Supplementary Figure 1 online

Meta-analysis of p53 loss of function. Dot and bars; mean and 95% CI of mean p53 activity as measured by transactivation with 6 promoters. 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. For sake of space, only two cancer types, HNSCC (Fig 1 A to 1G) and Eso SCC (Fig 1 H to 1O), are shown. HNSCC is the cancer with the highest rate of out of range studies (7 studies) . All these studies display a similar behaviour with each transcription promoters and no new out of range study are highlighted in this analysis. A similar results in obtained with ESO SCC (1 out range study) and with other cancer (data not shown).

Supplementary Figure 2 online

Control of the global mean value: Six studies were used for this analysis. For five studies (1859 in oesophageal cancer, 1187 in ovarian cancer, 1896 in colorectal cancer, 2015 in bladder cancer and 1914 in breast cancer) p53 mutation analysis was performed simultaneously by direct sequencing and by DNA chips with a very good concordance between the two methodologies. For study 485 in breast cancer, p53 mutations were analysed on both DNA and RNA obtained from different parts of the same tumour and processed in two different Institutes. 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 also shown. CRC: Colorectal carcinoma; HNSCC: head and neck squamous cell carcinoma; NSCLC: Non-small cell lung cancer; HCC: hepatocellular carcinoma; C.L.: Cell lines; G.L.: germline mutation.

Supplementary Figure 3 online

Meta–analysis of p53 loss of function. 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 (see material and methods). The top figure corresponds to the graph shown in Figure 2 with a larger scale. The lower graph includes publications describing 4 or more p53 mutations.

Supplementary Figure 4 online

p53 mutant distribution according to their frequency in the database. p53 mutations have been classified into 3 categories according to their frequency. Frequent p53 mutations (represented at least 10 times in the database), light green; infrequent p53 mutations (represented 9 times or less in the database), red; mutations that do not change the amino acid, blue. Known p53 polymorphism of the p53 protein (codons 36, 72 and 213) was not included.
Out–of–range studies are shown at the bottom of each graph.

Supplementary Figure 5 online
Distribution of mutational events in lung cancer. Comparison of all lung cancers with known smoking status (A) versus the 1659–70 study (B). The number of cases is shown inside each graph. The 1659–70 study was not included in A.

