Supplemental Figures and Tables

Somatic mutations of the Parkinson's Disease gene *PARK2* in glioblastoma and other human malignancies

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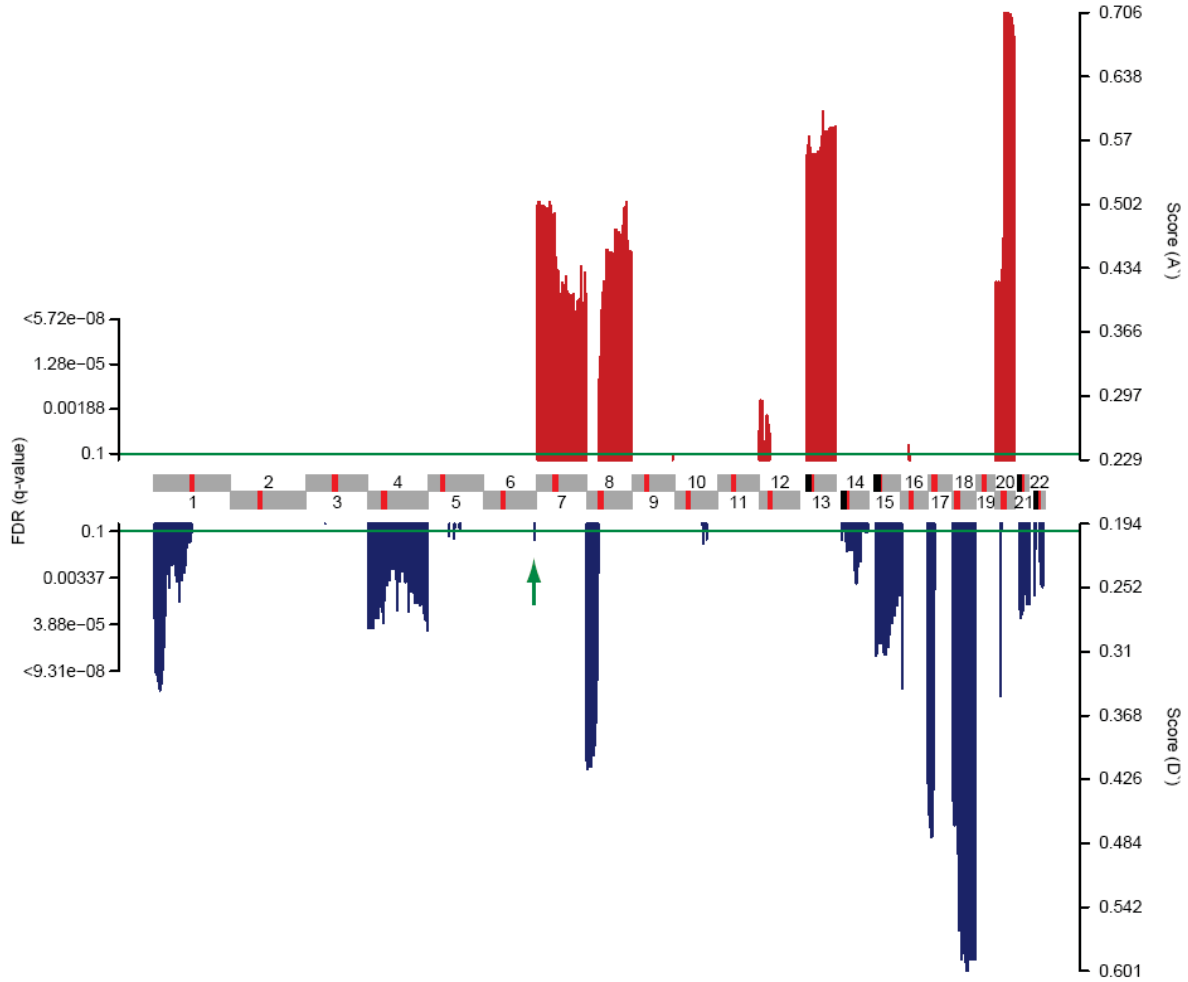
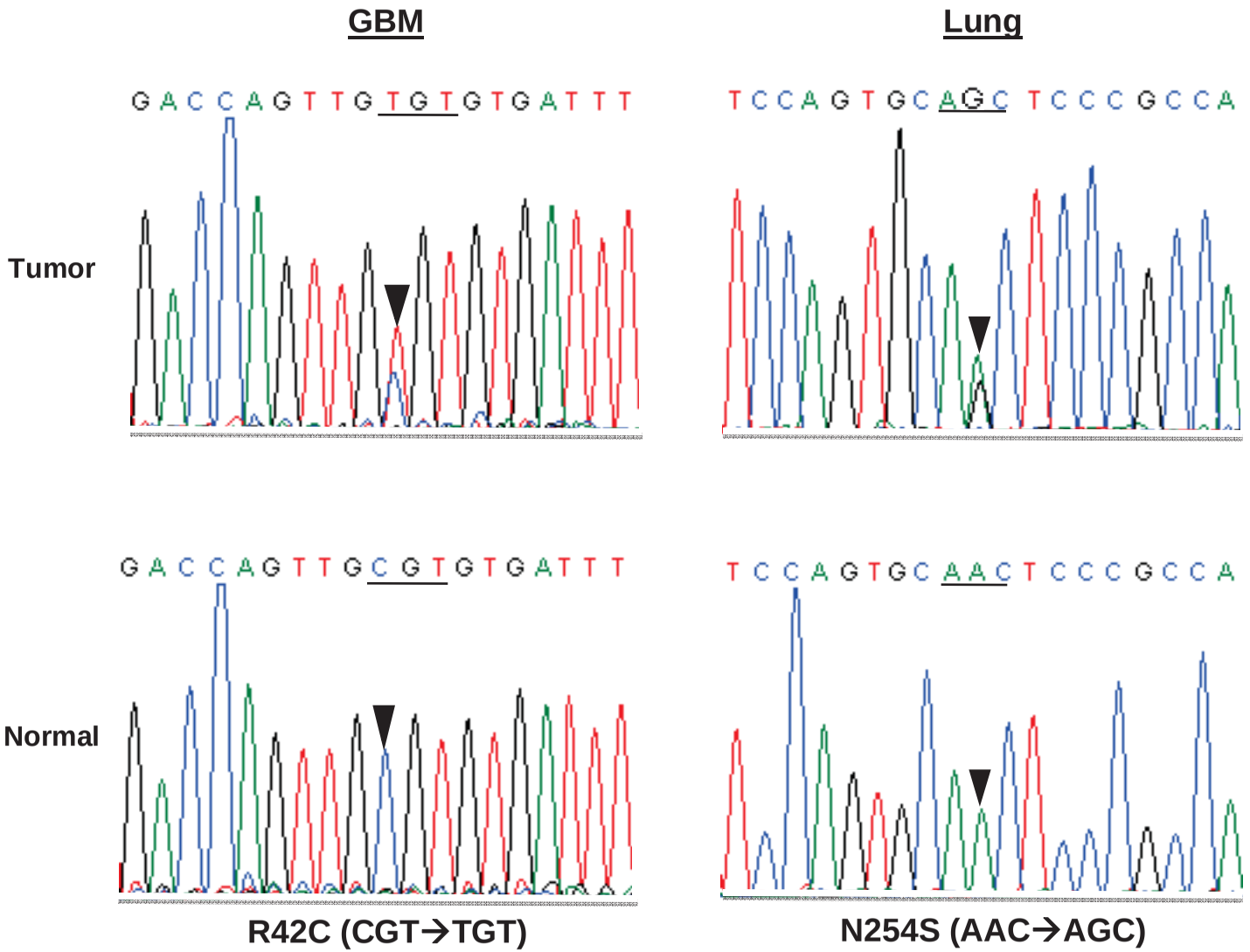


