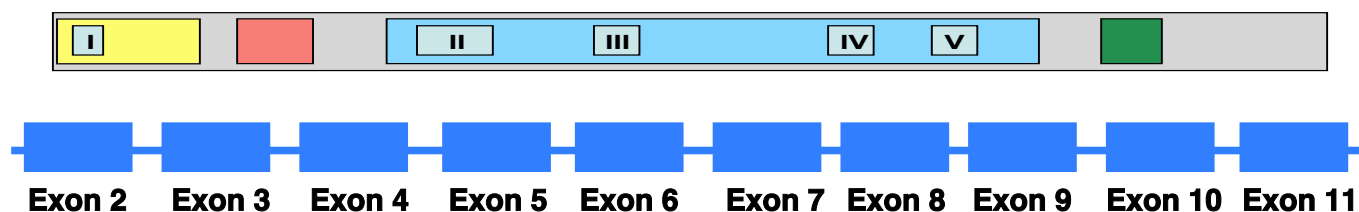
Other
- -
42 studies

Prescreening

Studies with prescreening	**62**		Studies without prescreening	**41**

SSCP	52	IHC	1
DGGE/CDGE	7	dHPLC	0
Yeast Assay	4	Other	1

OVARIAN CARCINOMA

p53 mutation frequency

Number of missense mutations	1368	77%
Number of nonsense mutations	150	8%
Number of frameshift mutations	259	15%
Total number of mutations	1777	100%
Number of polymorphisms	47	3%

p53 mutant frequency

Number of missense mutants	406	67%
Number of nonsense mutants	46	8%
Number of frameshift mutants	155	26%
Total number of mutants	607	100%
Number of polymorphisms	36	6%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
175	CGC	CAC	Arg	His	Ts	Yes	85
273	CGT	CAT	Arg	His	Ts	Yes	76
248	CGG	CAG	Arg	Gln	Ts	Yes	49
220	TAT	TGT	Tyr	Cys	Ts	No	44
273	CGT	TGT	Arg	Cys	Ts	Yes	44
248	CGG	TGG	Arg	Trp	Ts	Yes	40
282	CGG	TGG	Arg	Trp	Ts	Yes	31
245	GGC	AGC	Gly	Ser	Ts	Yes	28
237	ATG	ATA	Met	Ile	Ts	No	25
195	ATC	ACC	Ile	Thr	Ts	No	22

Exon Distribution

EXON 2-4

36%
45%
19%

EXON 5-8

12%
7%
80%

EXON 9-11

41%
38%
21%

Frameshift   Nonsense   Missense

OVARIAN CARCINOMA

p53 mutation distribution

I II III IV V

FREQUENCY (%)

273

248

175

p53 CODON

p53 mutational events

FREQUENCY (%)

■ mutation at CpG

■ mutation outside CpG

GC->AT   AT->GC   GC->CG   GC->TA   AT->CG   AT->TA   Fr.
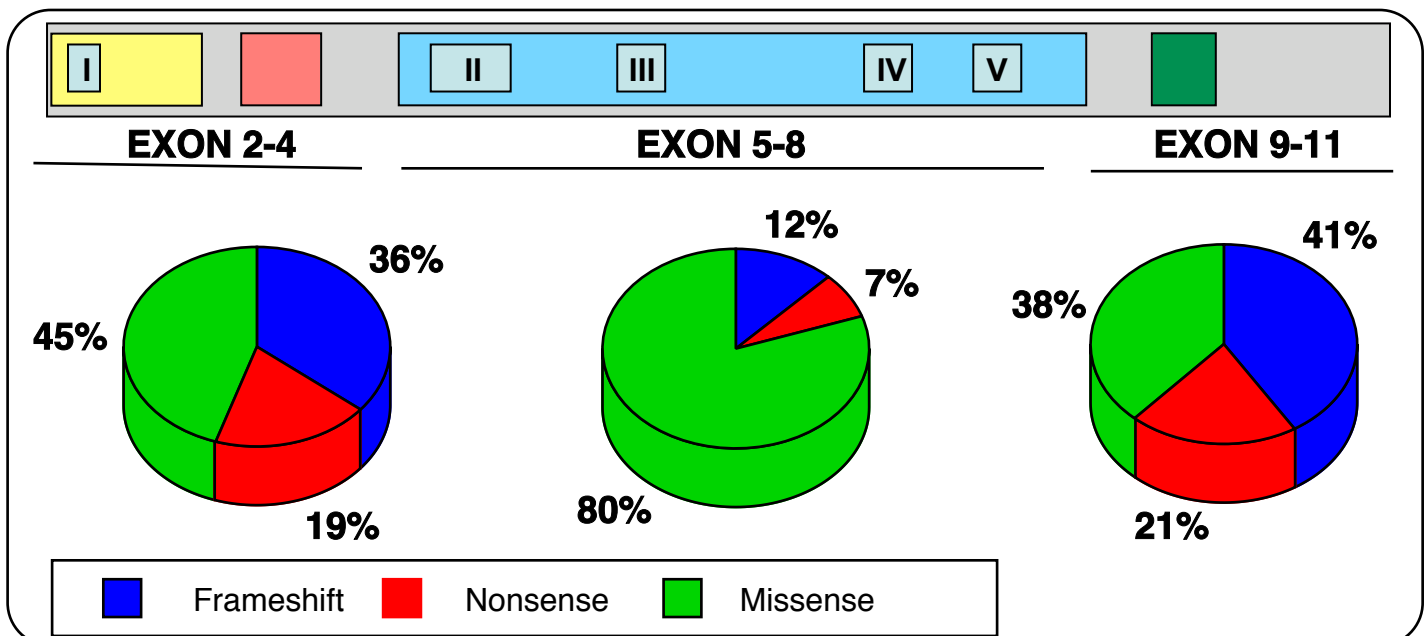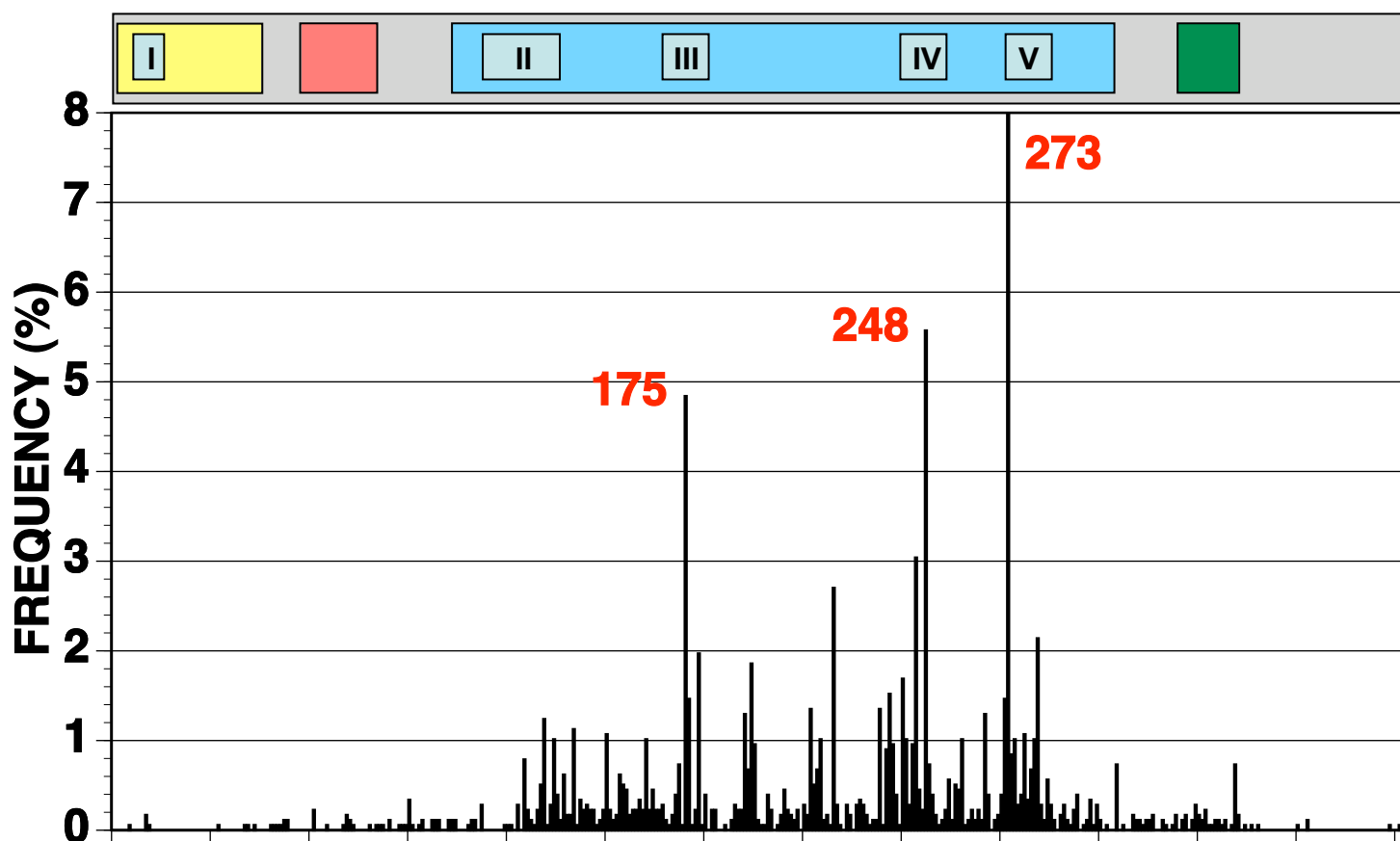
MUTATIONAL EVENTS
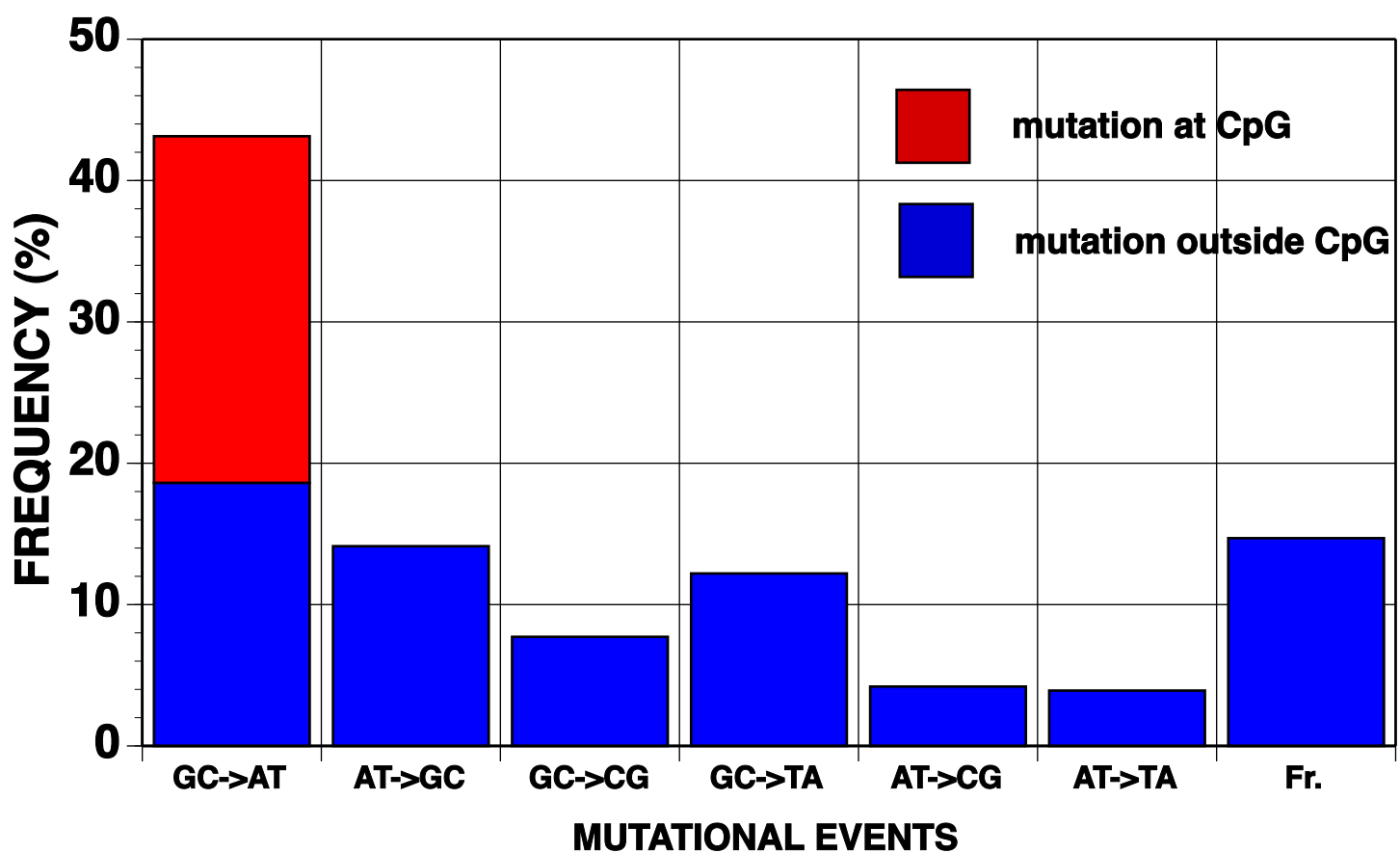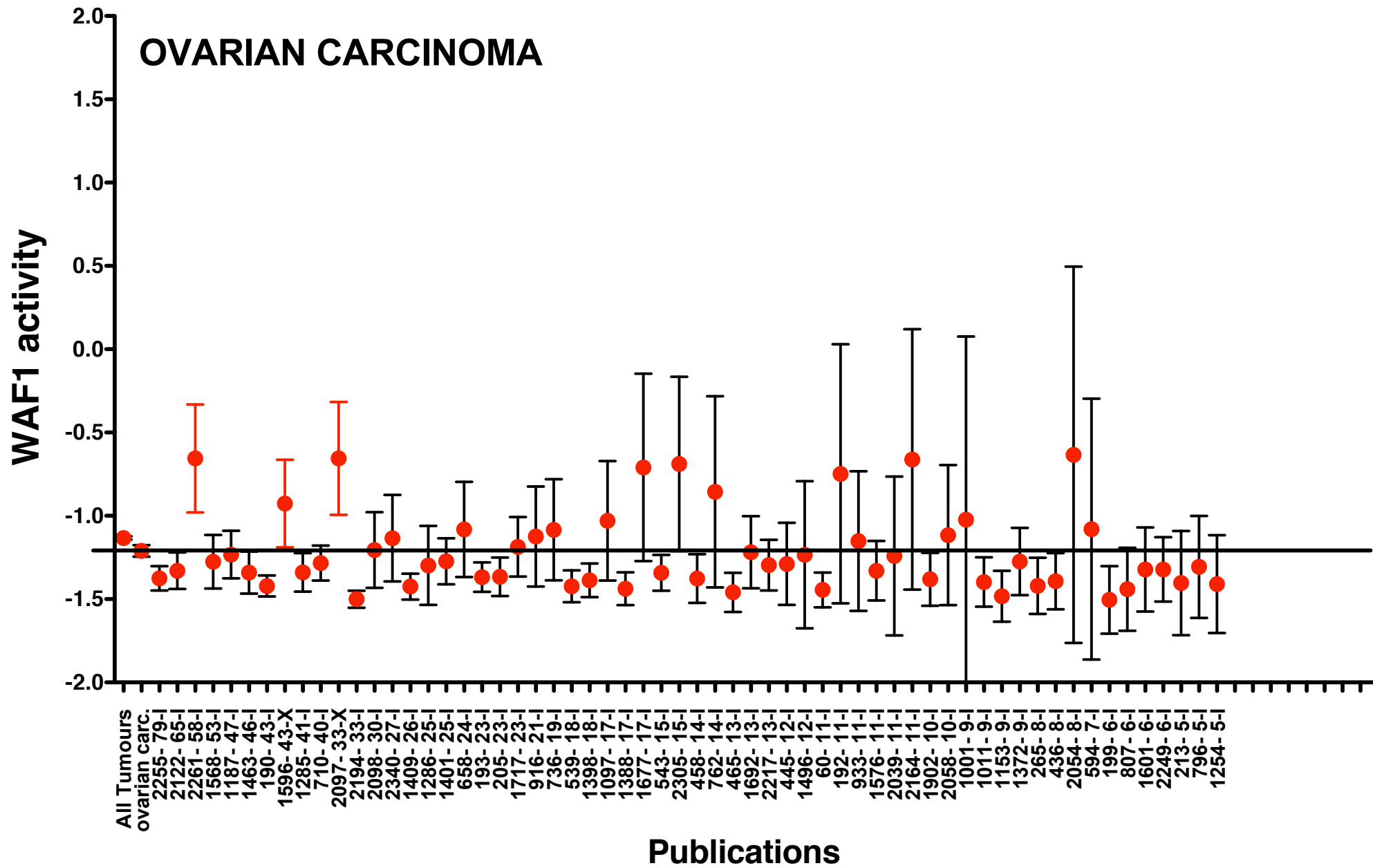
p53 MUTATION DATABASE ANALYSIS