Supplementary Figure 6 online

Distribution of p53 loss of function in breast cancer. Dot and bars; mean and 95% CI of mean p53 activity as measured by transactivation with the 8 promoters. Data from Crook et al. are derived from a single study that describes 44 tumours in BRCA patients and 7 sporadic cases.
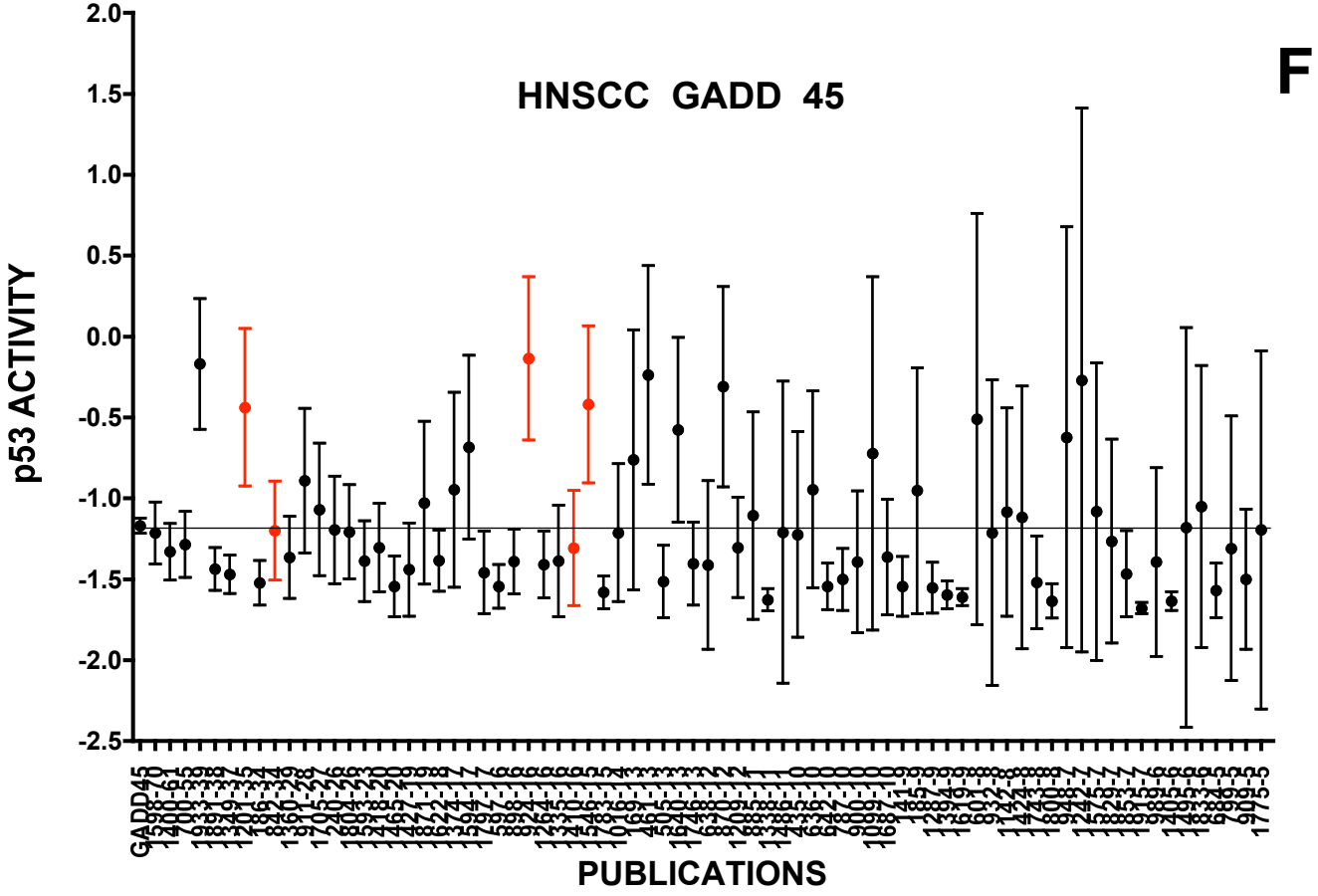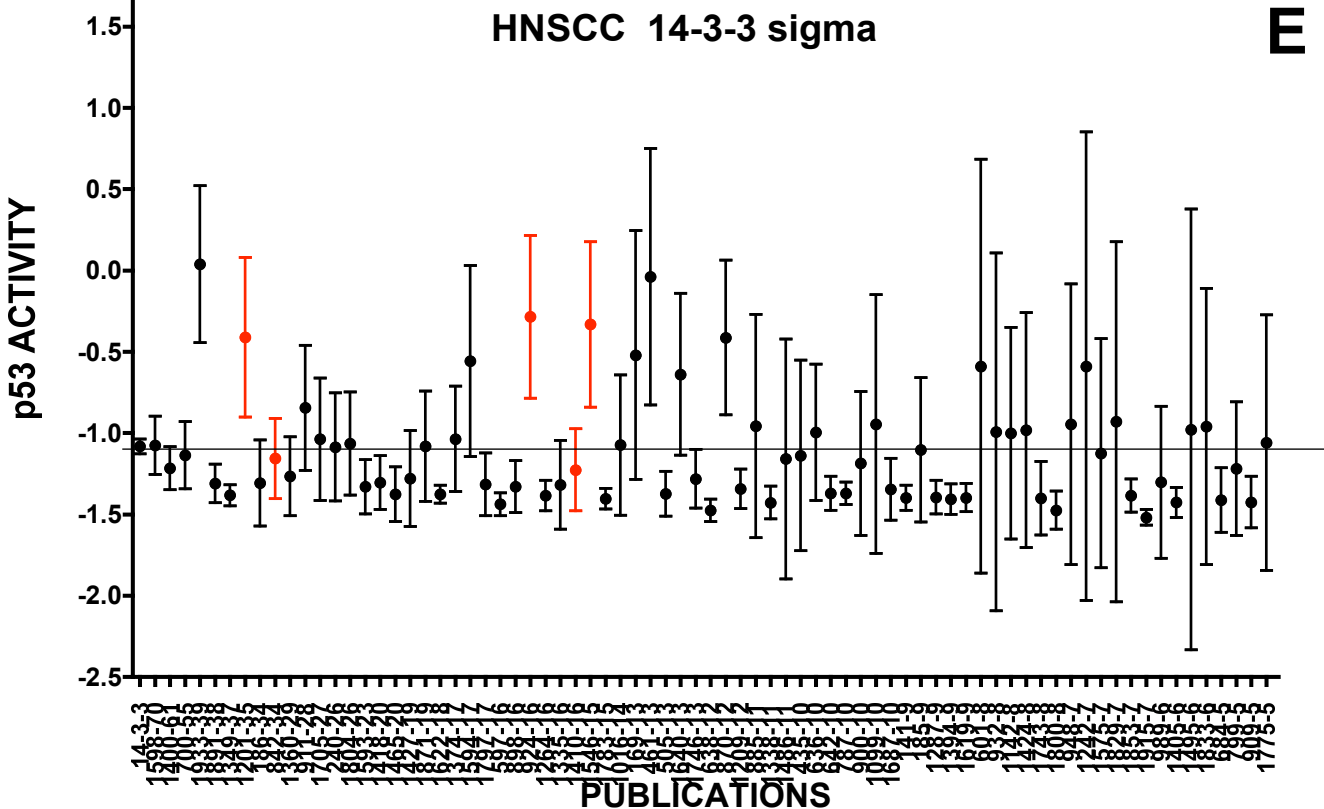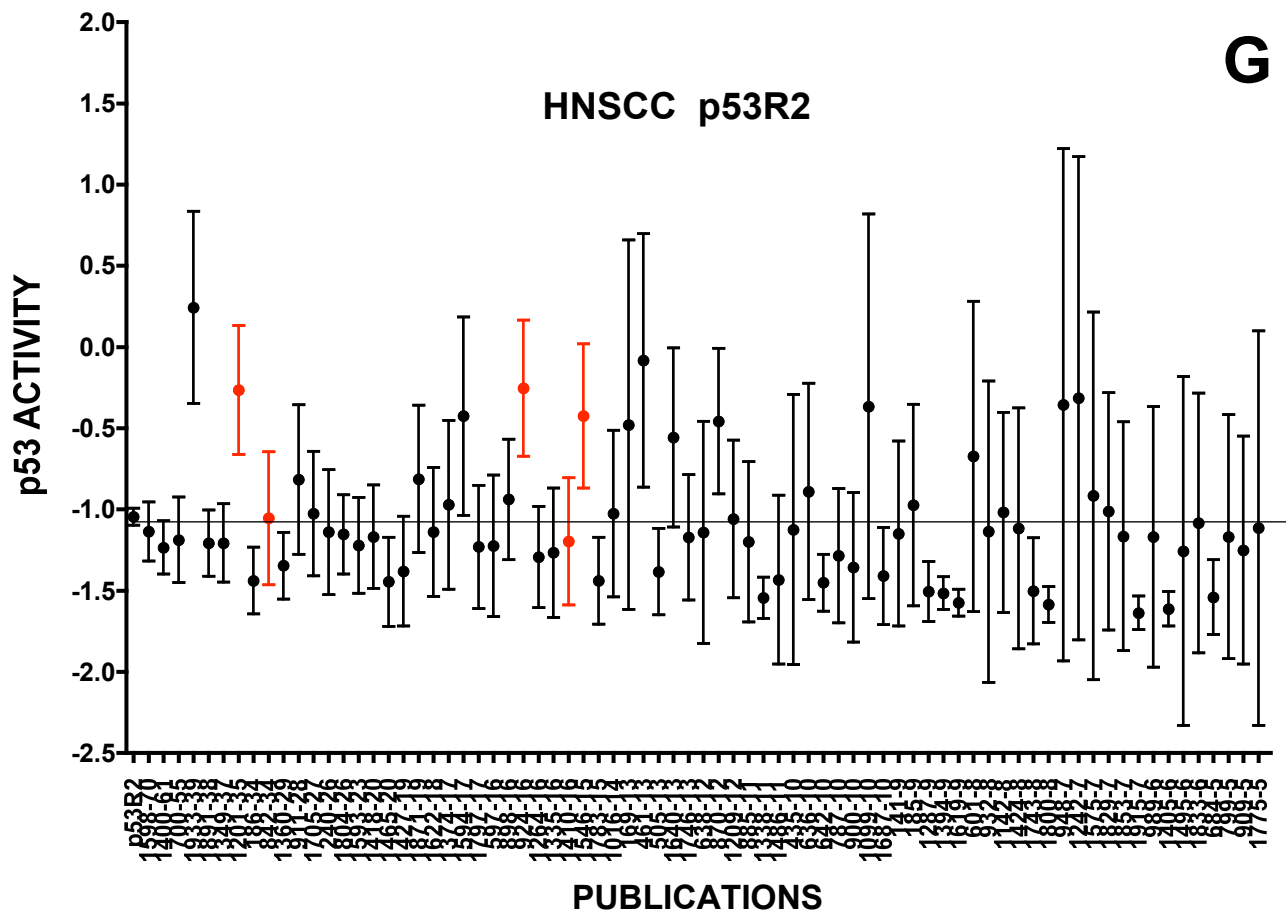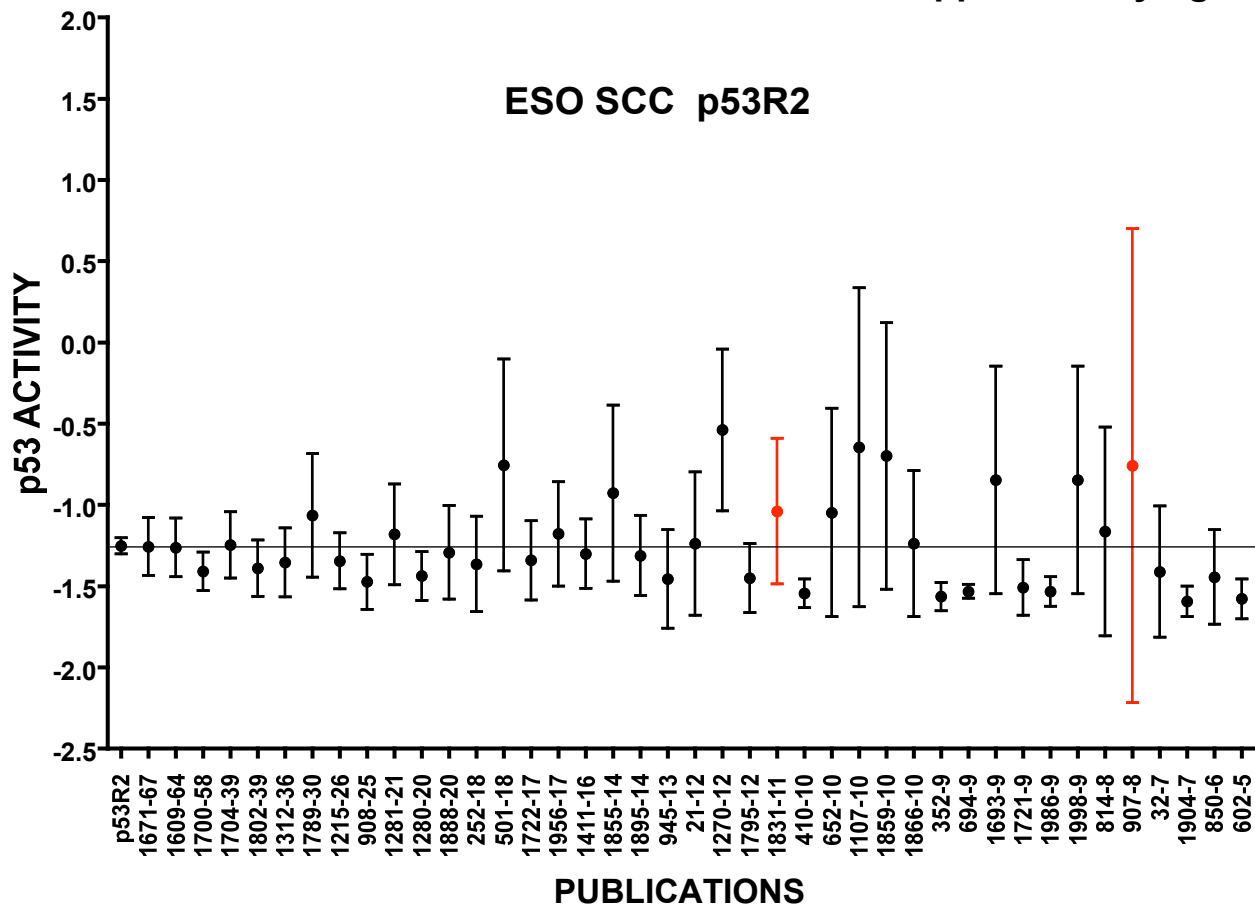
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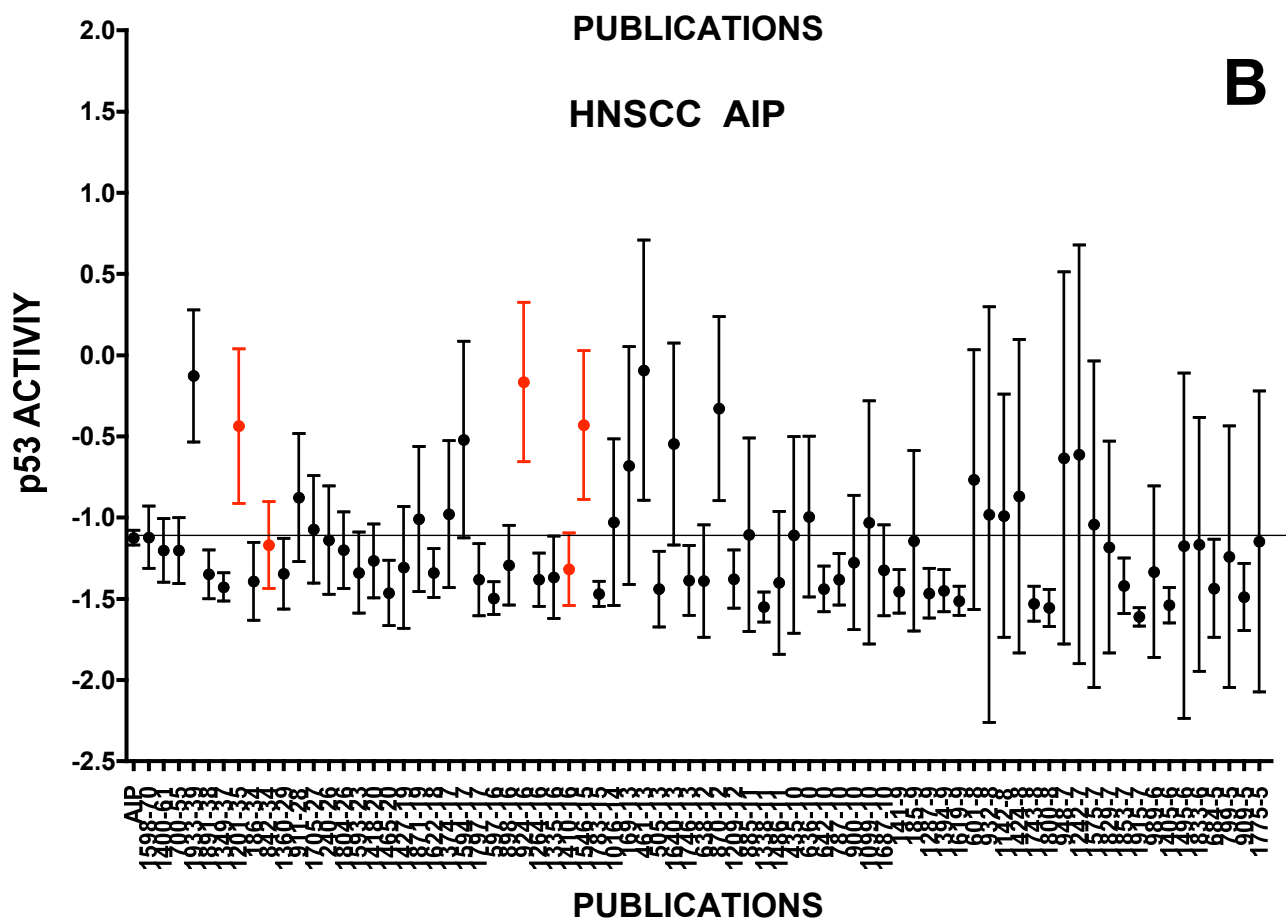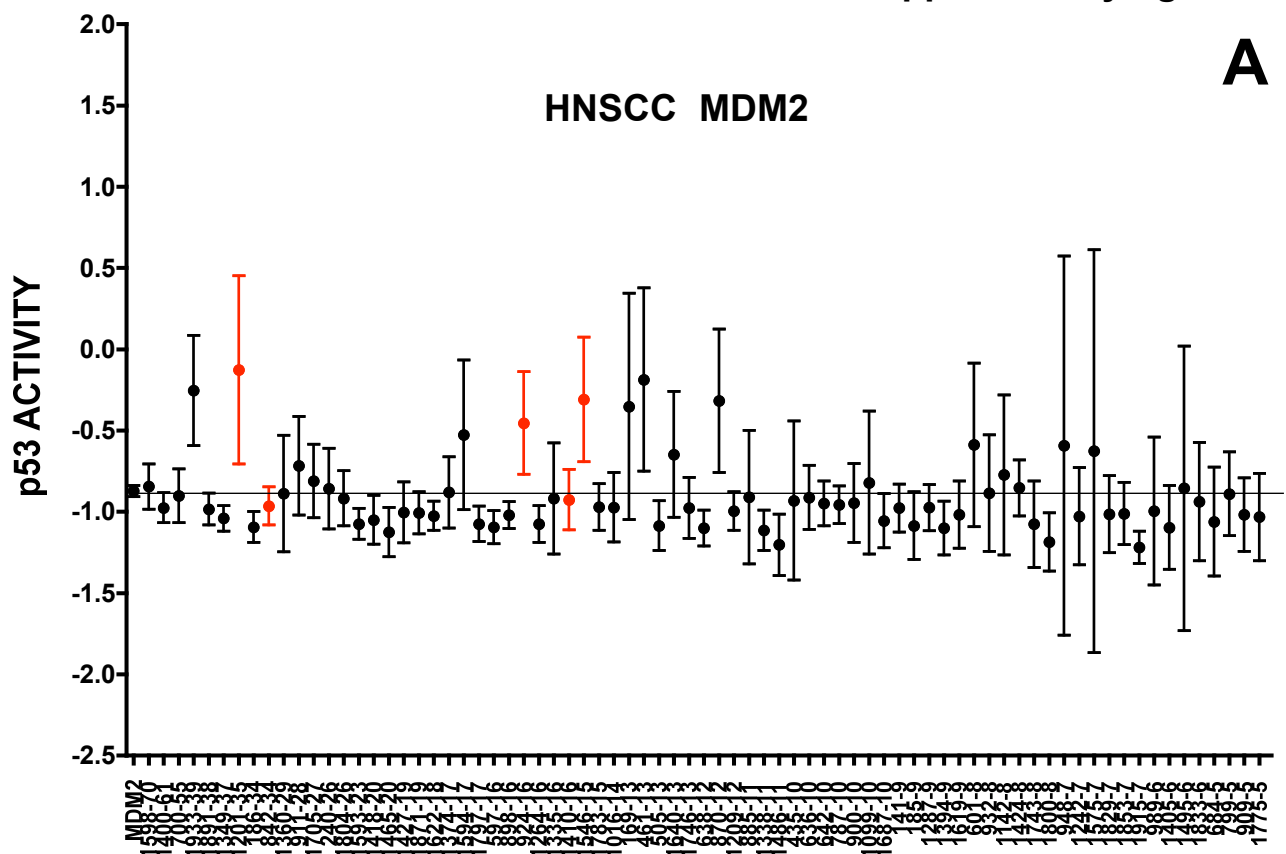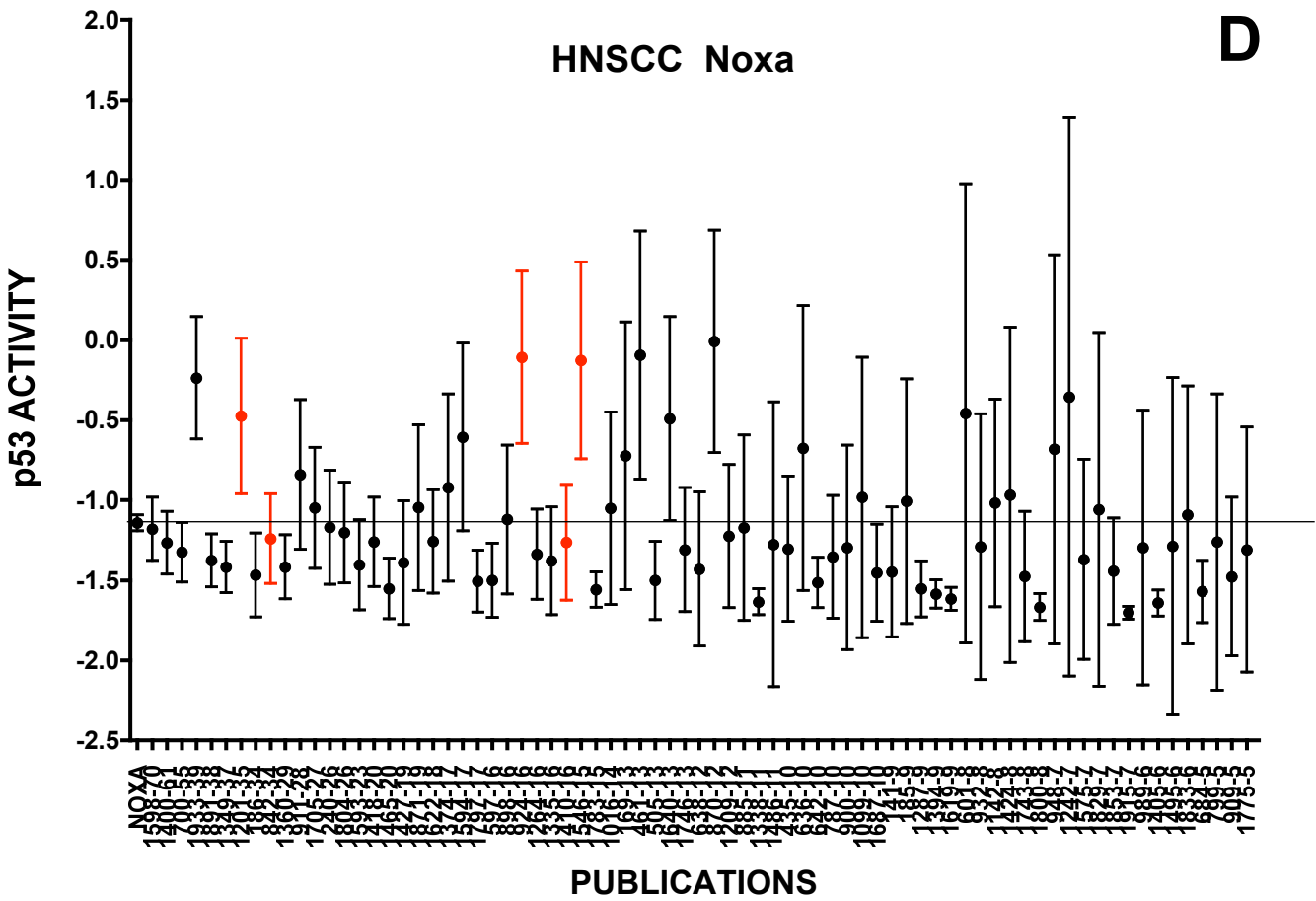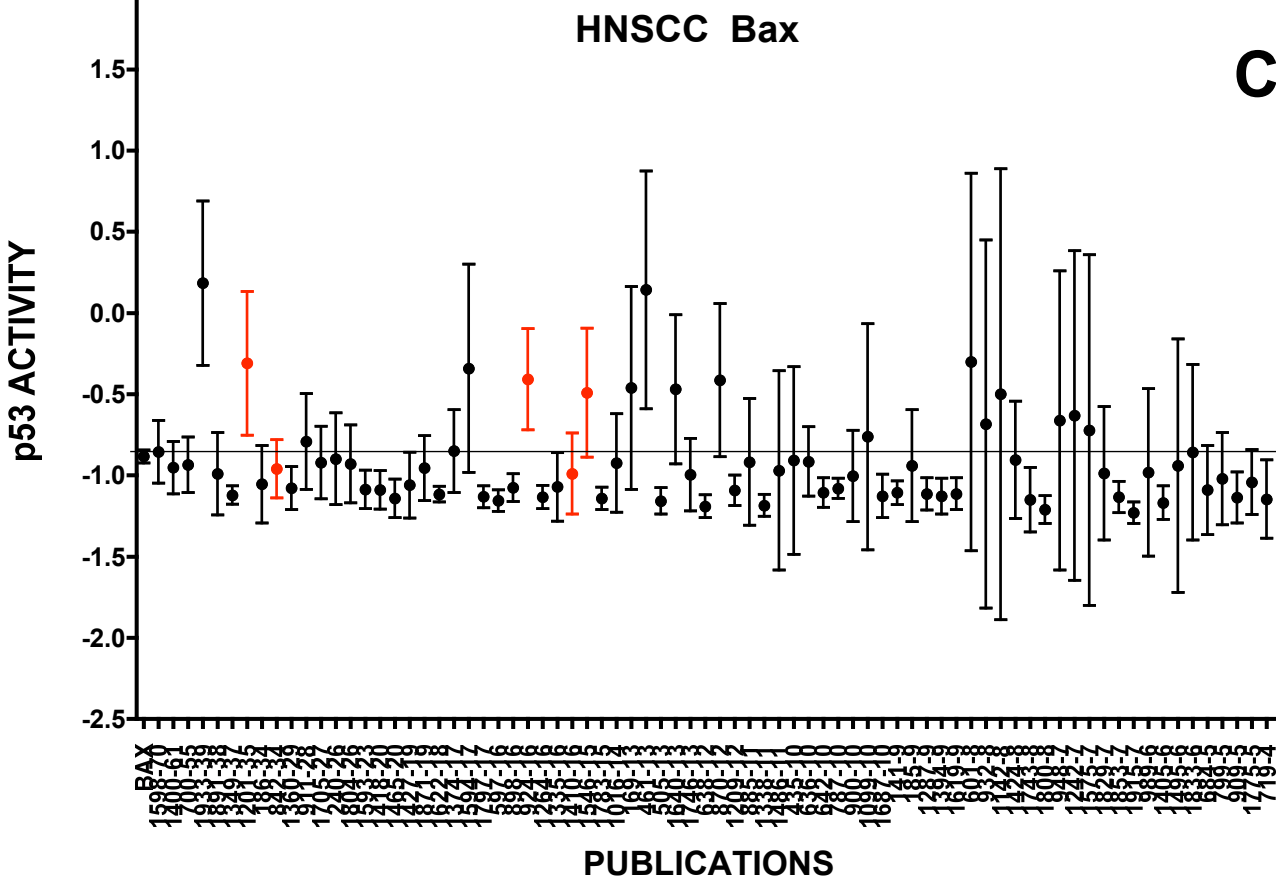
HNSCC MDM2