Supplemental Figure 1. Statistically significant genome-wide copy number aberrations in colon cancer. Amplifications (red) and deletions (blue) are indicated across the 22 autosomes in genomic coordinates (center; green line, FDR<10% left axis). Analysis and scores were calculated by RAE as described in Methods. The green arrow indicates the discrete region of significance that spans *PARK2*.



Supplemental Figure 2. Sequencing traces of representative tumors with *PARK2* mutations. Arrows point to sites of mutation.

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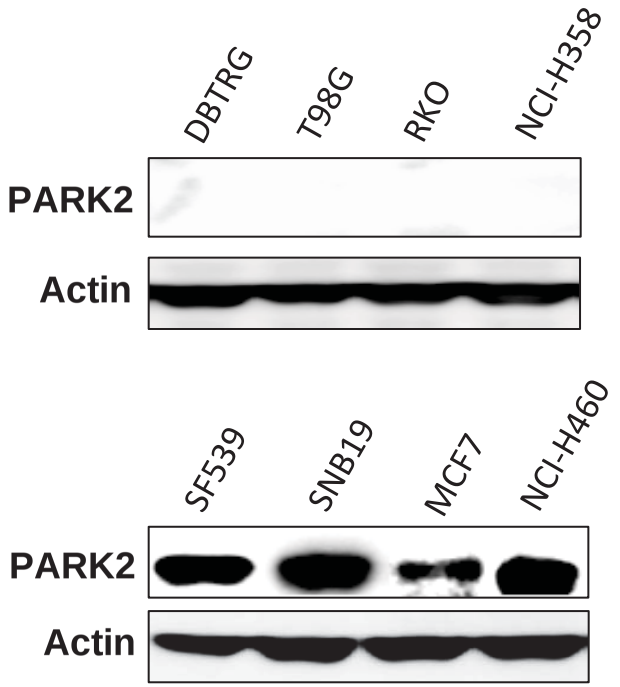

Supplemental Figure 3. PARK2 protein expression in human cancer cell lines. Western blot analysis of human cancer cell lines using anti-PARK2 antibody. Actin is used as a loading control. Equal amounts of protein (5ug) were loaded in all lanes.

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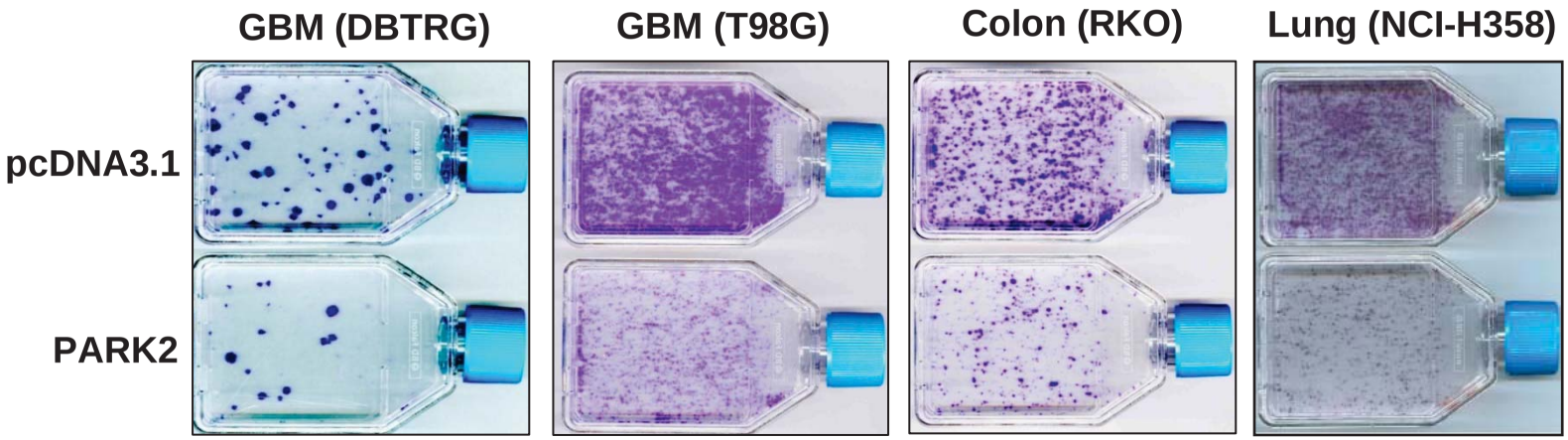
a