Analysis summary

Number of studies	2384
Number of tumors	25847
Number of mutations	28513
Number of tumors with 1 mutation	23217
Number of tumors with 2 mutations	1621
Number of tumors with more than 2 mutations	346
In studies	2330
Out studies 95	31
Out studies 99	23

Strategy of analysis

Exon 2 Exon 3 Exon 4 Exon 5 Exon 6 Exon 7 Exon 8 Exon 9 Exon 10 Exon 11

Exon 5-8
723 studies

Exon 4-9
156 studies

Exon 2-11
297 studies
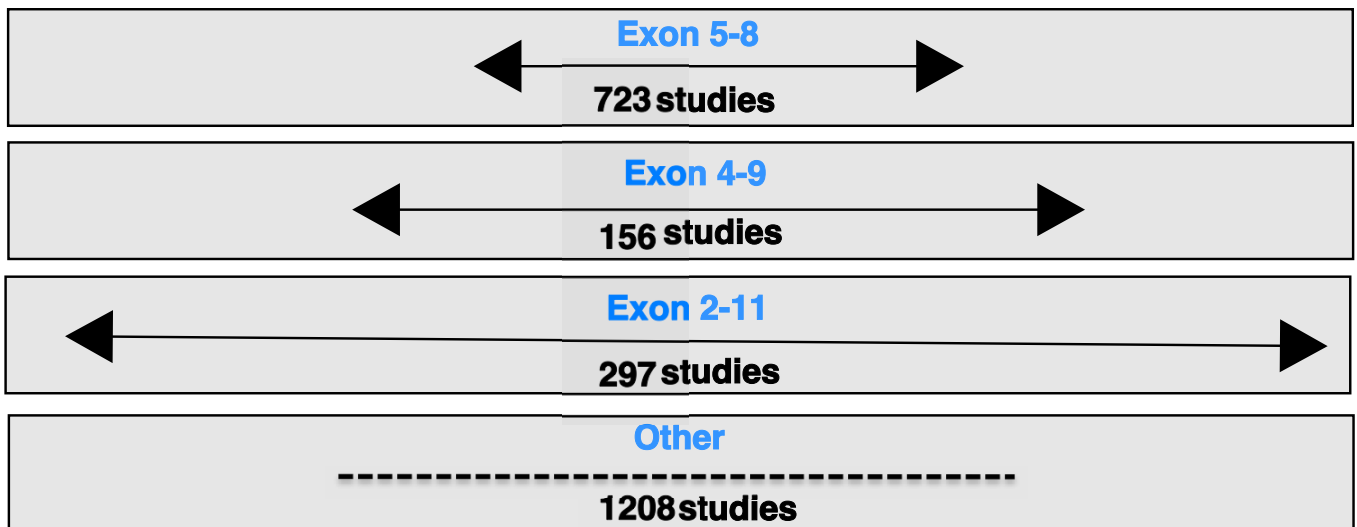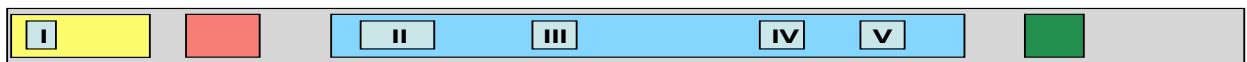
Other
- -
1208 studies

Prescreening

Studies with prescreening 1258

Studies without prescreening 1126

SSCP	982	IHC	39
DGGE/CDGE	158	dHPLC	20
Yeast Assay	49	Other	44

p53 MUTATION DATABASE ANALYSIS

p53 mutation frequency

Number of missense mutations	22629	81%
Number of nonsense mutations	2233	8%
Number of frameshift mutations	2920	11%
Total number of mutations	27782	100%
Number of polymorphisms	1336	5%

p53 mutant frequency

Number of missense mutants	1690	74%
Number of nonsense mutants	91	4%
Number of frameshift mutants	491	22%
Total number of mutants	2272	100%
Number of polymorphisms	236	10%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
175	CGC	CAC	Arg	His	Ts	Yes	1233
248	CGG	CAG	Arg	Gln	Ts	Yes	940
273	CGT	CAT	Arg	His	Ts	Yes	825
248	CGG	TGG	Arg	Trp	Ts	Yes	761
273	CGT	TGT	Arg	Cys	Ts	Yes	721
282	CGG	TGG	Arg	Trp	Ts	Yes	635
245	GGC	AGC	Gly	Ser	Ts	Yes	458
249	AGG	AGT	Arg	Ser	Tv	No	439
220	TAT	TGT	Tyr	Cys	Ts	No	375
213	CGA	TGA	Arg	Stop	Ts	Yes	328