A

p53 ACTIVITY

PUBLICATIONS

HNSCC AIP

B

p53 ACTIVIY

PUBLICATIONS

Supplementary figure 1

C

HNSCC Bax

D

HNSCC Noxa

Supplementary figure 1

E HNSCC 14-3-3 sigma

F HNSCC GADD 45

Supplementary figure 1

HNSCC p53R2

G

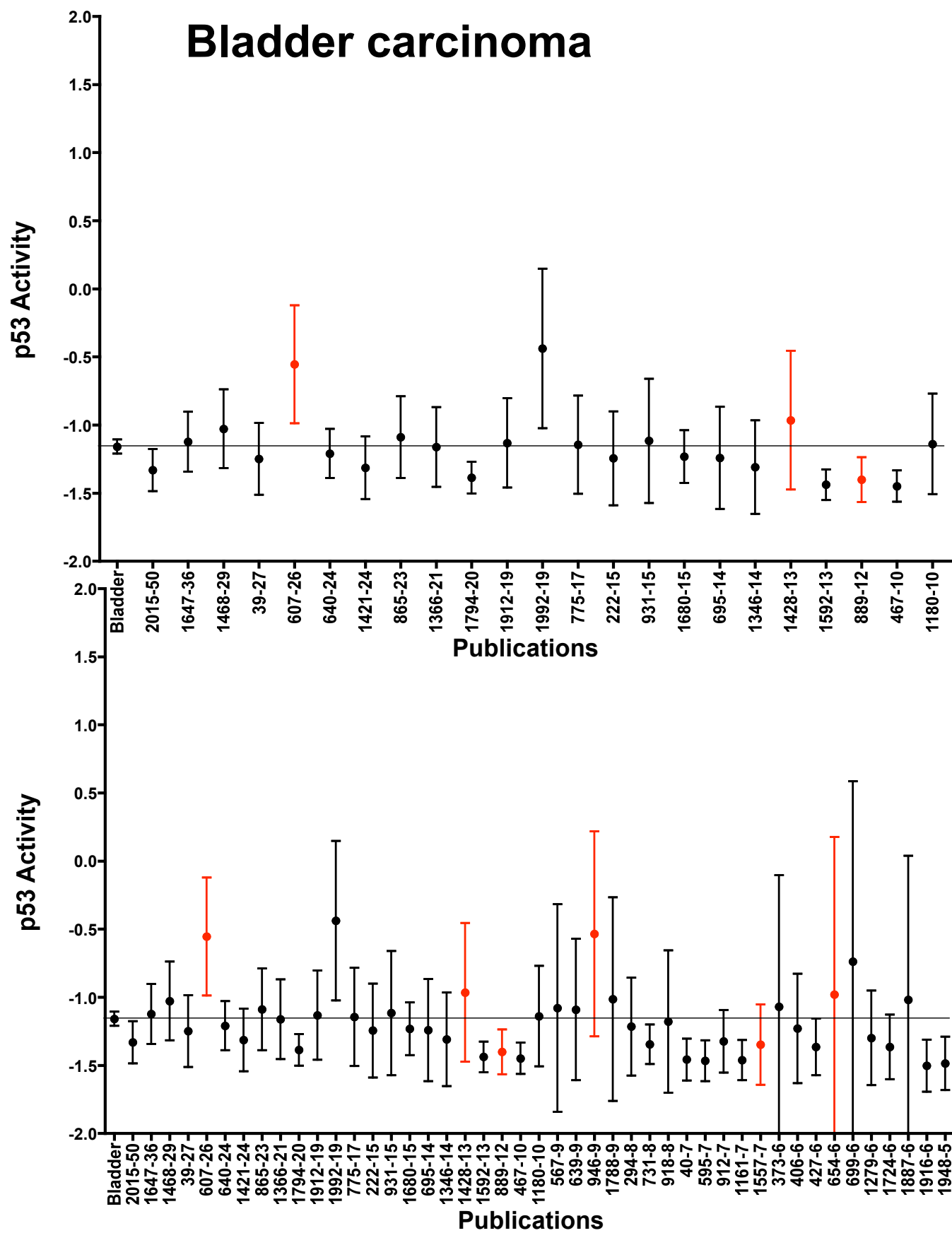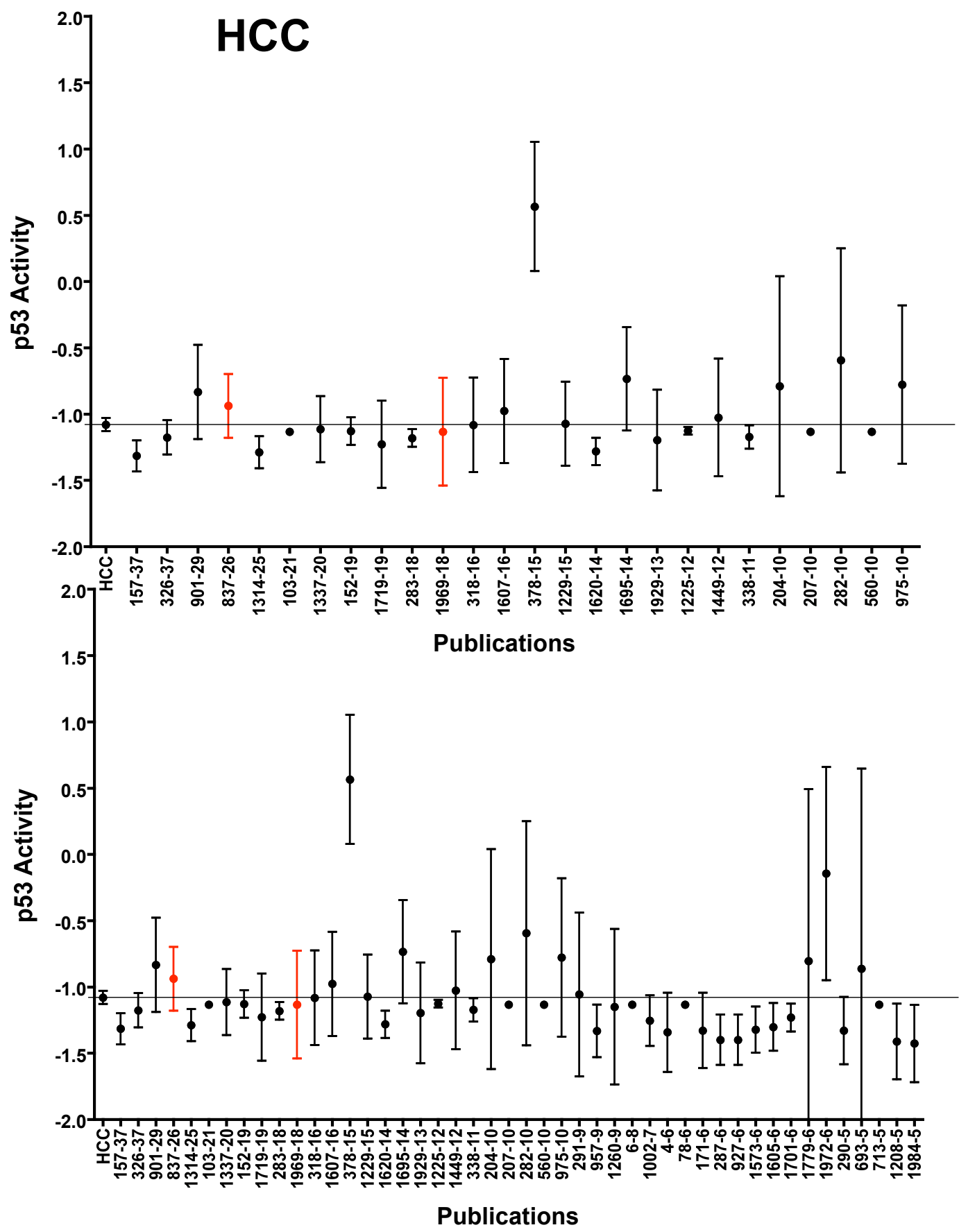Supplementary figure 1

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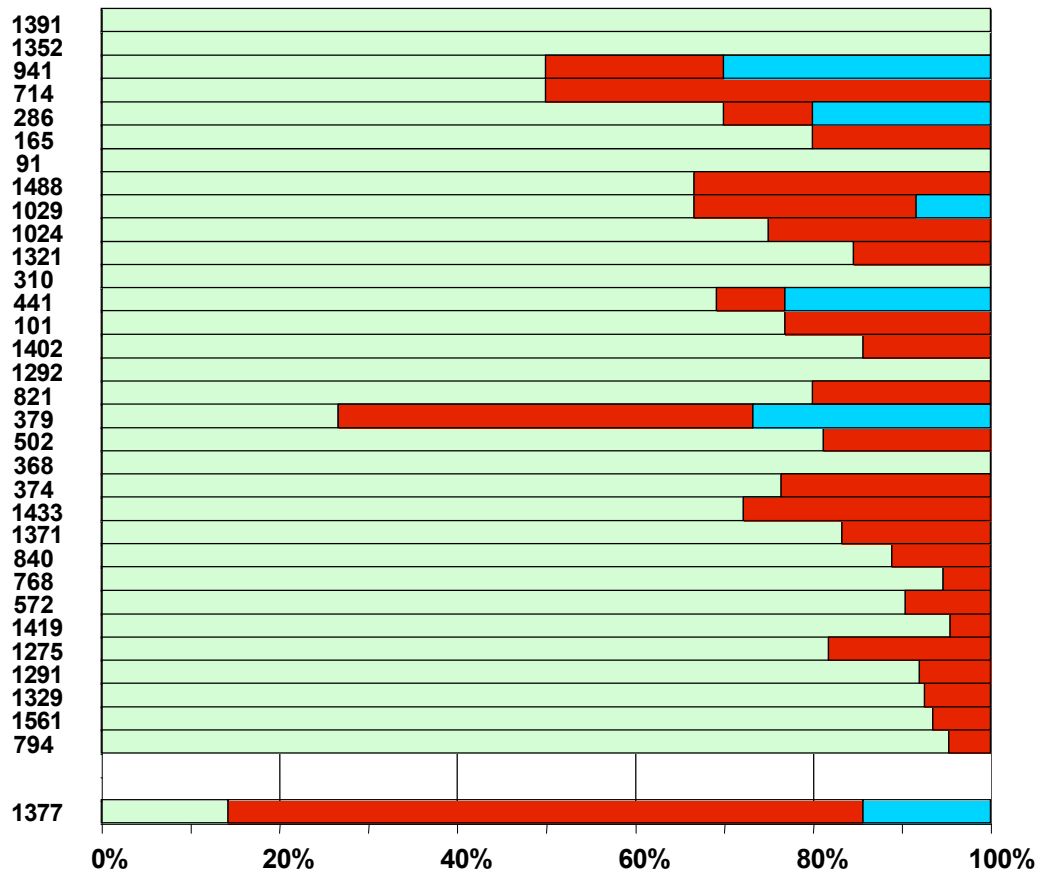
Supplementary figure 1