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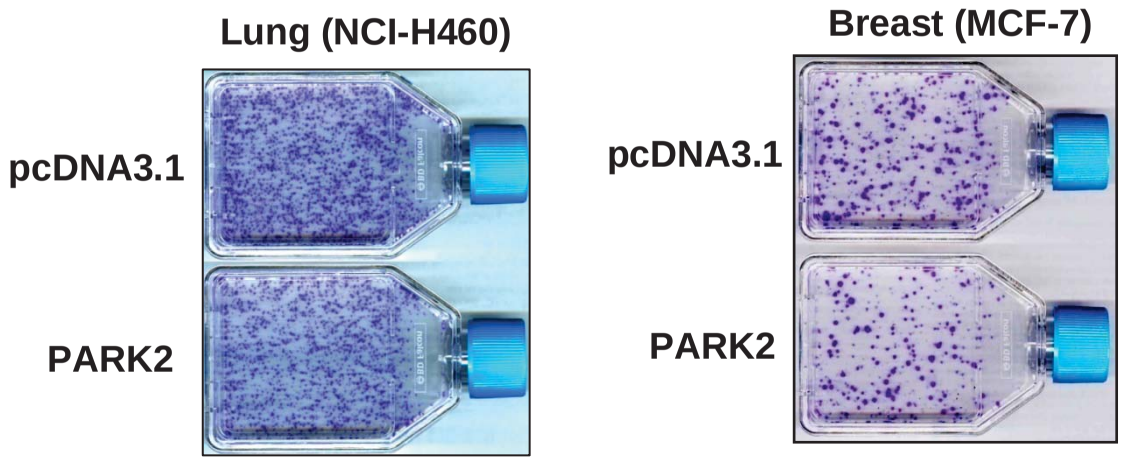
b

PARK2 (+) expression cell lines



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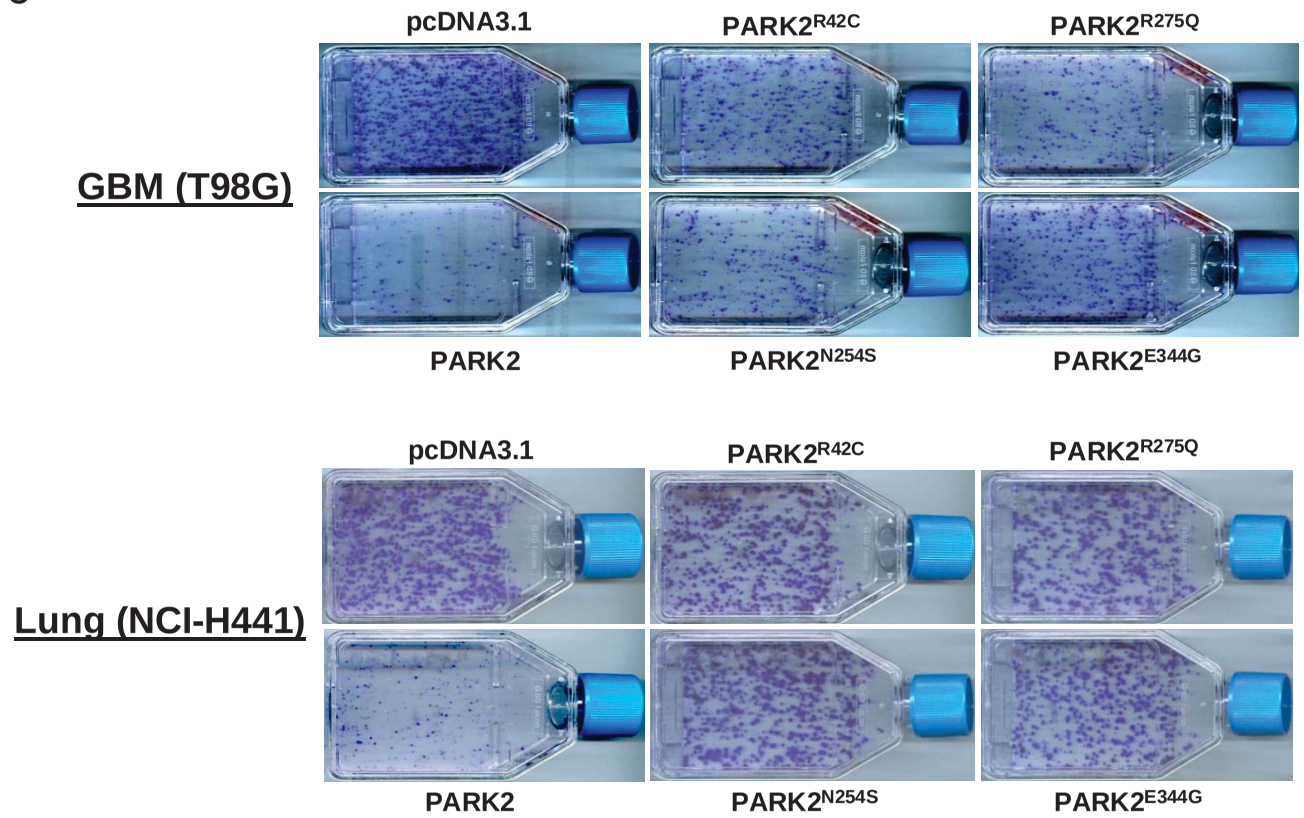
C