Exon Distribution

EXON 2-4 — 29% 14% 58%

EXON 5-8 — 10% 7% 83%

EXON 9-11 — 19% 25% 56%

Frameshift   Nonsense   Missense
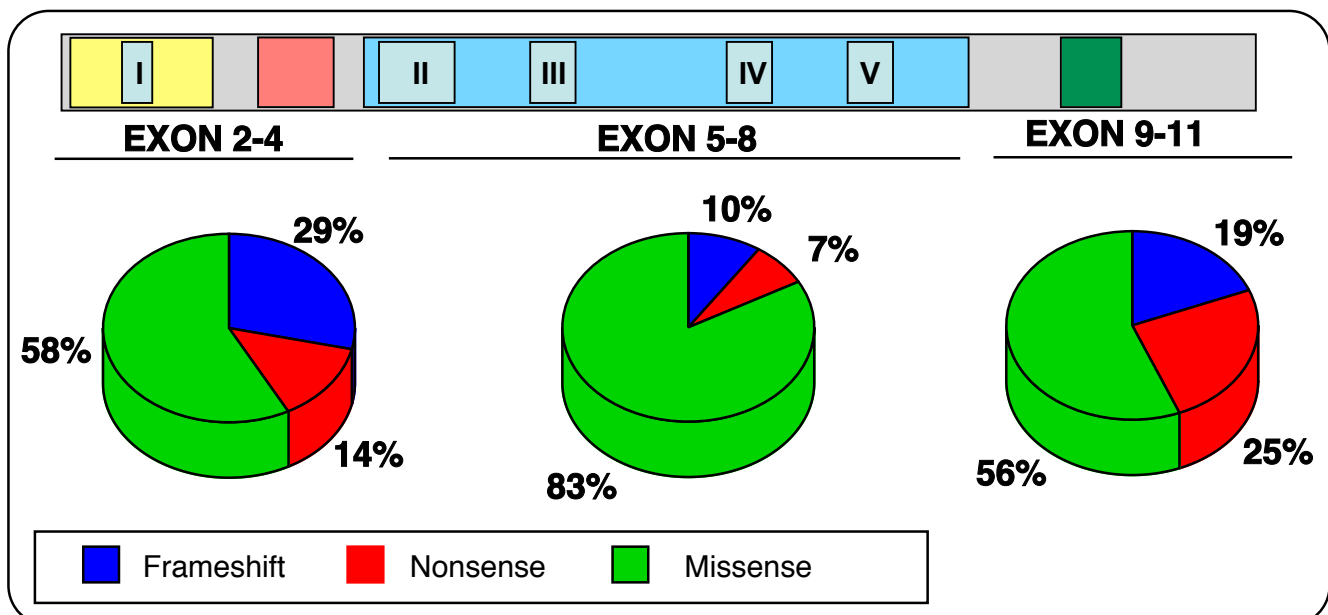
p53 MUTATION DATABASE ANALYSIS

p53 mutation distribution
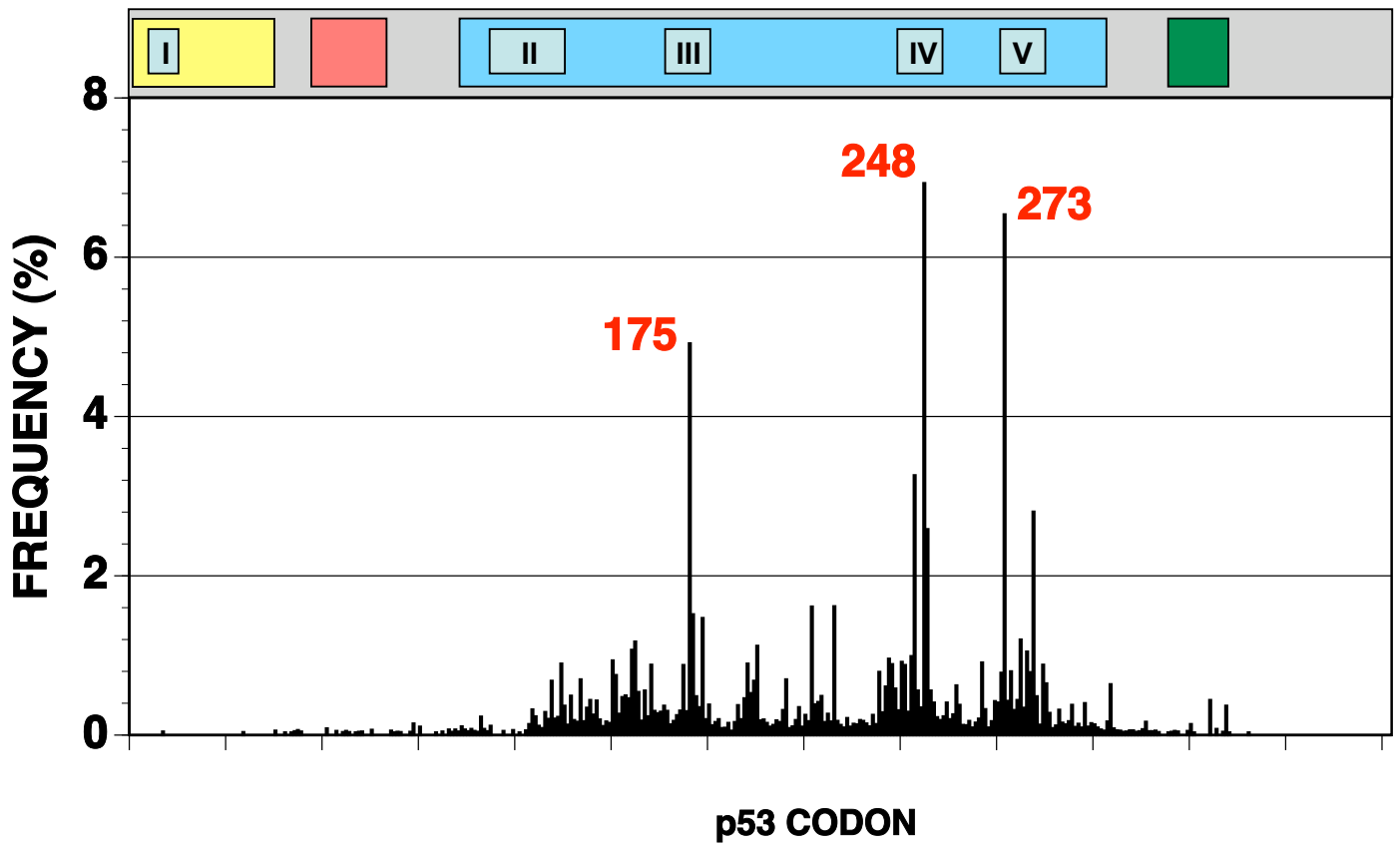
p53 mutational events
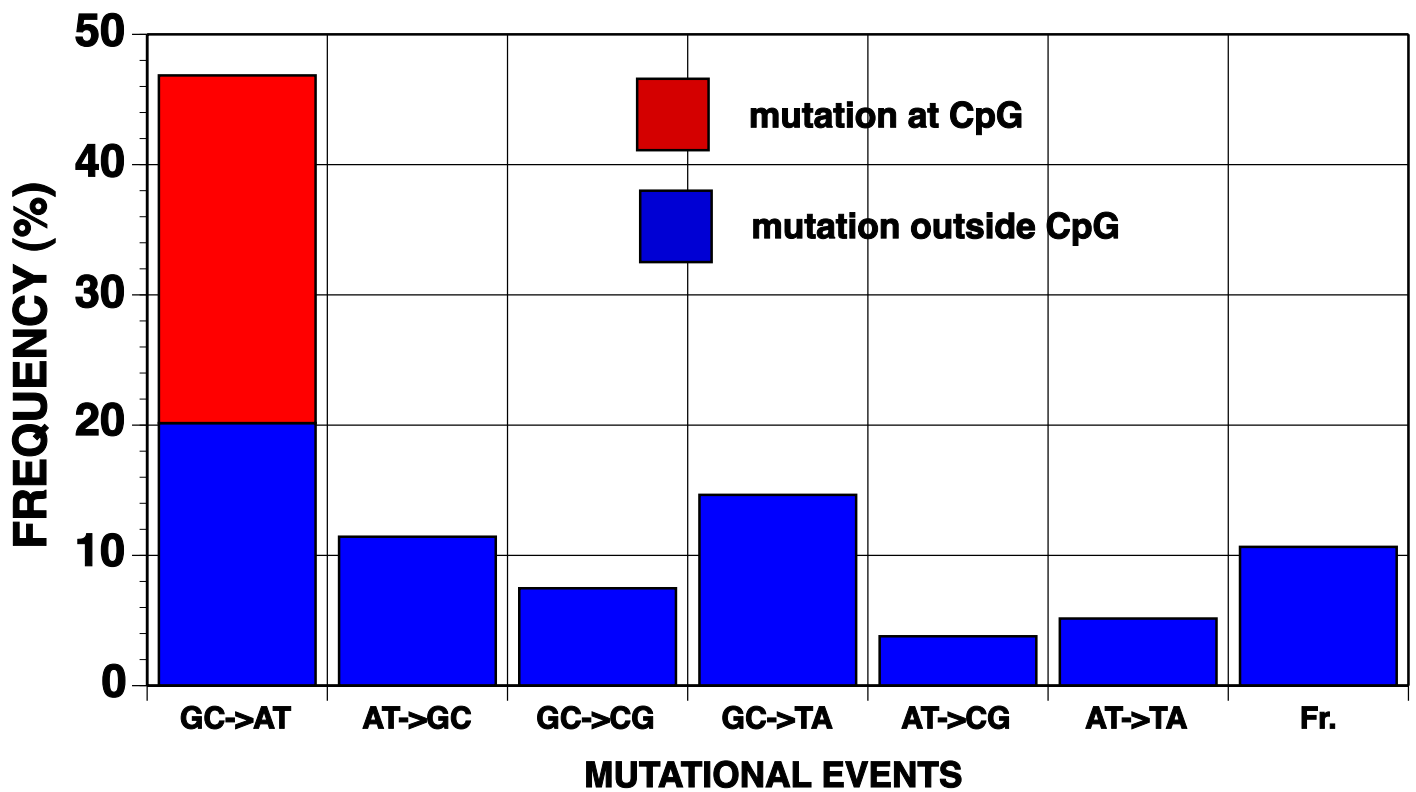
PANCREATIC CANCER