Eso SCC 14-3-3 sigma

M

Eso SCC GADD 45

N

Supplementary figure 1

ESO SCC p53R2

O

BASE LINE DEFINITION

Supplementary figure 3

COLORECTAL CARCINOMA

Supplementary figure 3

GASTRIC CARCINOMA

Supplementary figure 3

BREAST CARCINOMA

Supplementary figure 3

Supplementary figure 3

Supplementary figure 3

Esophageal SCC
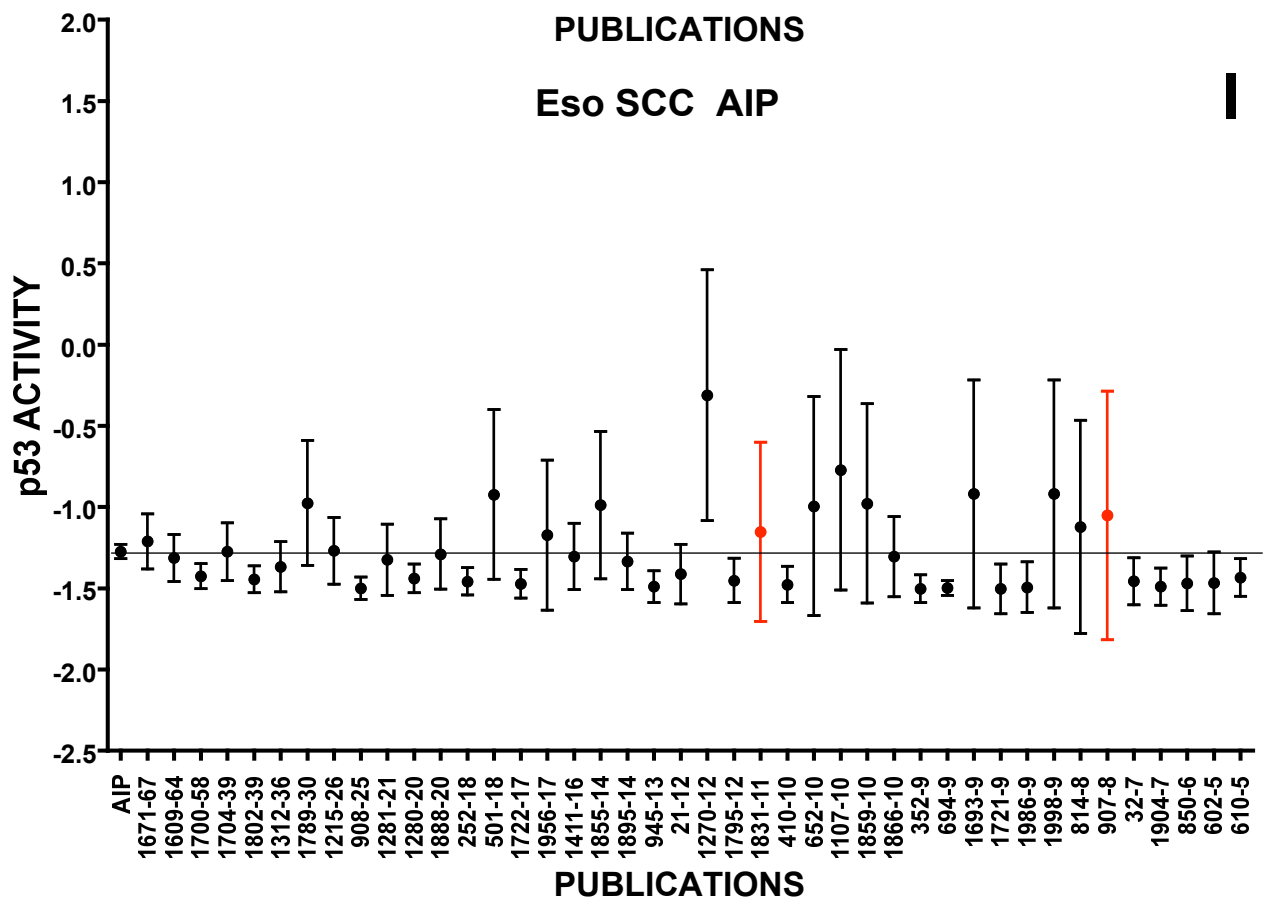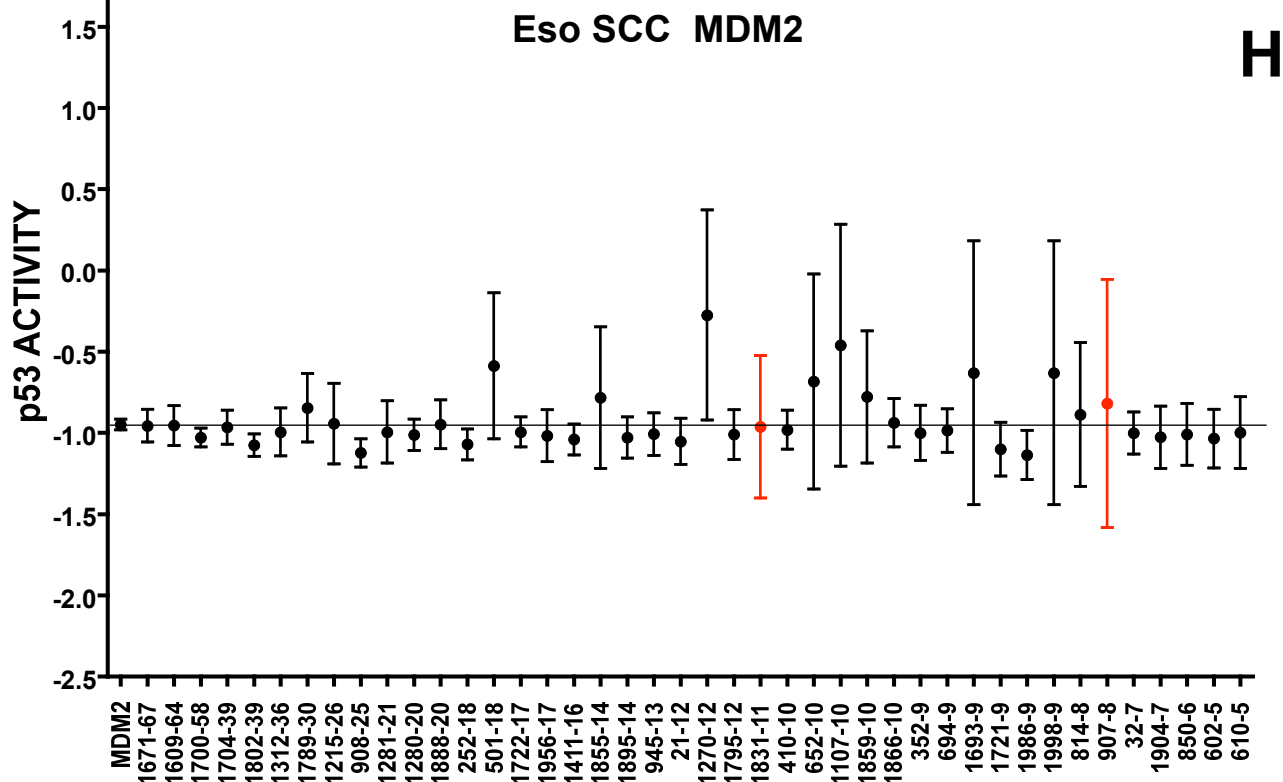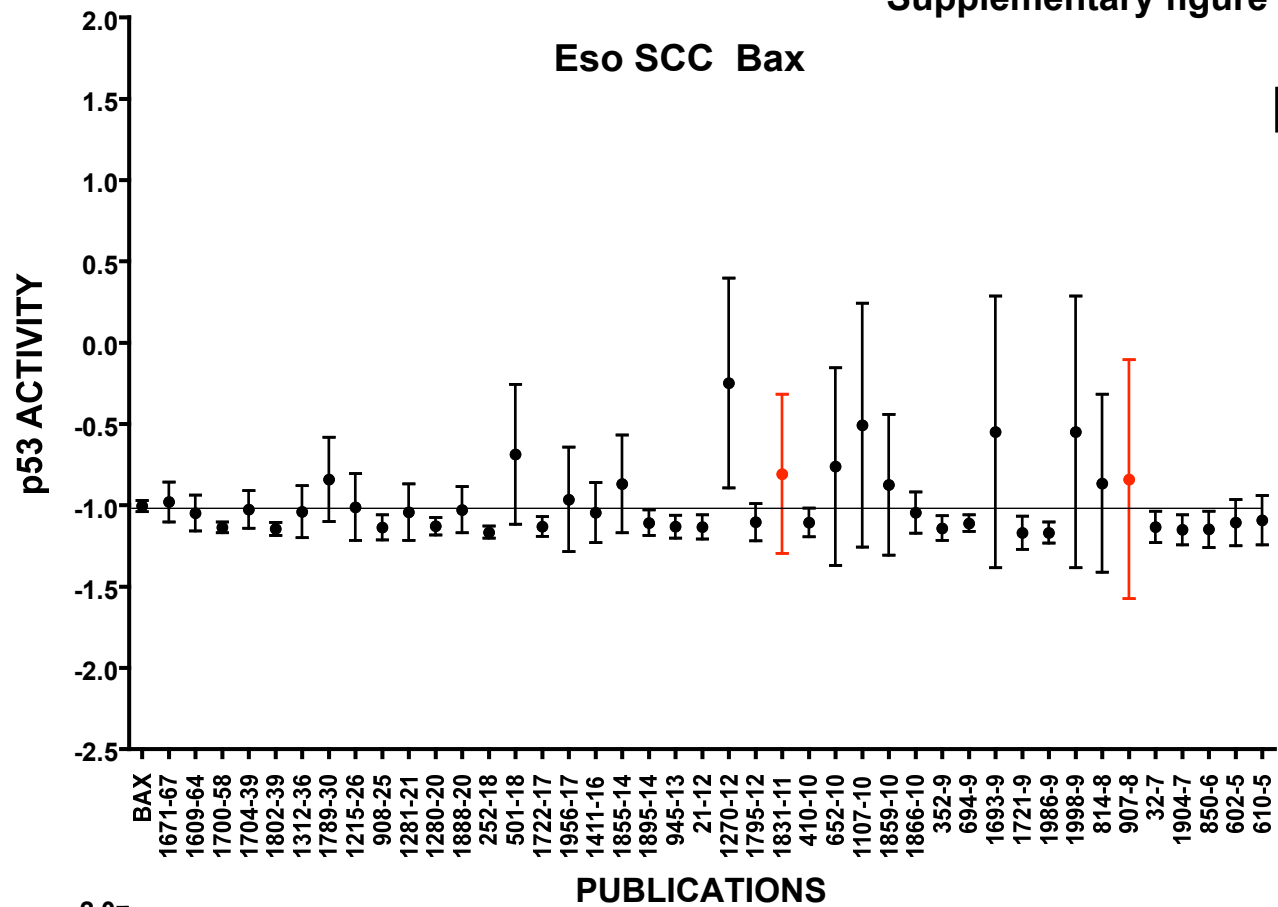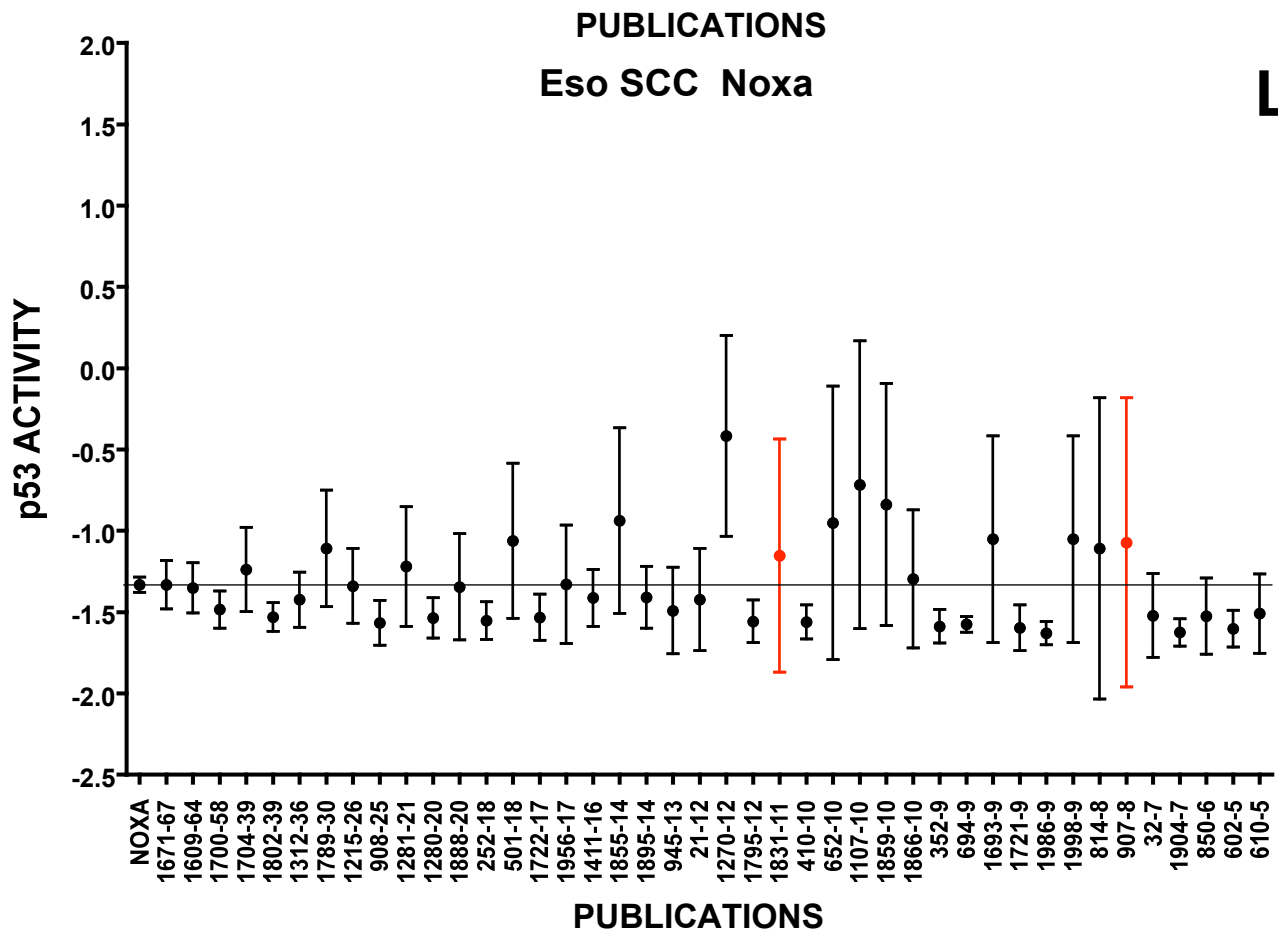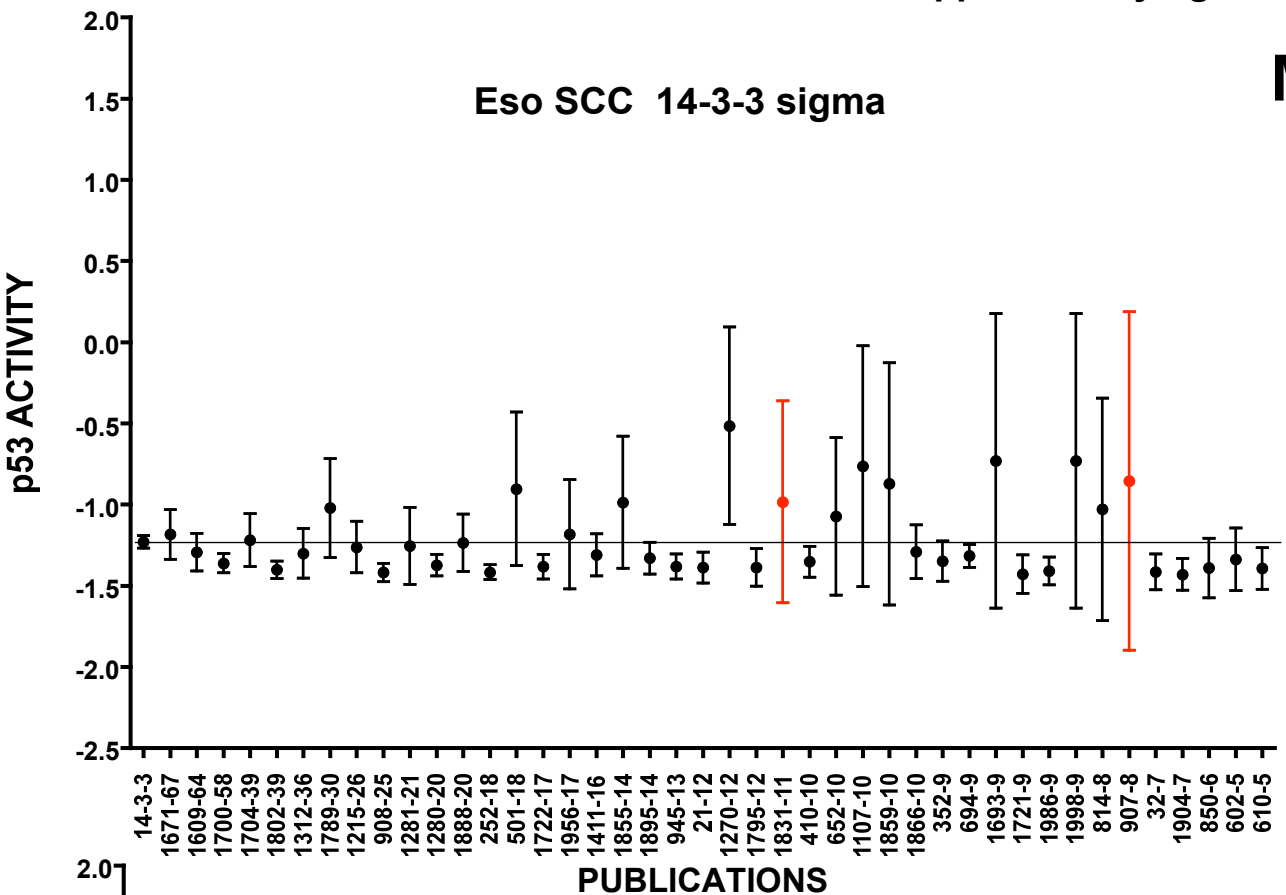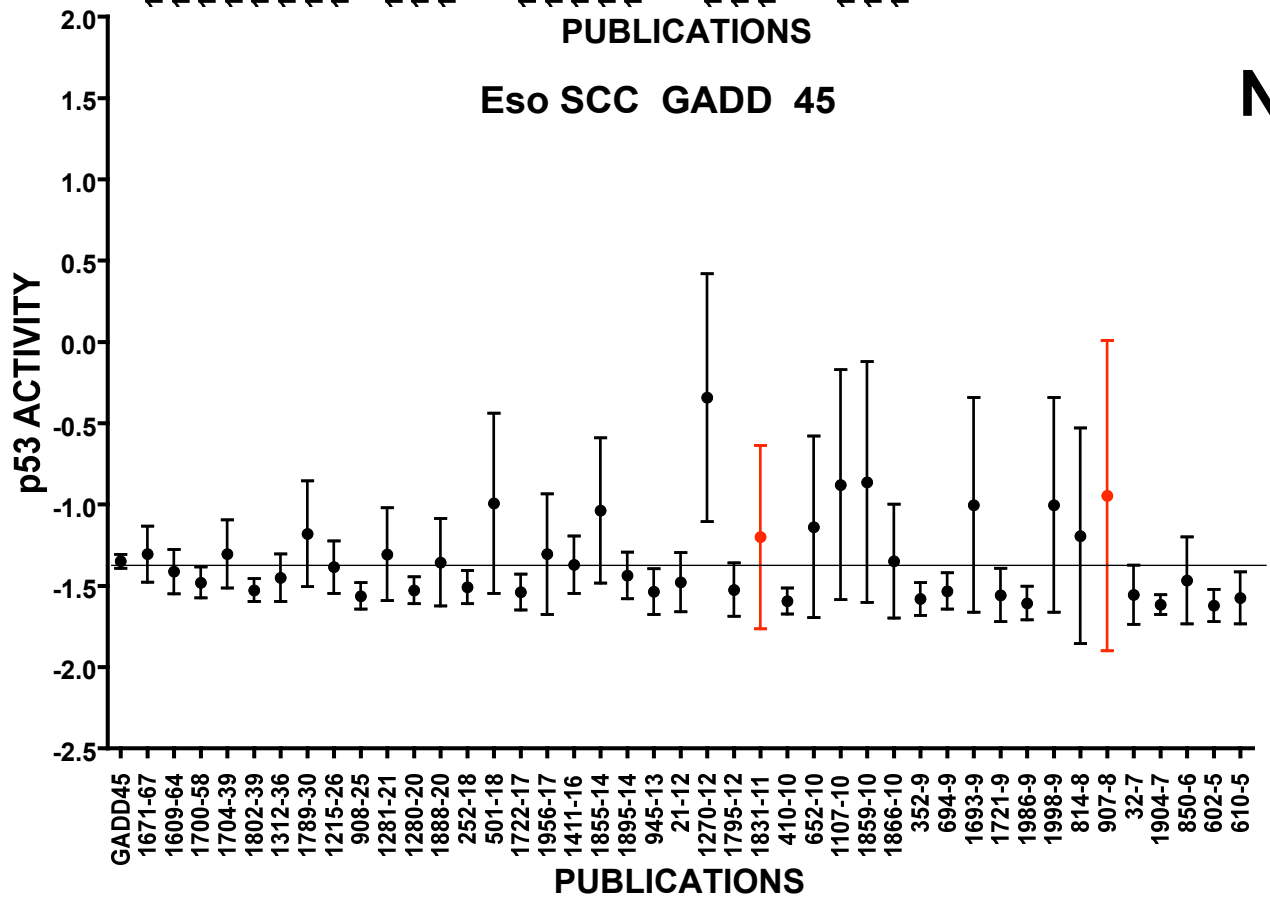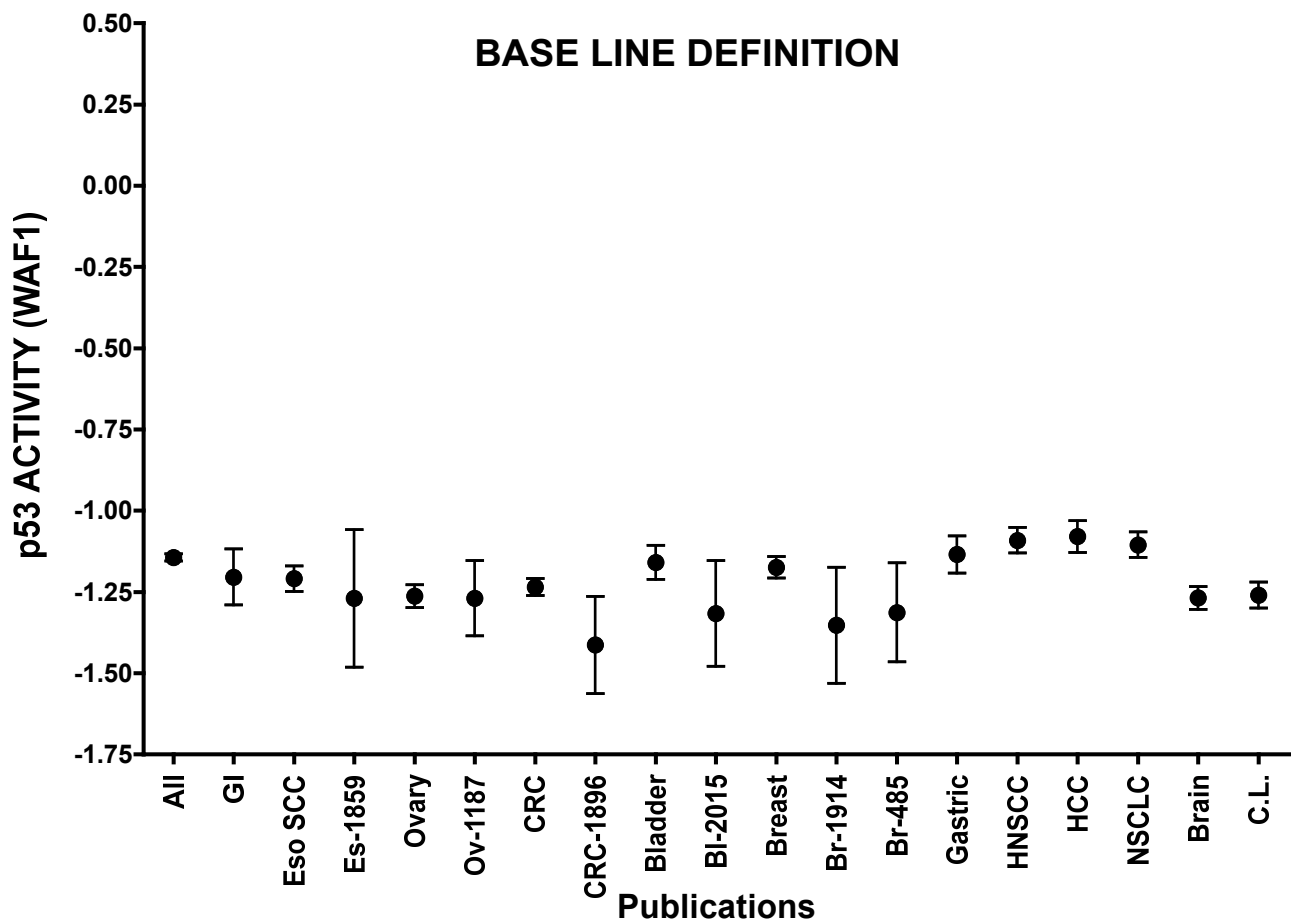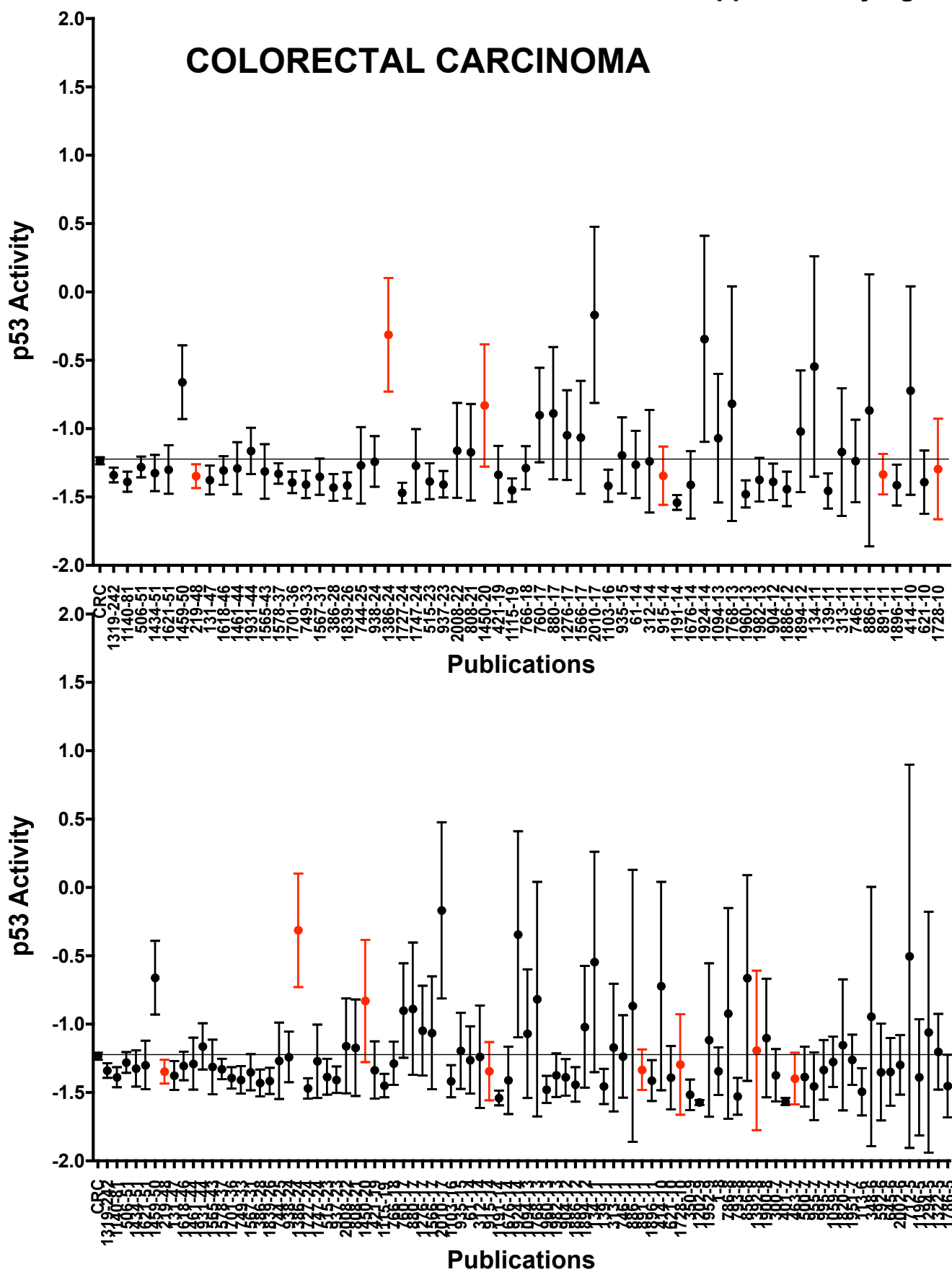
Supplementary figure 3