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Supplemental Figure 4. Growth suppressive effects of wild-type and mutant PARK2. Quantitation of results in Fig. 3. **(a)** Colony formation assays demonstrating that wild-type PARK2 suppresses cell growth in cells lacking PARK2 protein. Representative flasks are shown for vector-only control (pcDNA3.1) and vector + PARK2 cDNA (PARK2). **(b)** Colony formation assays demonstrating that wild-type PARK2 does not significantly suppress growth in cell lines with normal PARK2 protein expression. Representative flasks are shown for vector-only control (pcDNA3.1) and vector + PARK2 cDNA (PARK2). **(c)** Colony formation assays demonstrating that cancer-specific mutations in PARK2 compromise its growth suppressive ability. Representative flasks are shown for vector-only control (pcDNA3.1) and vector + PARK2 cDNA (PARK2).

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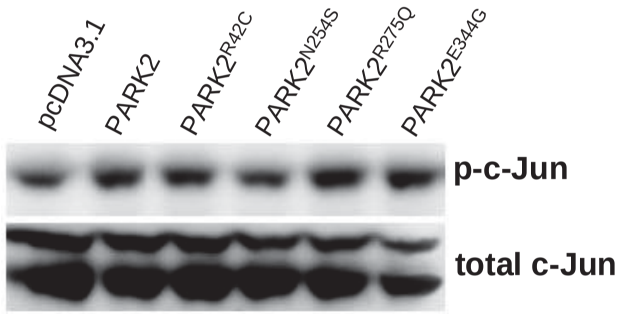

Supplemental Figure 5. Expression of wt or mutant PARK2 does not alter c-Jun phosphorylation. T98G cells were stably transfected with the vector alone (pcDNA3.1) or the indicated PARK2 cDNAs. All proteins were expressed (see main text). Western blot detection was performed using antibody specific for phospho-c-Jun or total c-Jun.

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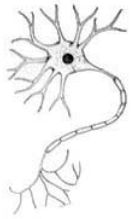
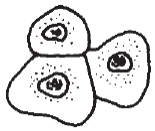
Familial Parkinson's Disease



neuron

Germ-line *PARK2* mutation → Loss of PARK2 E3 ligase activity → Increased cyclin E (and others?) → neuronal death and neurodegenerative disease

Cancer



dividing somatic cell (ie. astrocytes, colon epithelial cells)

Initial mutations → Somatic *PARK2* mutation → Loss of PARK2 E3 ligase activity → Increased cyclin E (and others?) → clonal advantage and cancer

Supplemental Figure 6. Model of differential effects of *PARK2* mutation in Parkinson's Disease and cancer.

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Supplemental Table 1. Frequencies of Mutations

Cancer type	Total samples with alterations	Total samples analyzed	Frequency
Mutations			
Glioblastoma	7	75	9.3%
Lung	4	61	6.5%
Squamous, H/N	0	24	0%
Colon	1	82	1.2%
Total		242	

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Supplementary note for clinical samples

Glioma aCGH samples analyzed were from the tumors procured by The Cancer Genome Atlas (TCGA) as described above. Informed consent was obtained by the member institutions of the TCGA. The glioma, lung, and colon samples analyzed were from the Memorial Sloan Kettering Cancer Center and the University of California, Los Angeles. All samples were obtained following informed consent and in full accordance with the Institutional Review Board of each institution.