Analysis summary

Number of studies	46
Number of tumors	467
Number of mutations	480
Number of tumors with 1 mutation	367
Number of tumors with 2 mutations	12
Number of tumors with more than 2 mutations	0
In studies	45
Out studies 95	1
Out studies 99	0

Strategy of analysis

Exon 5-8
14 studies

Exon 4-9
2 studies

Exon 2-11
5 studies
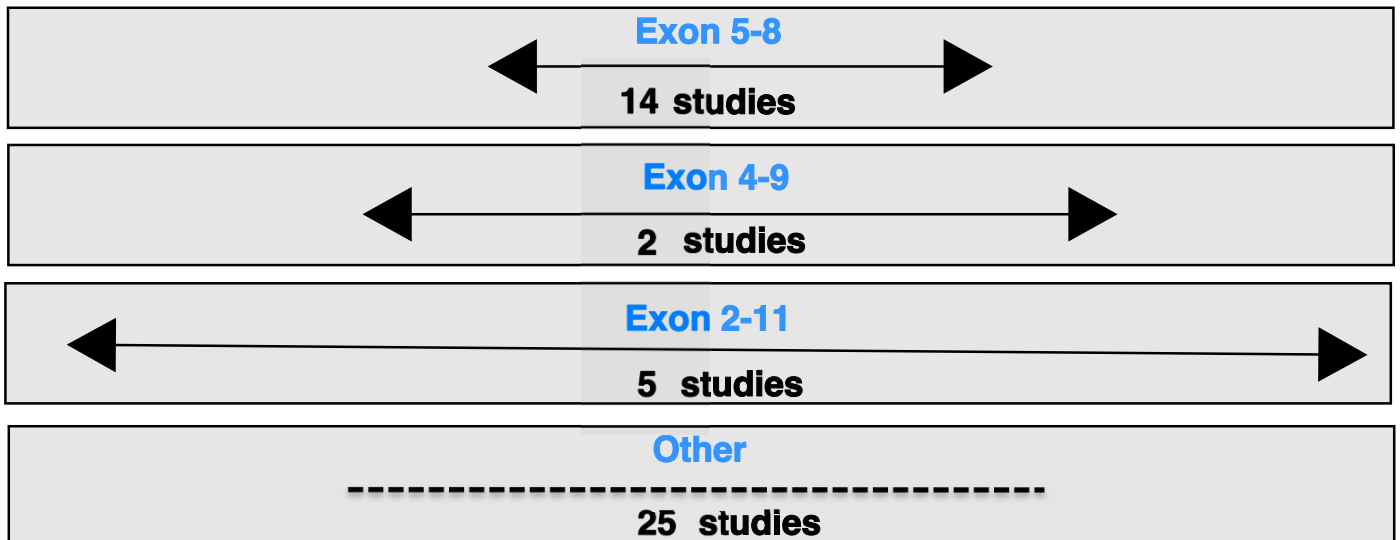
Other
25 studies

Prescreening

Studies with prescreening 23

SSCP	17	IHC	2
DGGE/CDGE	3	dHPLC	0
Yeast Assay	1	Other	0

Studies without prescreening 23

p53 mutation frequency

Number of missense mutations	303	78%
Number of nonsense mutations	19	5%
Number of frameshift mutations	67	17%
Total number of mutations	389	100%
Number of polymorphisms	14	4%

p53 mutant frequency

Number of missense mutants	150	71%
Number of nonsense mutants	11	5%
Number of frameshift mutants	49	23%
Total number of mutants	210	100%
Number of polymorphisms	12	6%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
273	CGT	CAT	Arg	His	Ts	Yes	26
175	CGC	CAC	Arg	His	Ts	Yes	17
273	CGT	TGT	Arg	Cys	Ts	Yes	17
282	CGG	TGG	Arg	Trp	Ts	Yes	12
248	CGG	TGG	Arg	Trp	Ts	Yes	11
248	CGG	CAG	Arg	Gln	Ts	Yes	8
220	TAT	TGT	Tyr	Cys	Ts	No	7
179	CAT	CGT	His	Arg	Ts	No	6
213	CGA	CTA	Arg	Leu	Tv	No	6
245	GGC	GAC	Gly	Asp	Ts	No	5

Exon Distribution
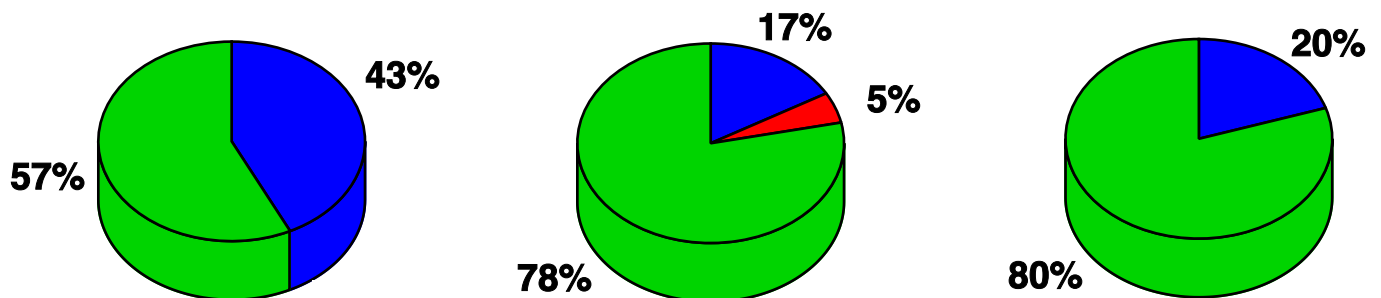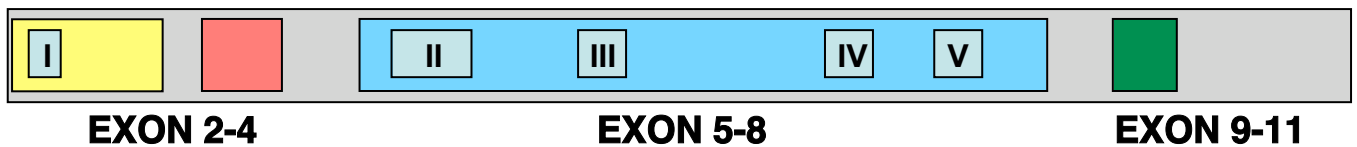
PANCREATIC CANCER