Brain tumors
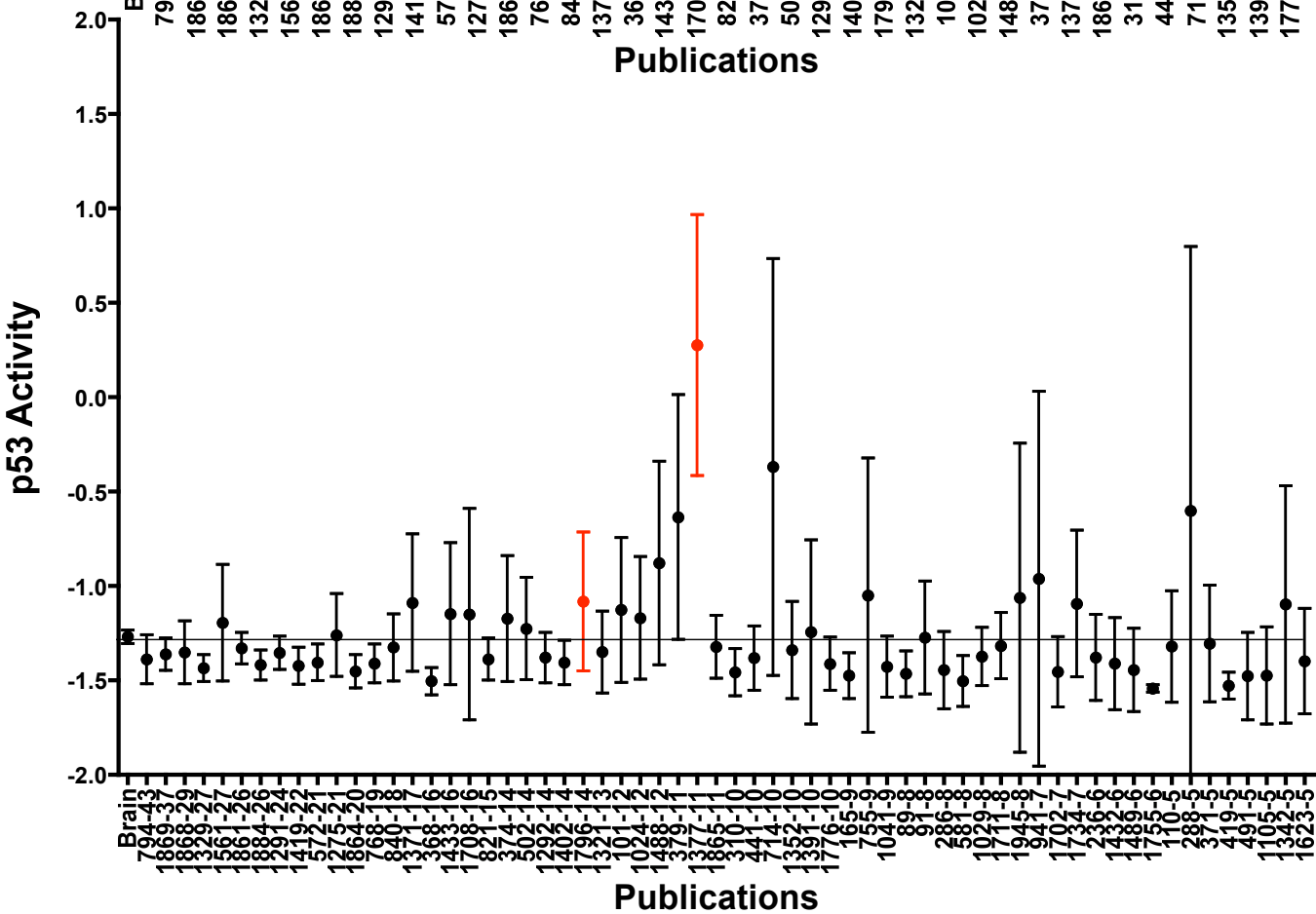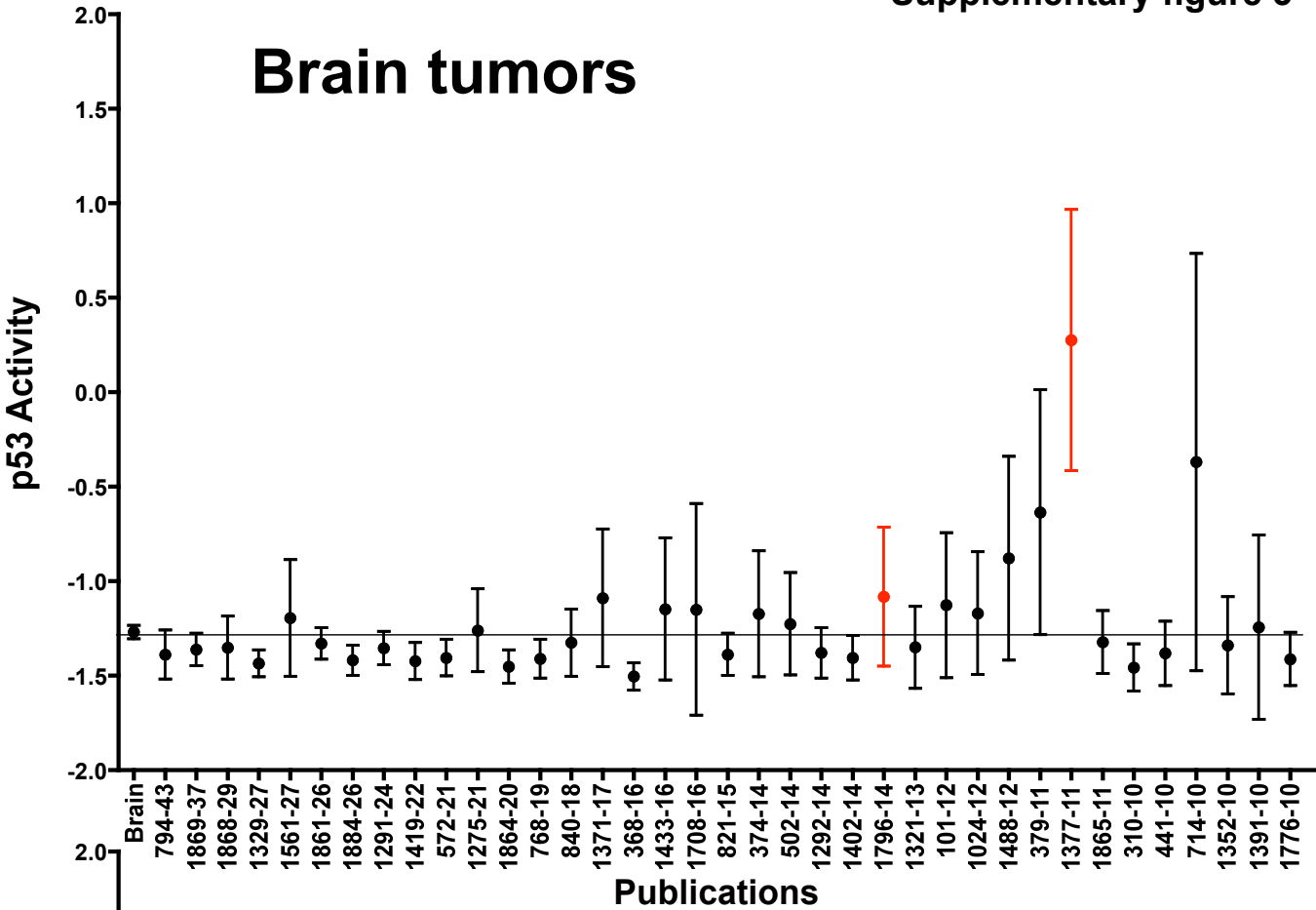
Bladder carcinoma

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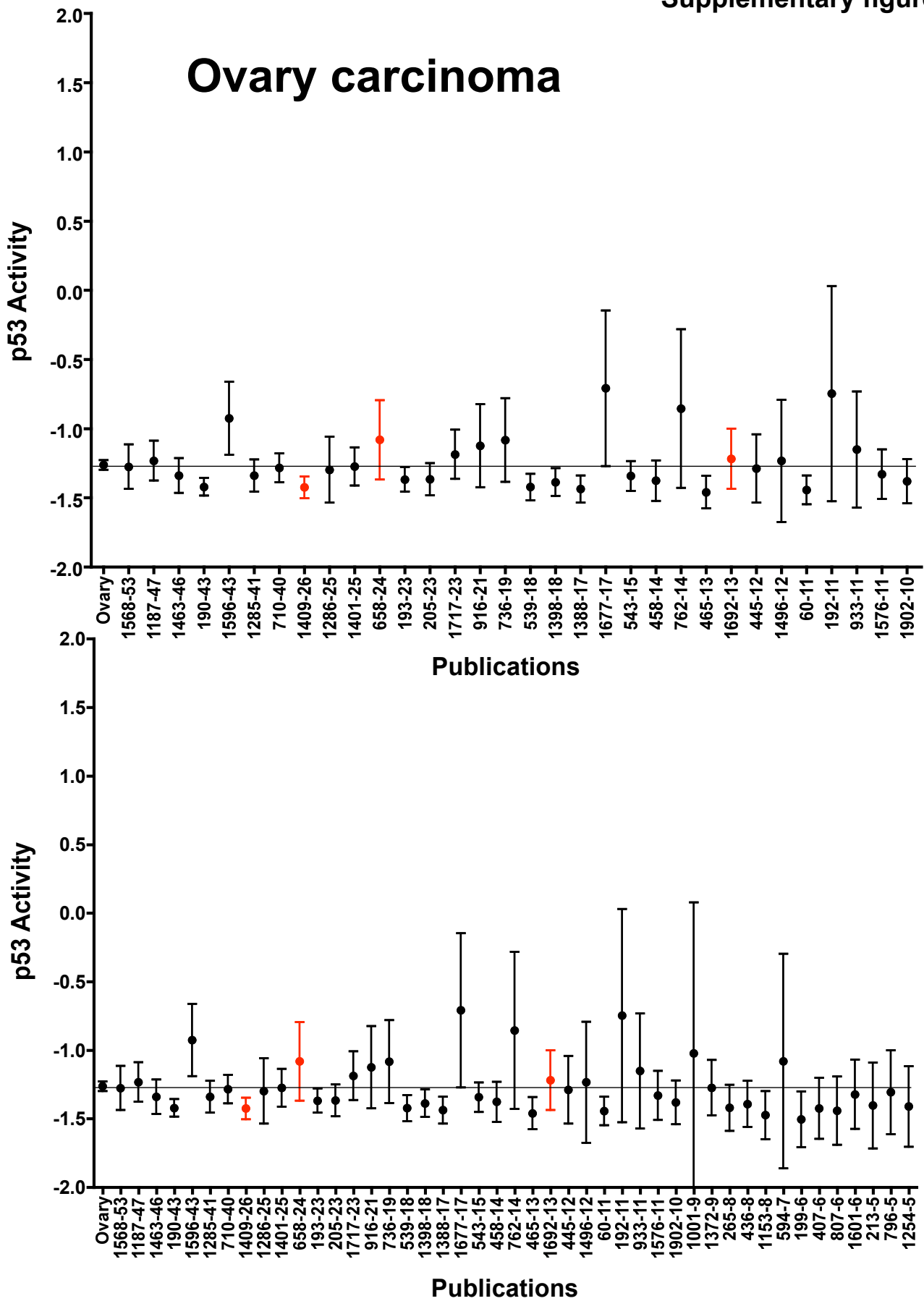
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Ovary carcinoma
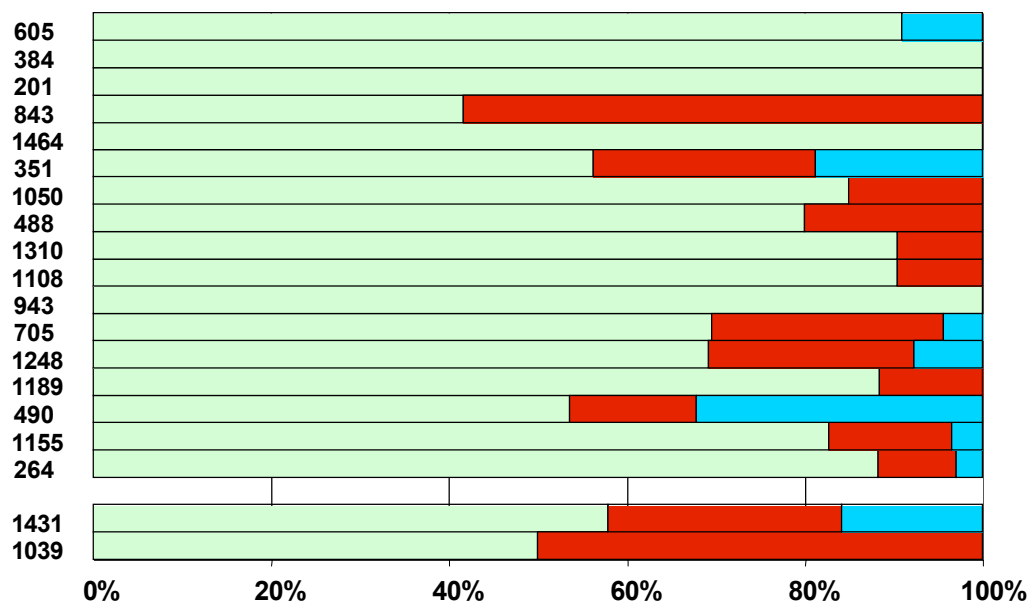
Esophageal carcinoma
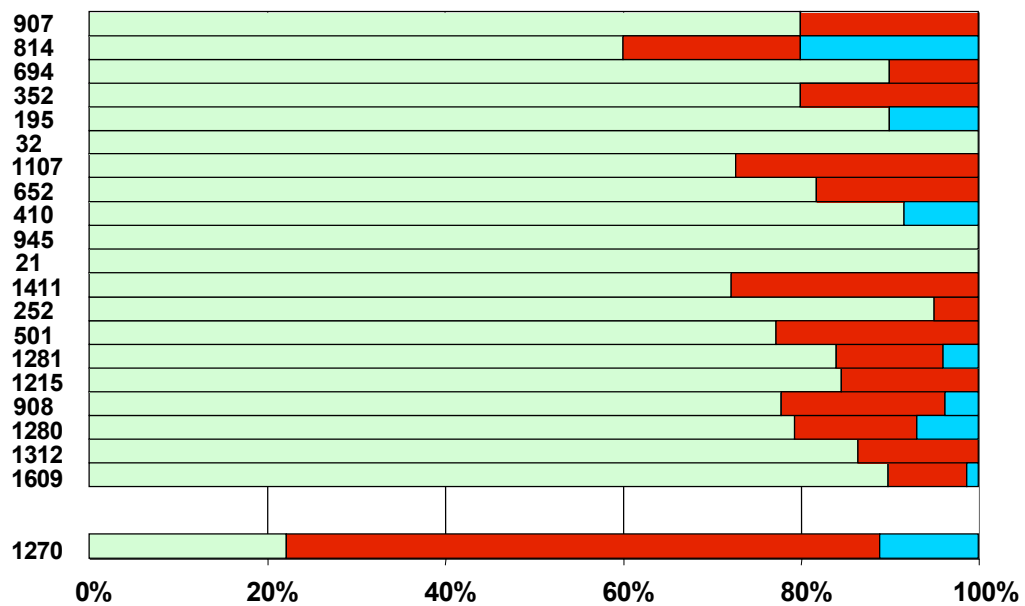
Brain tumors