p53 mutation distribution
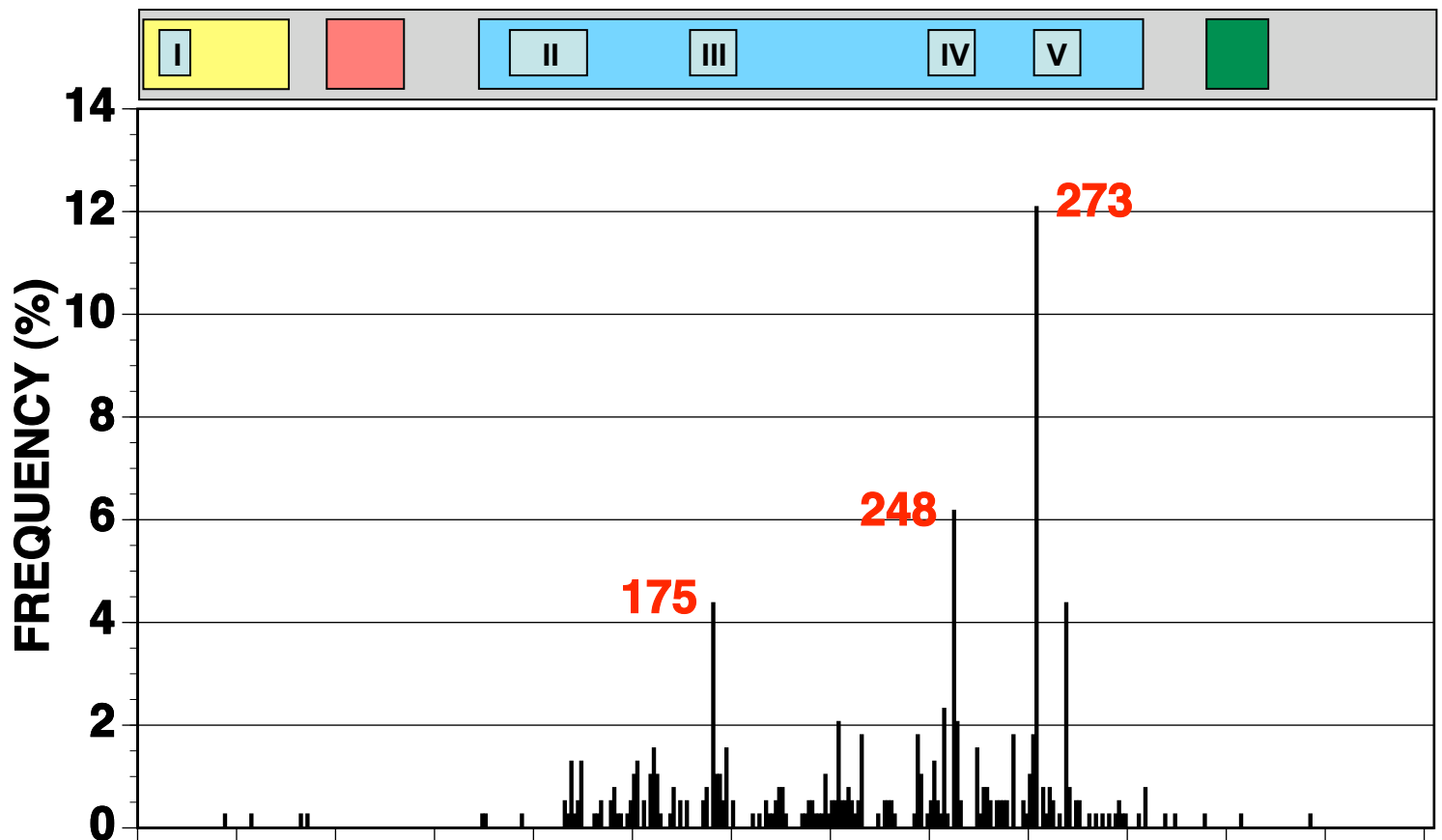
p53 mutational events
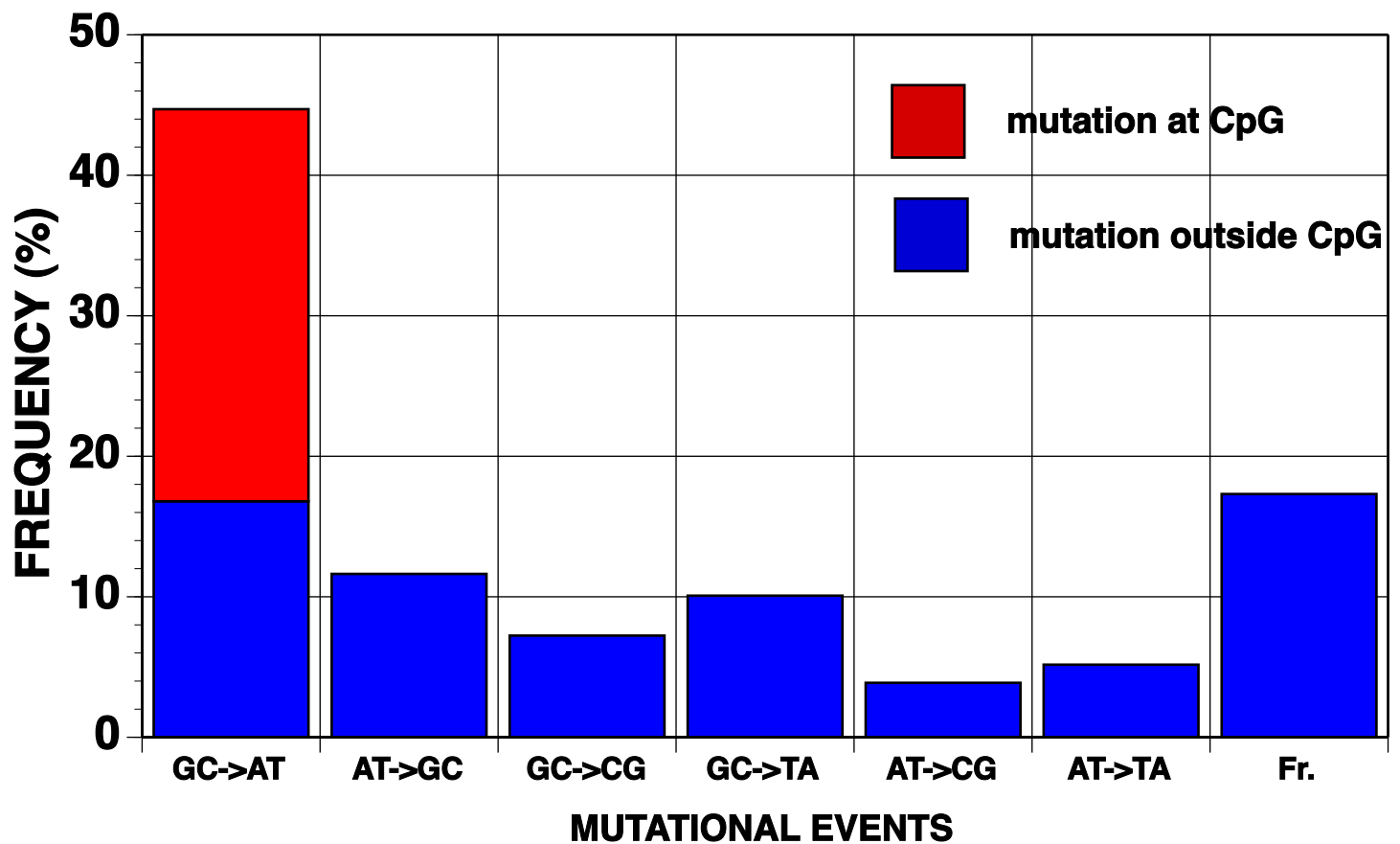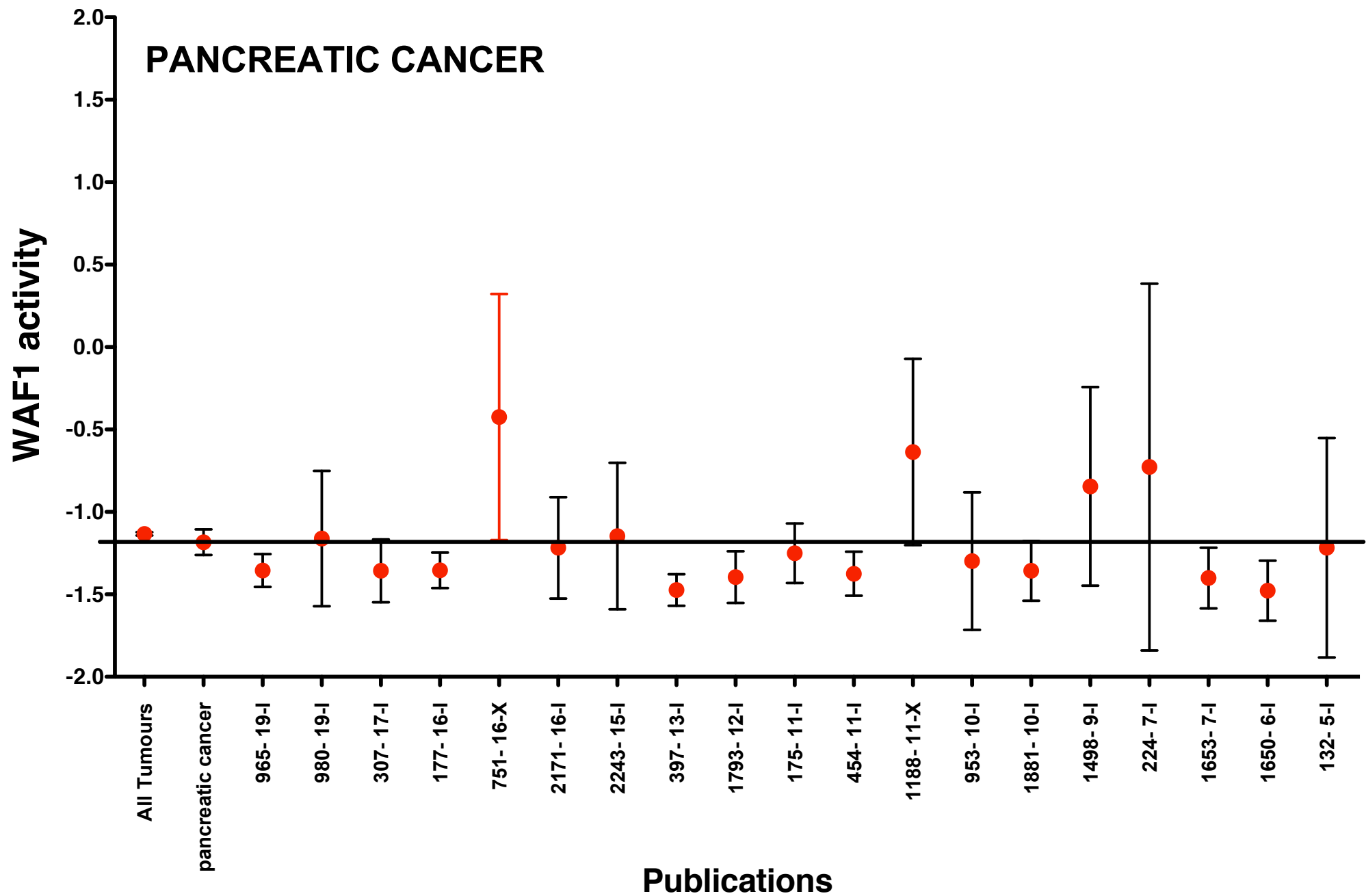
PROSTATE CANCER

Analysis summary

Number of studies	41
Number of tumors	258
Number of mutations	299
Number of tumors with 1 mutation	220
Number of tumors with 2 mutations	30
Number of tumors with more than 2 mutations	7
In studies	38
Out studies 95	3
Out studies 99	0

Strategy of analysis

Exon 2 Exon 3 Exon 4 Exon 5 Exon 6 Exon 7 Exon 8 Exon 9 Exon 10 Exon 11

Exon 5-8
13 studies

Exon 4-9
9 studies

Exon 2-11
5 studies
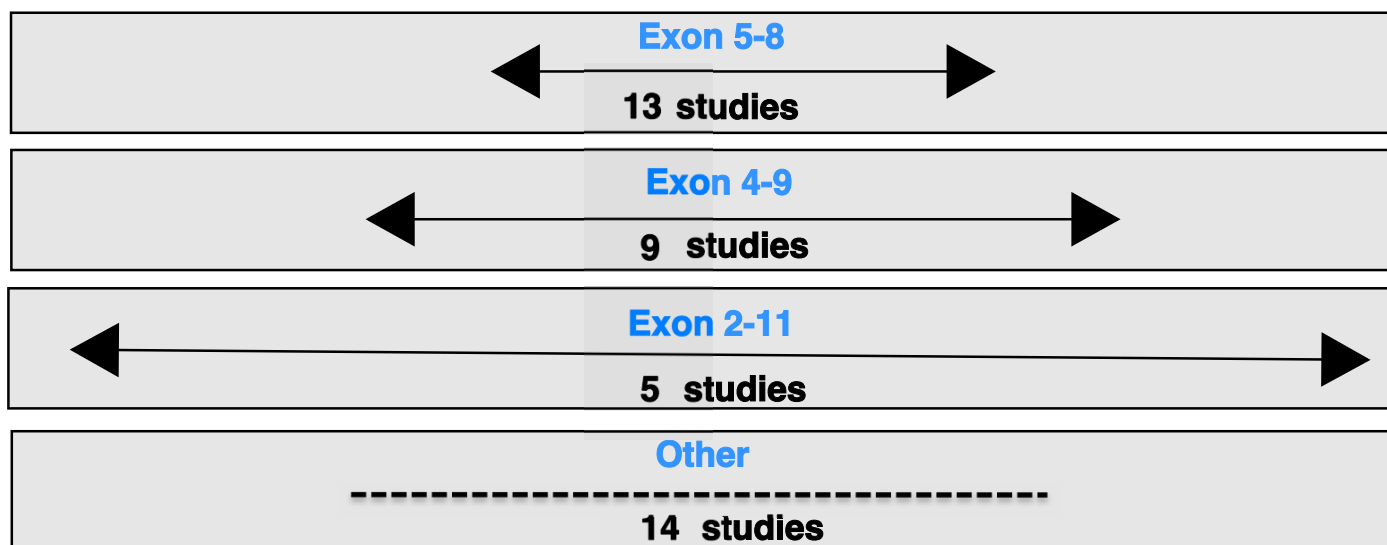
Other
----
14 studies