HNSCC
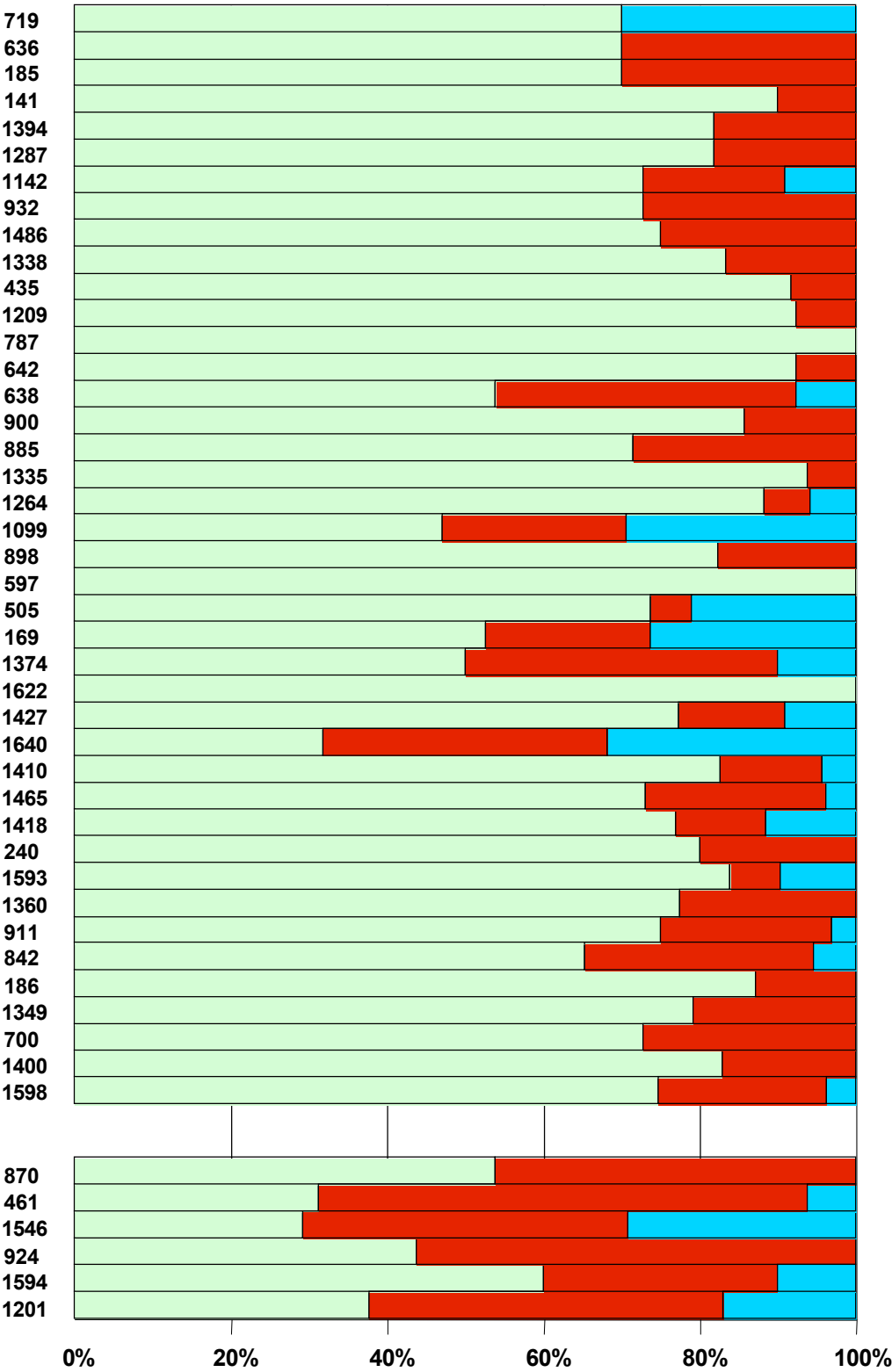
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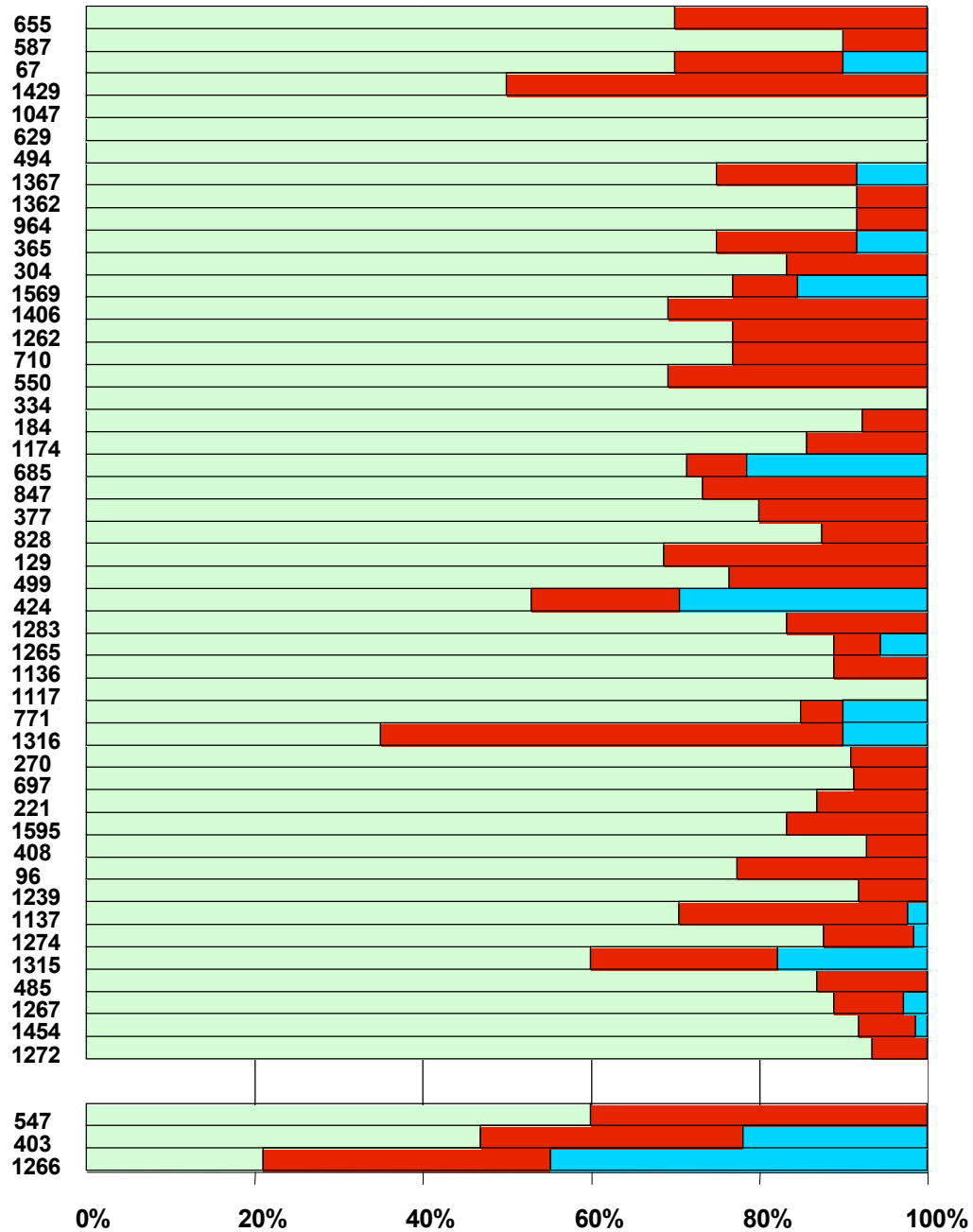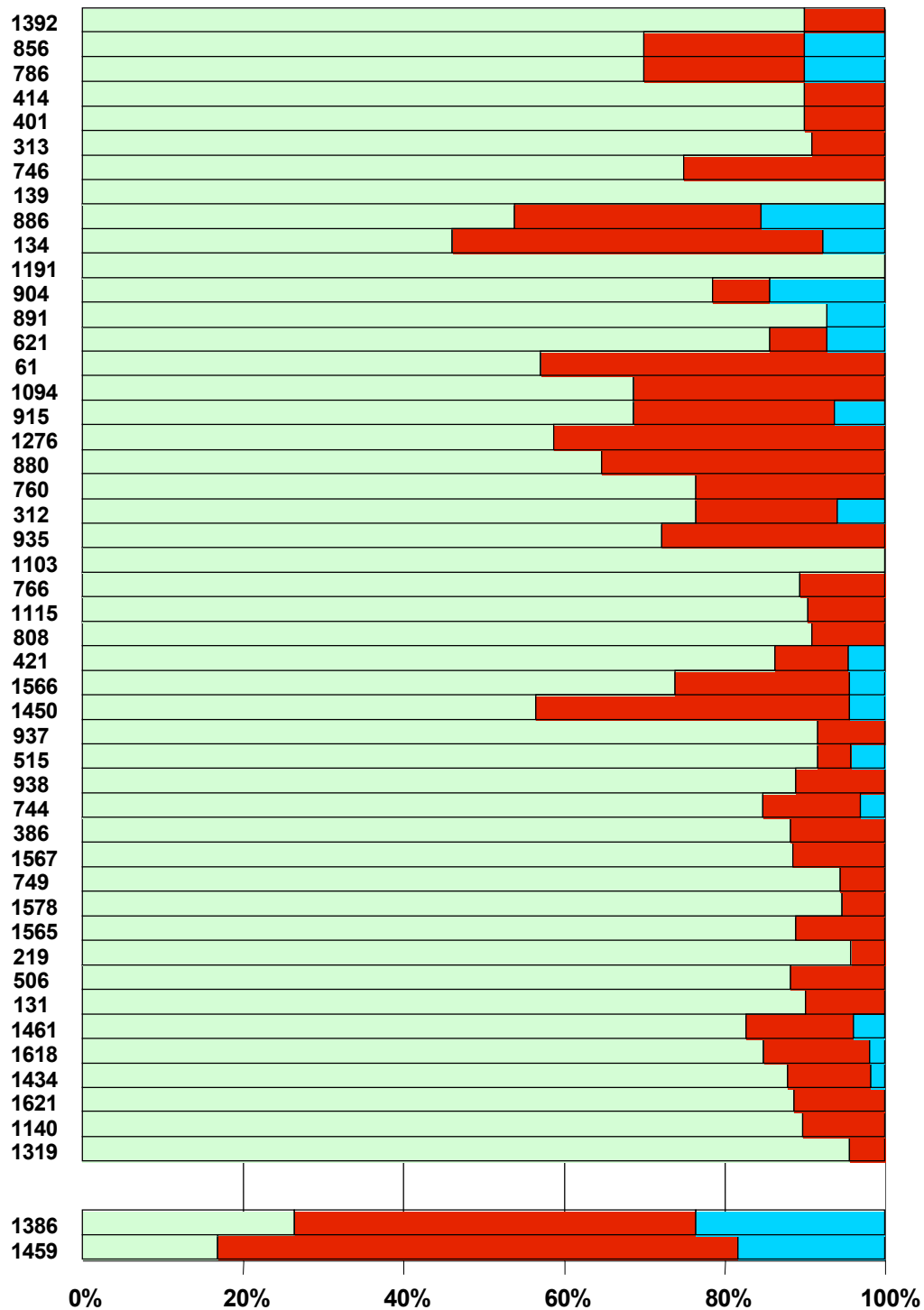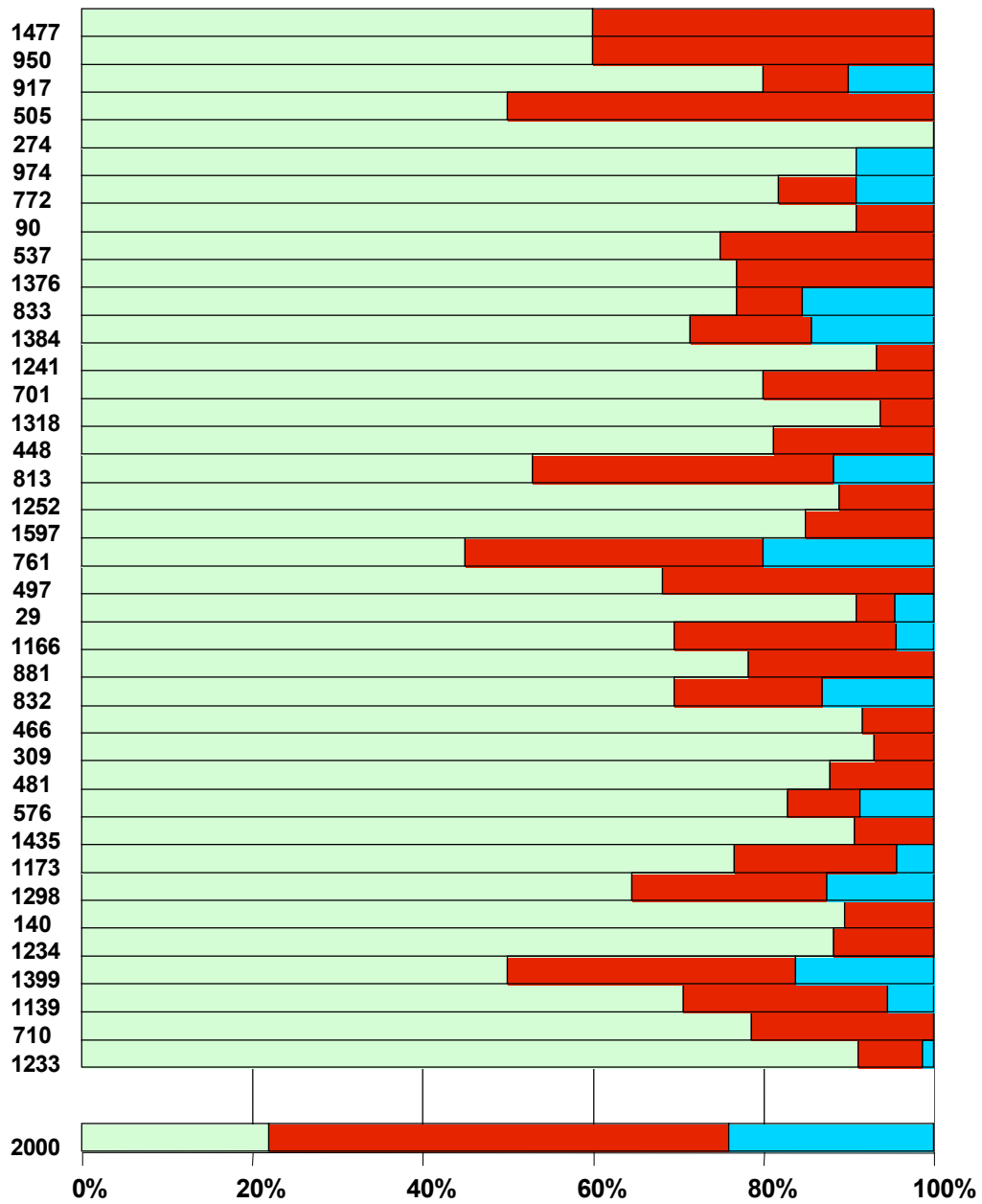
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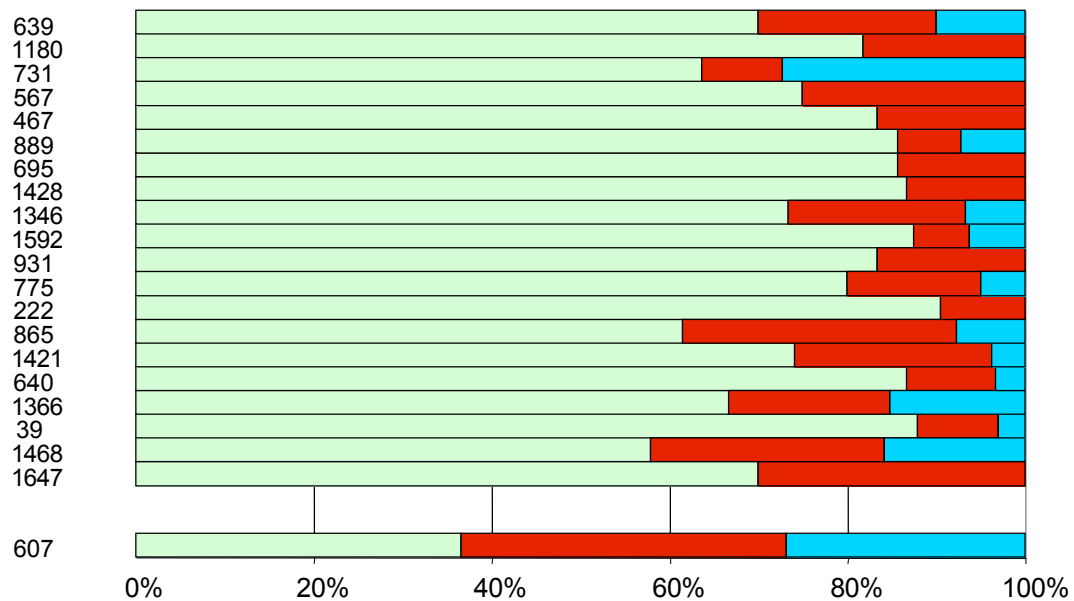
Gastric carcinoma