Prescreening

Studies with prescreening 34

Studies without prescreening 7

SSCP	29	IHC	3
DGGE/CDGE	2	dHPLC	1
Yeast Assay	1	Other	1

p53 mutation frequency

Number of missense mutations	233	86%
Number of nonsense mutations	17	6%
Number of frameshift mutations	22	8%
Total number of mutations	272	100%
Number of polymorphisms	18	7%

p53 mutant frequency

Number of missense mutations	133	83%
Number of nonsense mutations	12	7%
Number of frameshift mutations	16	10%
Total number of mutations	161	100%
Number of polymorphisms	13	8%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
273	CGT	TGT	Arg	Cys	Ts	Yes	13
175	CGC	CAC	Arg	His	Ts	Yes	7
138	GCC	DEL1A	Ala	Fs.	Fr	Yes	6
251	ATC	AGC	Ile	Ser	Tv	No	6
273	CGT	CAT	Arg	His	Ts	Yes	6
214	CAT	CGT	His	Arg	Ts	No	5
248	CGG	TGG	Arg	Trp	Ts	Yes	5
274	GTT	TTT	Val	Phe	Tv	No	5
126	TAC	TGC	Tyr	Cys	Ts	No	4
152	CCG	CCA	Pro	Pro	Ts	Yes	4

Exon distribution

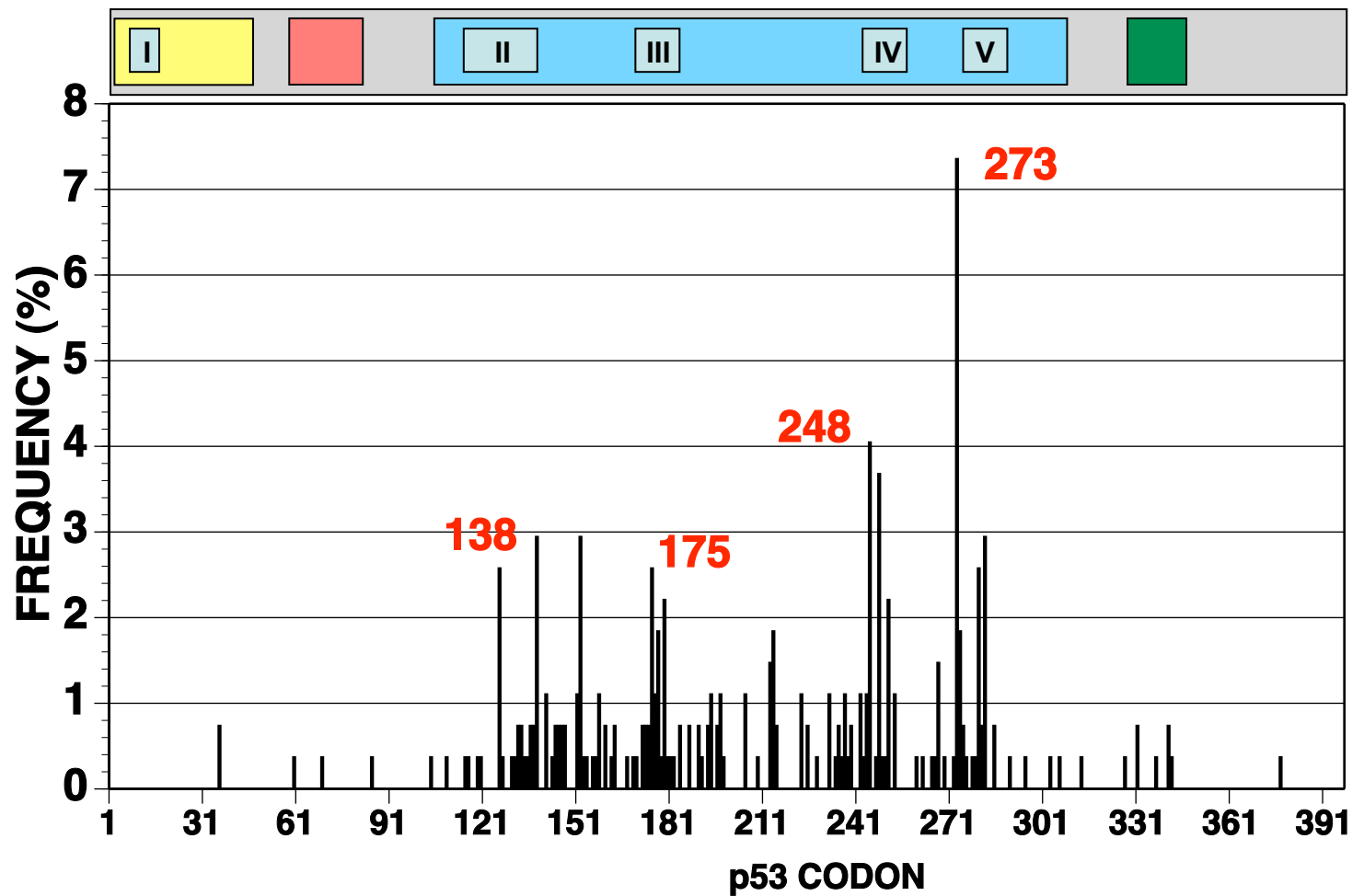EXON 2-4: 36%, 55%, 9%

EXON 5-8: 7%, 6%, 87%

EXON 9-11: 11%, 11%, 78%
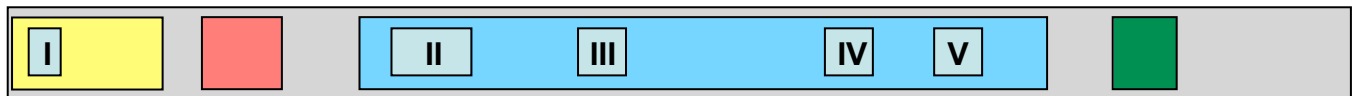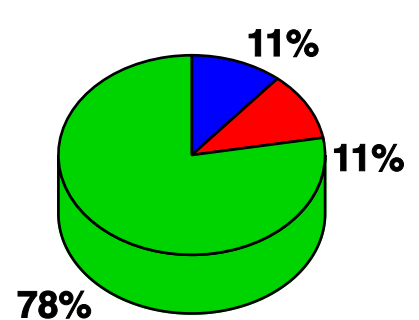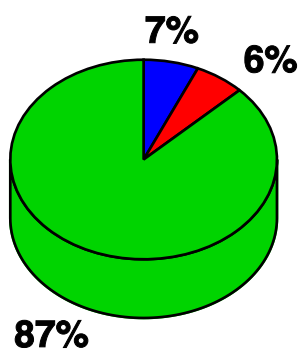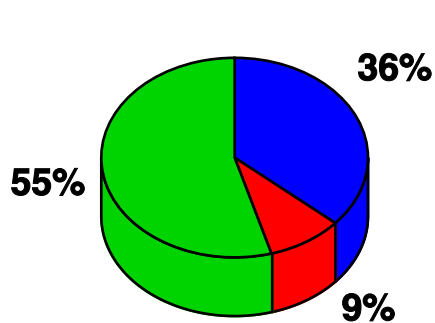
Frameshift Nonsense Missense

PROSTATE CANCER

p53 mutation distribution

p53 mutational events

PROSTATE CANCER

WAF1 activity (y-axis, ranging from -2.0 to 2.0)

Publications (x-axis): All Tumours, prostate ca., 2105- 40-I, 437- 20-I, 489- 16-I, 824- 11-X, 1420- 11-I, 741- 9-I, 2180- 9-I, 216- 8-I, 656- 8-I, 651- 7-I, 876- 7-I, 1991- 7-I, 530- 6-I, 281- 5-I, 456- 5-I, 818- 5-I
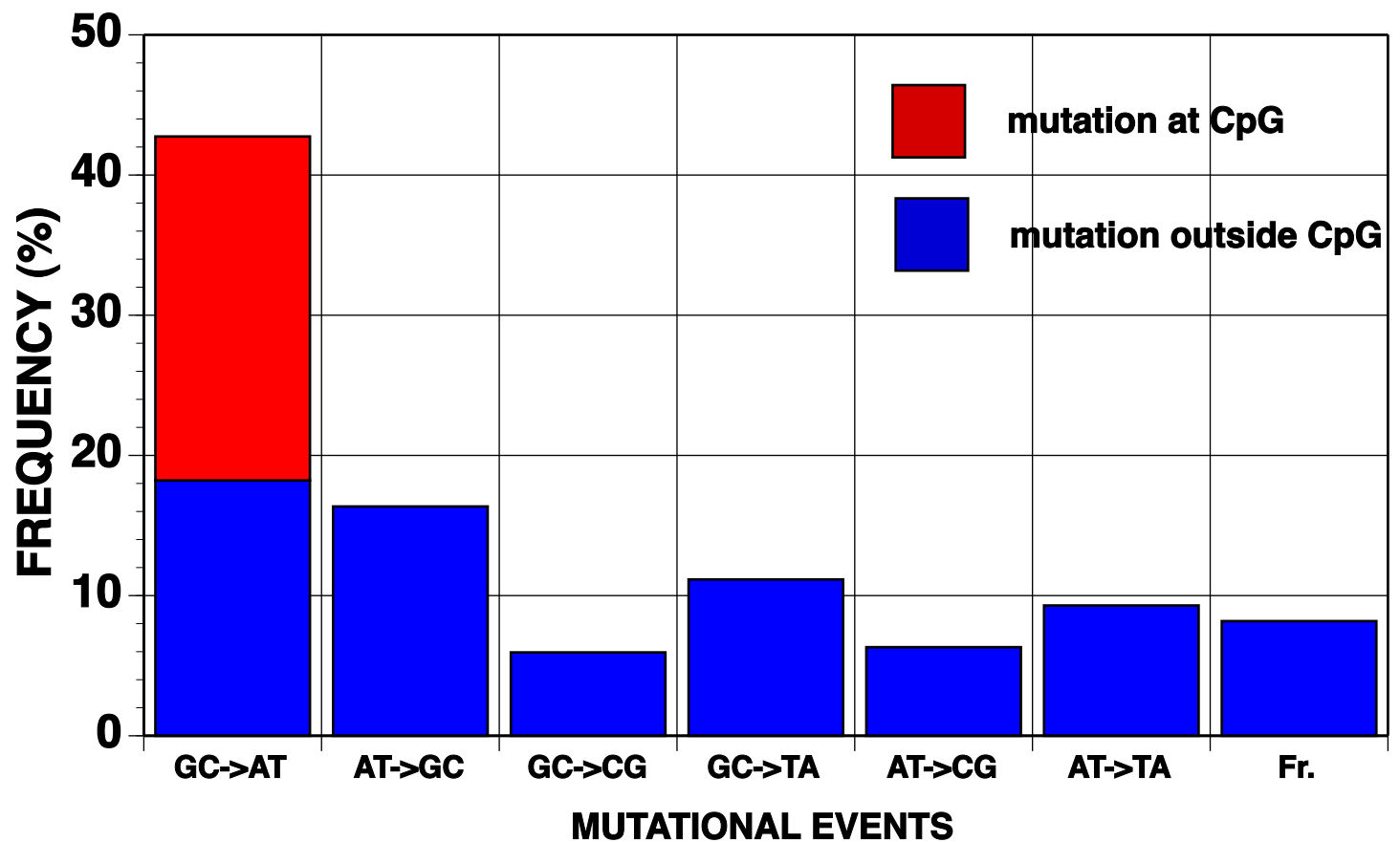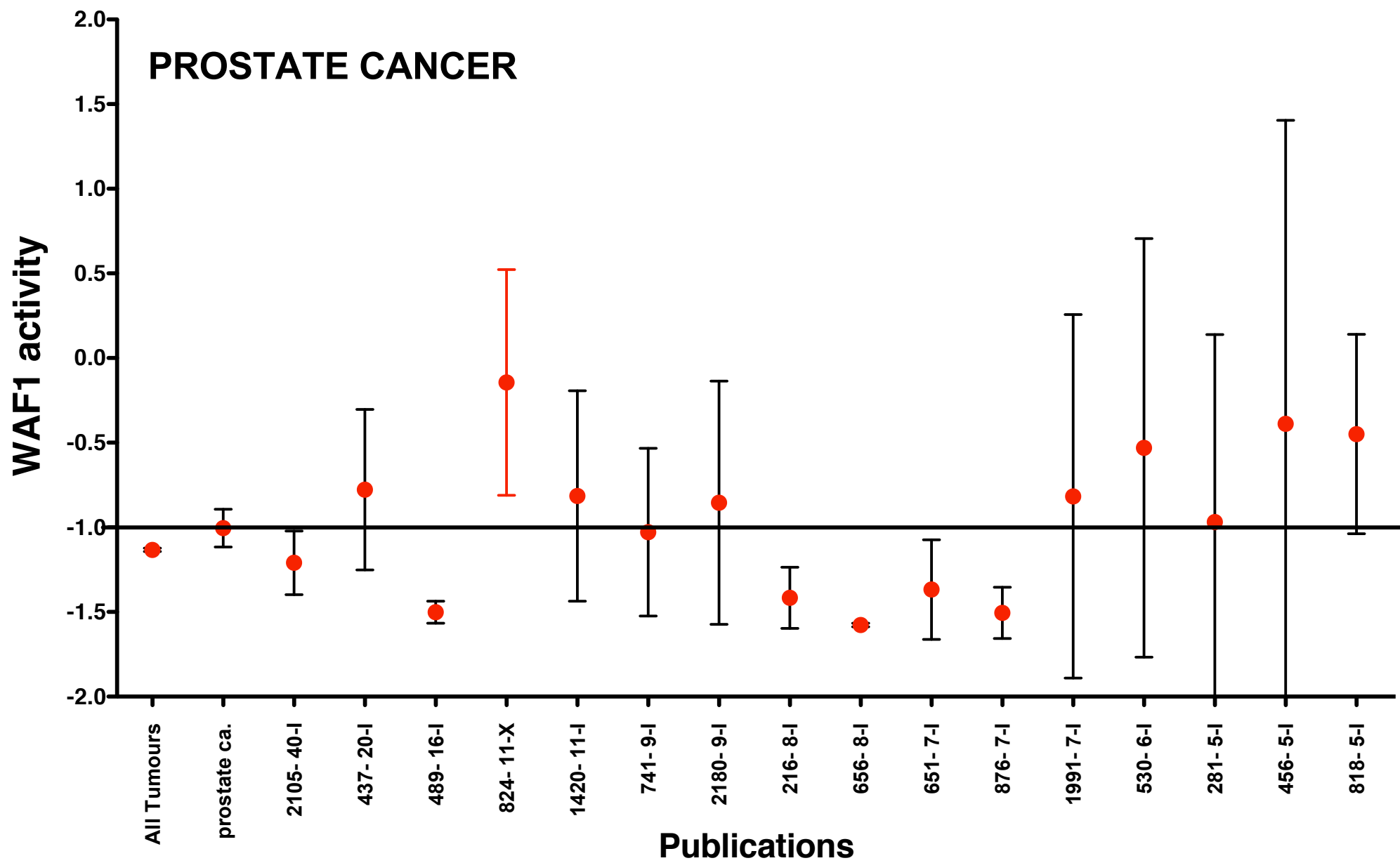
RENAL CELL CARCINOMA

Analysis summary

Number of studies	23
Number of tumors	106
Number of mutations	120
Number of tumors with 1 mutation	92
Number of tumors with 2 mutations	11
Number of tumors with more than 2 mutations	2
In studies	23
Out studies 95	0
Out studies 99	0

Strategy of analysis

Exon 2 Exon 3 Exon 4 Exon 5 Exon 6 Exon 7 Exon 8 Exon 9 Exon 10 Exon 11

Exon 5-8
9 studies

Exon 4-9
4 studies

Exon 2-11
2 studies
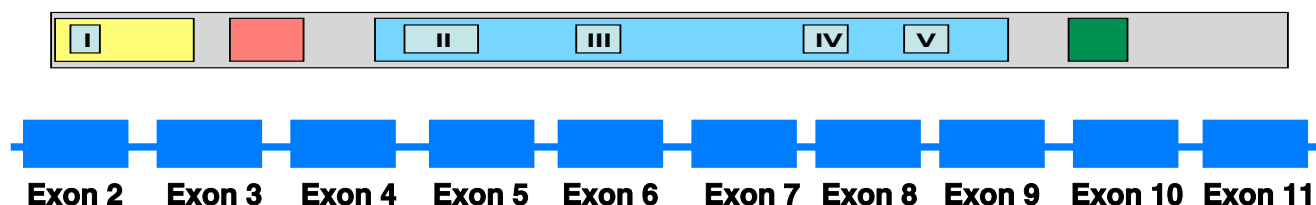
Other
8 studies

Prescreening

Studies with prescreening	16		
SSCP	15	IHC	0
DGGE/CDGE	0	dHPLC	0
Yeast Assay	1	Other	0

Studies without prescreening   7

RENAL CELL CARCINOMA

p53 mutation frequency

Number of missense mutations	93	78%
Number of nonsense mutations	7	6%
Number of frameshift mutations	19	16%
Total number of mutations	119	100%
Number of polymorphisms	7	6%

p53 mutant frequency

Number of missense mutants	65	74%
Number of nonsense mutants	5	6%
Number of frameshift mutants	18	20%
Total number of mutants	88	100%
Number of polymorphisms	7	8%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
278	CCT	CTT	Pro	Leu	Ts	No	8
244	GGC	TGC	Gly	Cys	Tv	No	8
294	GAG	TAG	Glu	Stop	Tv	No	3
176	TGC	TTC	Cys	Phe	Tv	No	3
173	GTG	GGG	Val	Gly	Tv	No	2
275	TGT	TAT	Cys	Tyr	Ts	No	2
273	CGT	CAT	Arg	His	Ts	Yes	2
248	CGG	CAG	Arg	Gln	Ts	Yes	2
157	GTC	TTC	Val	Phe	Tv	No	2
175	CGC	CAC	Arg	His	Ts	Yes	2

Exon Distribution

I		II	III	IV	V	

EXON 2-4   **EXON 5-8**   **EXON 9-11**

15%

5%

80%
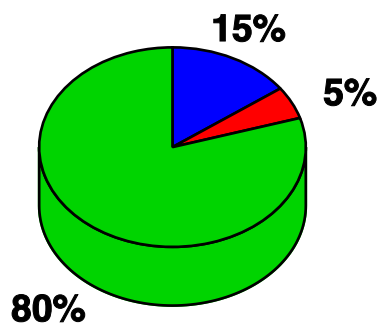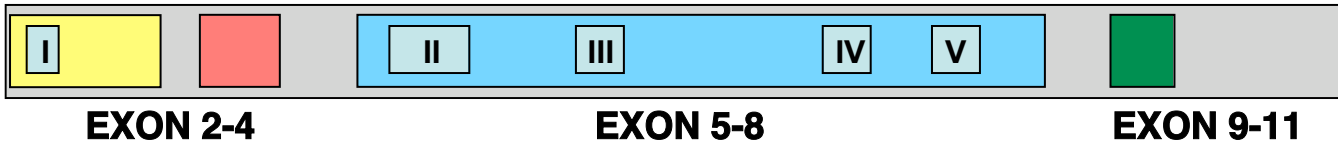
	Frameshift		Nonsense		Missense