Colorectal carcinoma
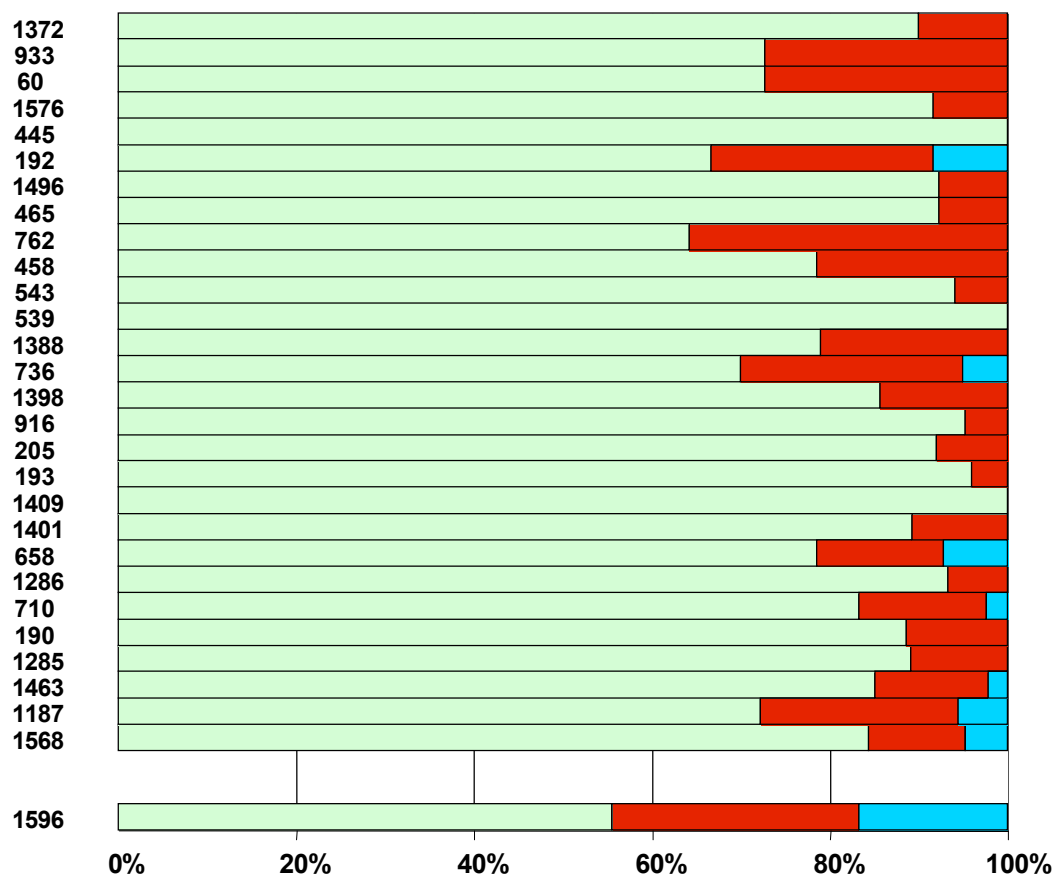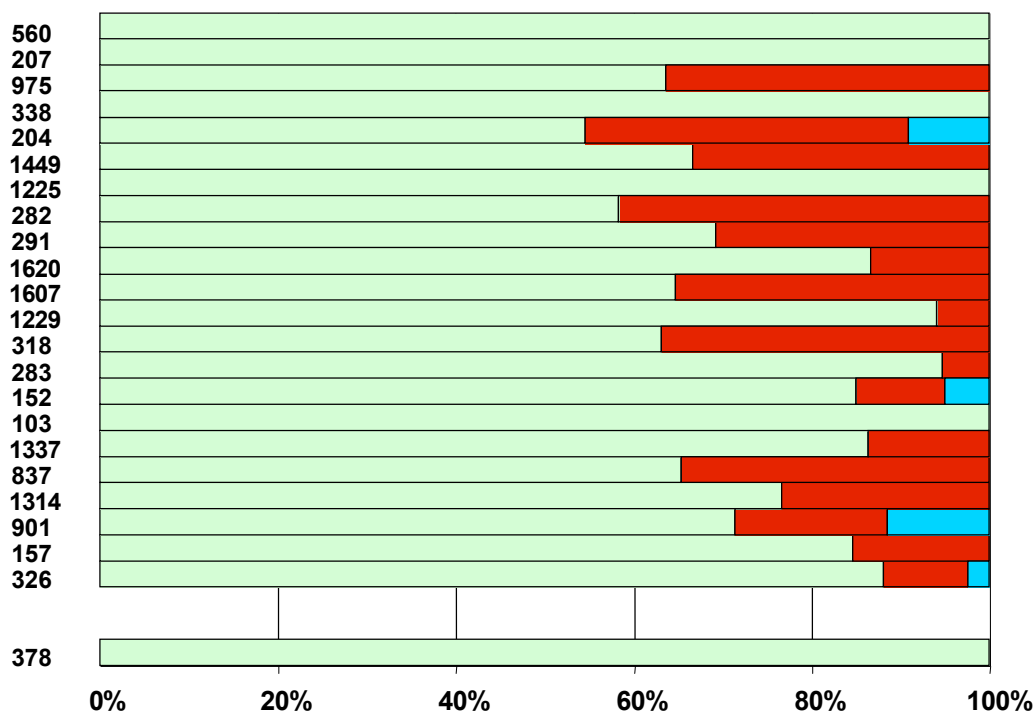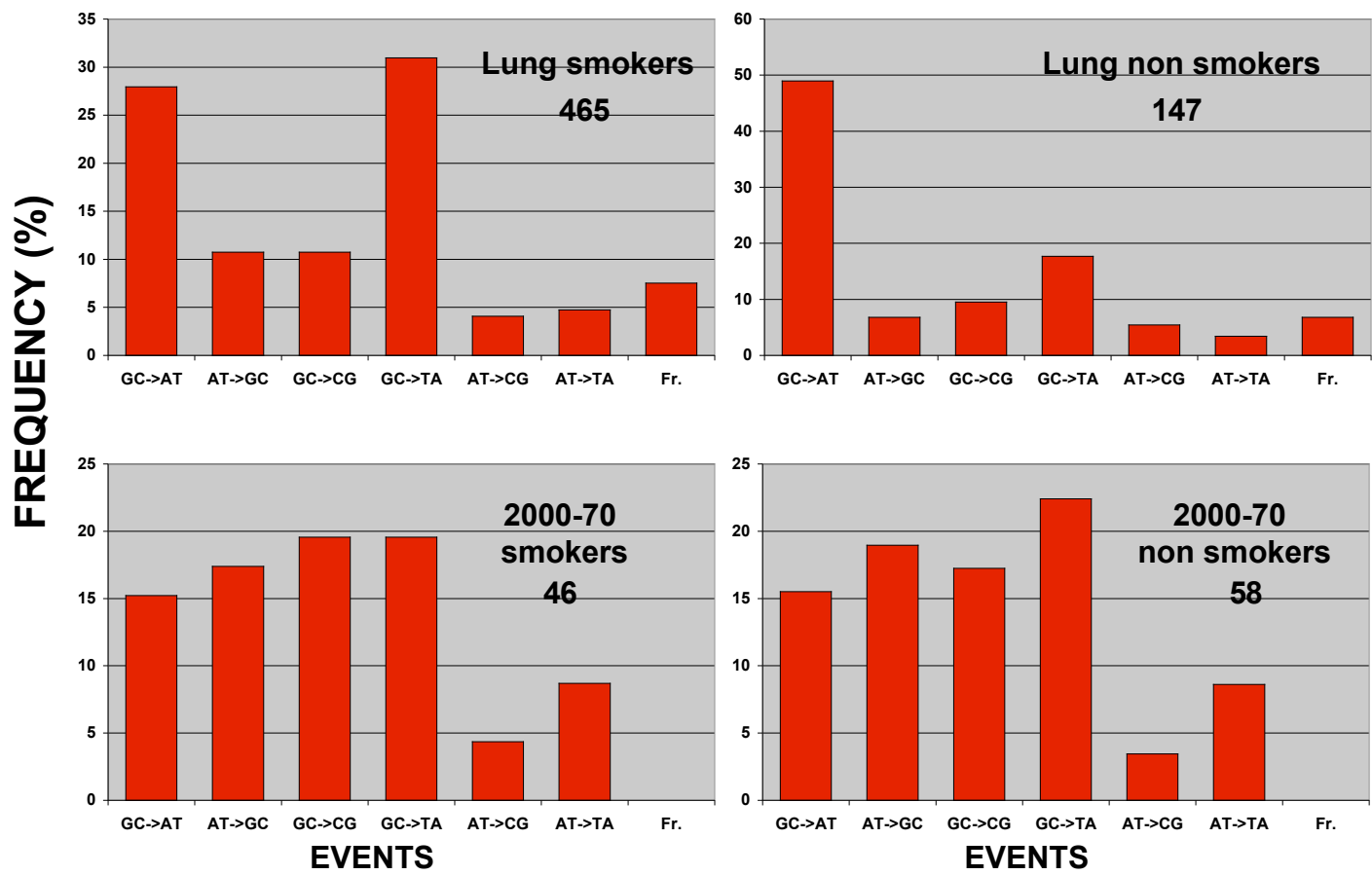
NSCLC

Ovary carcinoma

HCC

Supplementary figure 5

Supplementary figure 6