RENAL CELL CARCINOMA

p53 mutation distribution
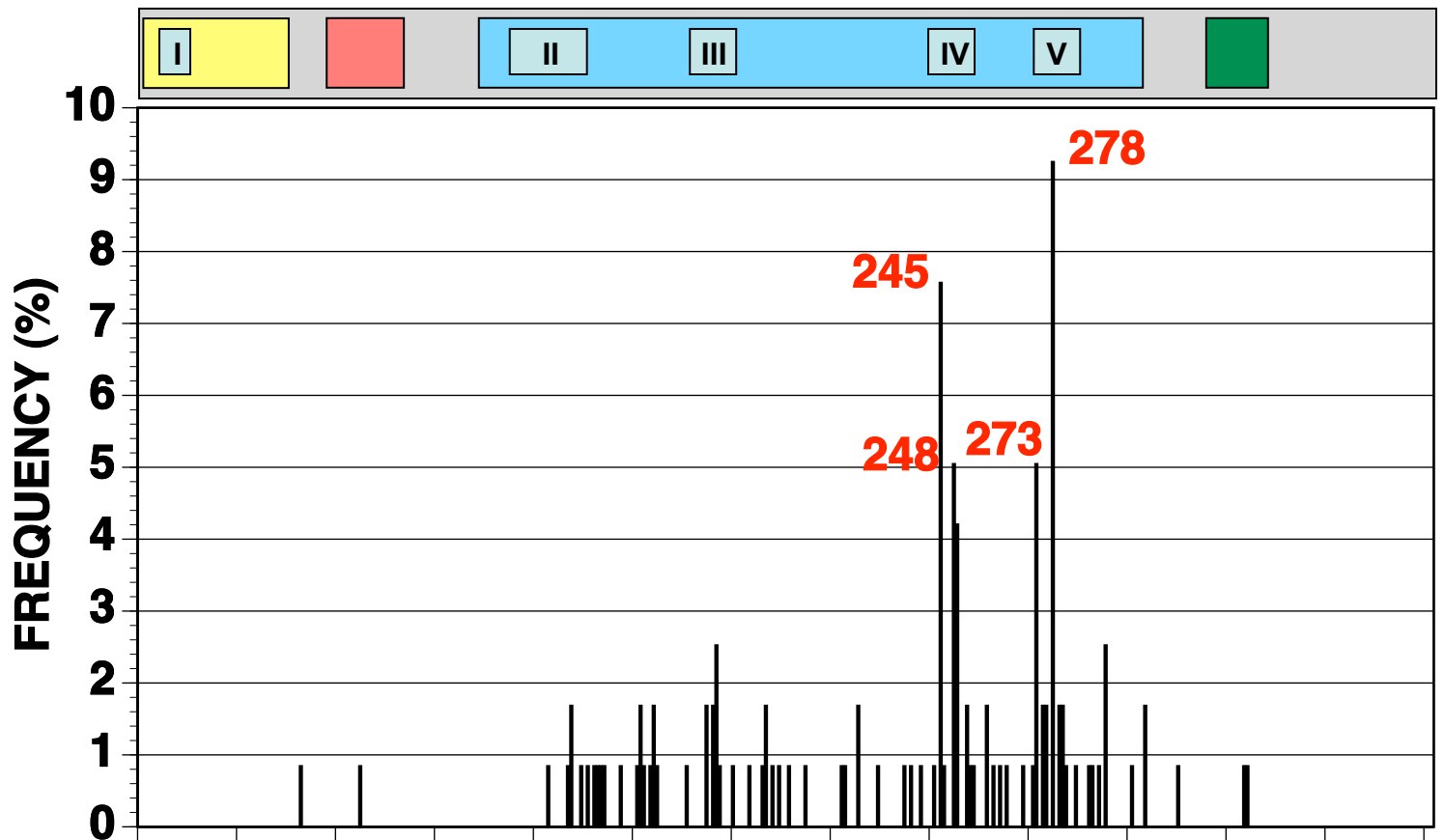
p53 mutational events
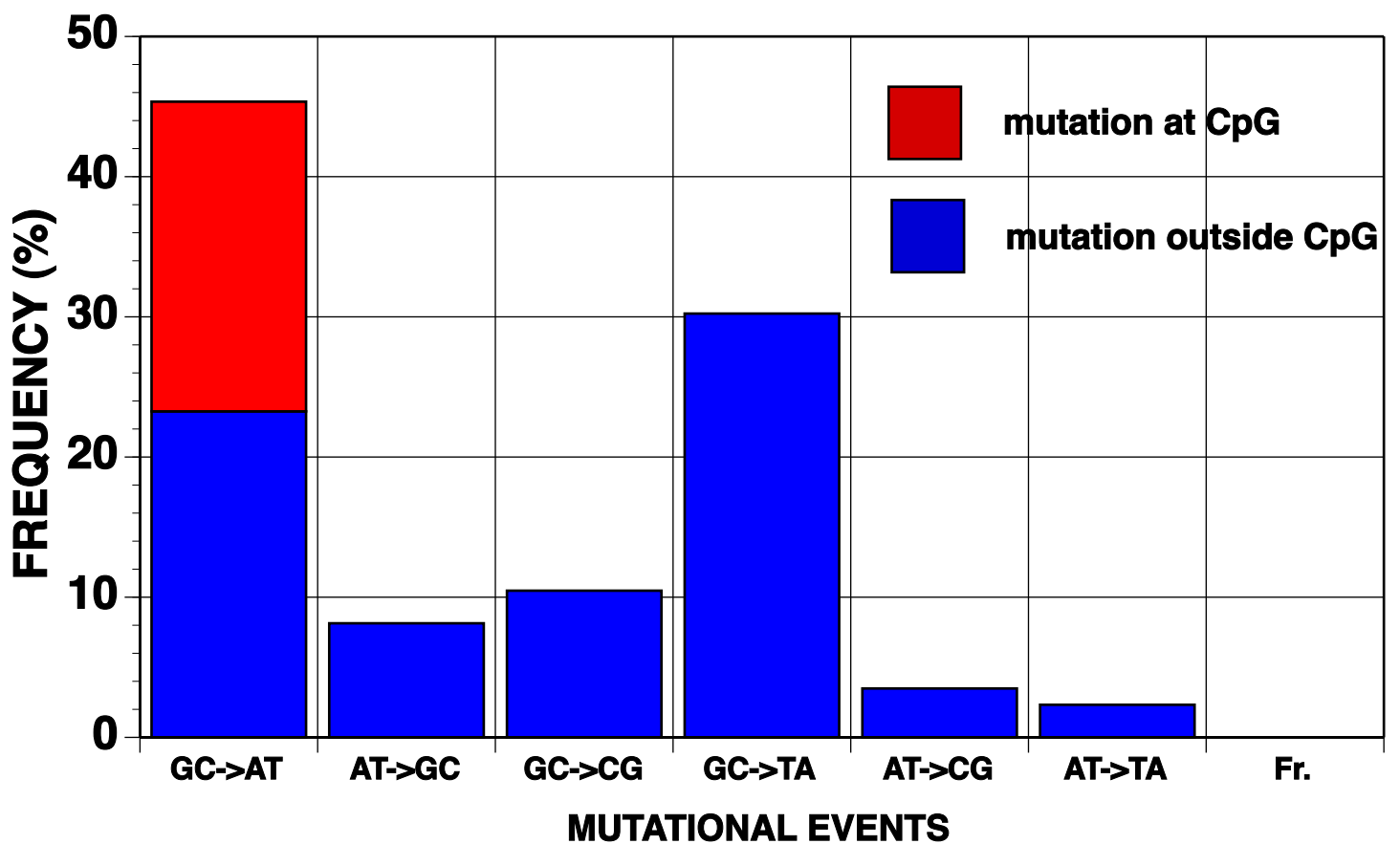
SKIN SCC

Analysis summary

Number of studies	36
Number of tumors	215
Number of mutations	303
Number of tumors with 1 mutation	178
Number of tumors with 2 mutations	25
Number of tumors with more than 2 mutations	5
In studies	34
Out studies 95	2
Out studies 99	0

Strategy of analysis

Exon 2 · Exon 3 · Exon 4 · Exon 5 · Exon 6 · Exon 7 · Exon 8 · Exon 9 · Exon 10 · Exon 11

Exon 5-8
9 studies

Exon 4-9
5 studies

Exon 2-11
6 studies
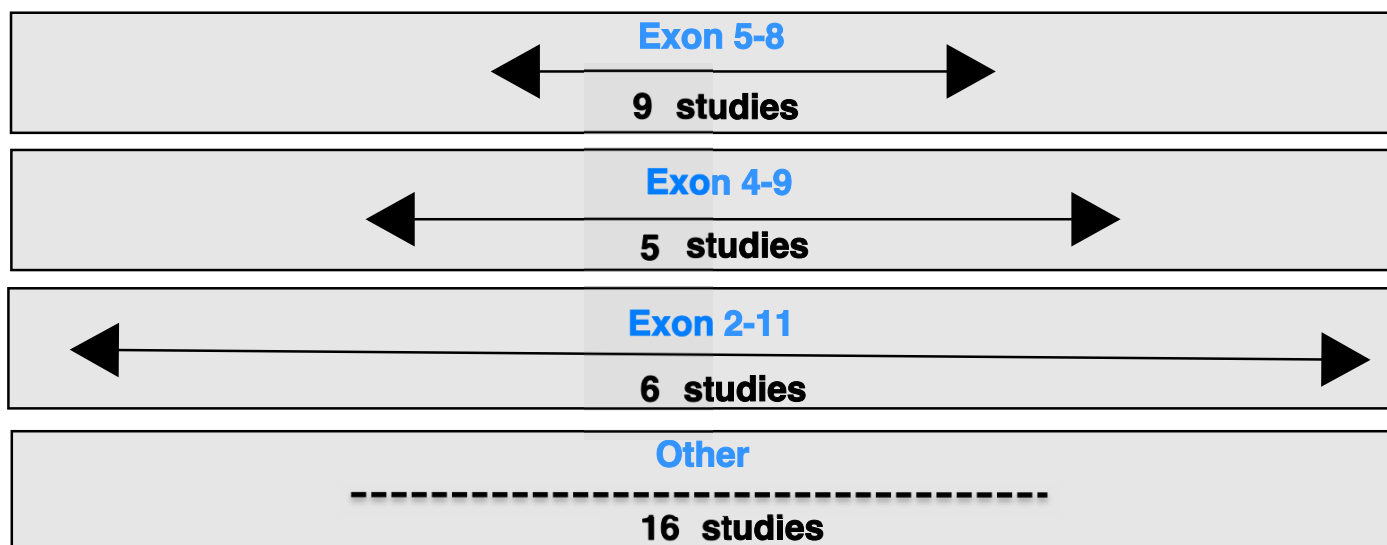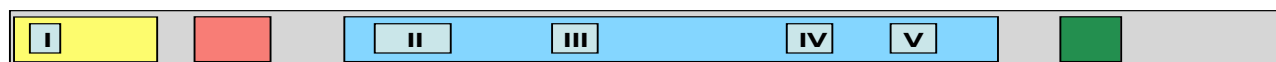
Other
16 studies

Prescreening

Studies with prescreening 17

SSCP	17	IHC	0
DGGE/CDGE	0	dHPLC	0
Yeast Assay	0	Other	0

Studies without prescreening 19

p53 mutation frequency

Number of missense mutations	262	86%
Number of nonsense mutations	30	10%
Number of frameshift mutations	11	4%
Total number of mutations	303	100%
Number of polymorphisms	57	19%

p53 mutant frequency

Number of missense mutants	143	88%
Number of nonsense mutants	13	8%
Number of frameshift mutants	7	4%
Total number of mutants	163	100%
Number of polymorphisms	26	16%

Hot spot mutations

Codon	WT Codon	Mutant Codon	WT AA	Mutant AA	Type	CpG	File Qty
282	CGG	TGG	Arg	Trp	Ts	Yes	16
248	CGG	TGG	Arg	Trp	Ts	Yes	15
179	CAT	TAT	His	Tyr	Ts	No	13
281	GAC	GAT	Asp	Asp	Ts	No	13
196	CGA	TGA	Arg	Stop	Ts	Yes	10
247	AAC	AAT	Asn	Asn	Ts	No	8
178	CAC	CAT	His	His	Ts	No	7
195	ATC	ATT	Ile	Ile	Ts	No	6
286	GAA	AAA	Glu	Lys	Ts	No	5
278	CCT	TTT	Pro	Phe	Ts	No	5

Exon Distribution

EXON 2-4

17%
17%
66%

EXON 5-8

2%
8%
90%

EXON 9-11

33%
67%

Frameshift   Nonsense   Missense

SKIN SCC

p53 mutation distribution

p53 mutational events