**Molecular subtyping of endometrial carcinoma cell lines uncovers subtype-specific targetable vulnerabilities**

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Supplementary Figures S1-9.
Supplementary Tables 1-2.
Supplementary Data 1-5.

**Supplementary Figures**

**Figure S1. Source data for Fig. 1c.**

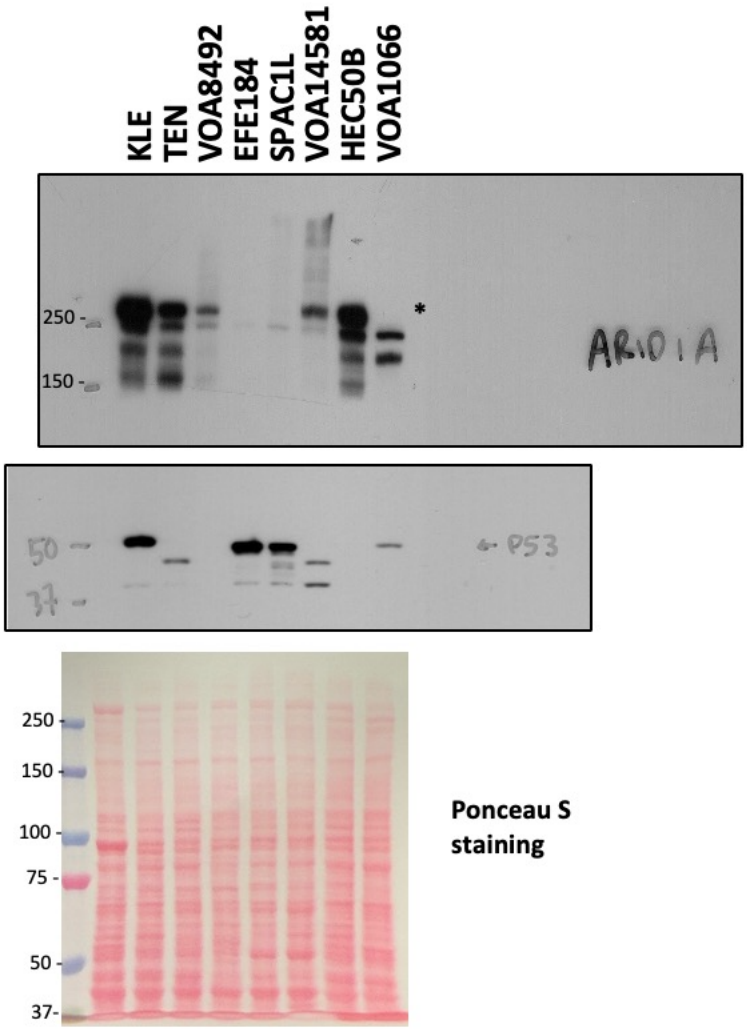


**Figure S2. Source data for Fig. 2d.**

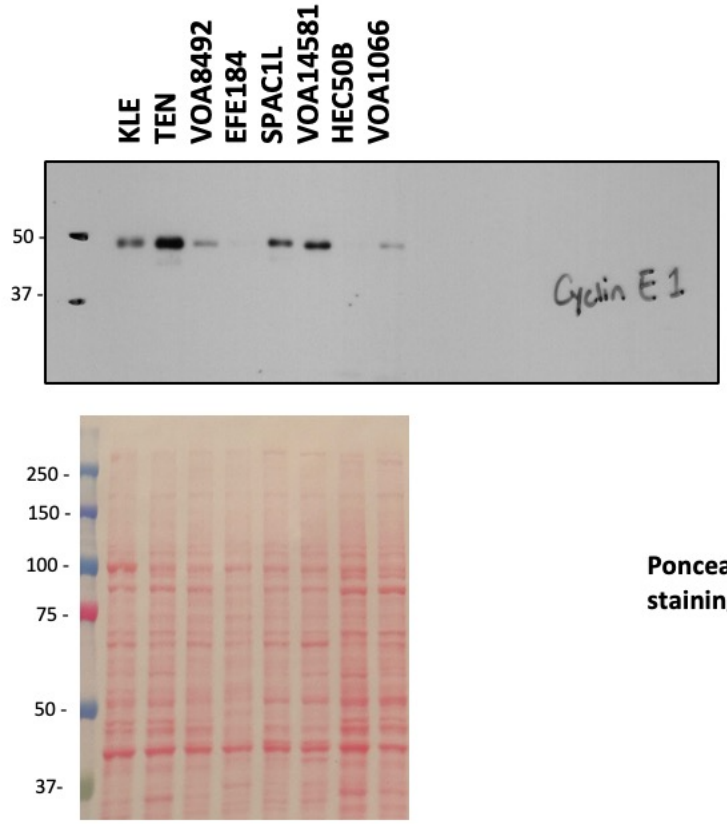


**Figure S3. Source data for Fig. 3a.**

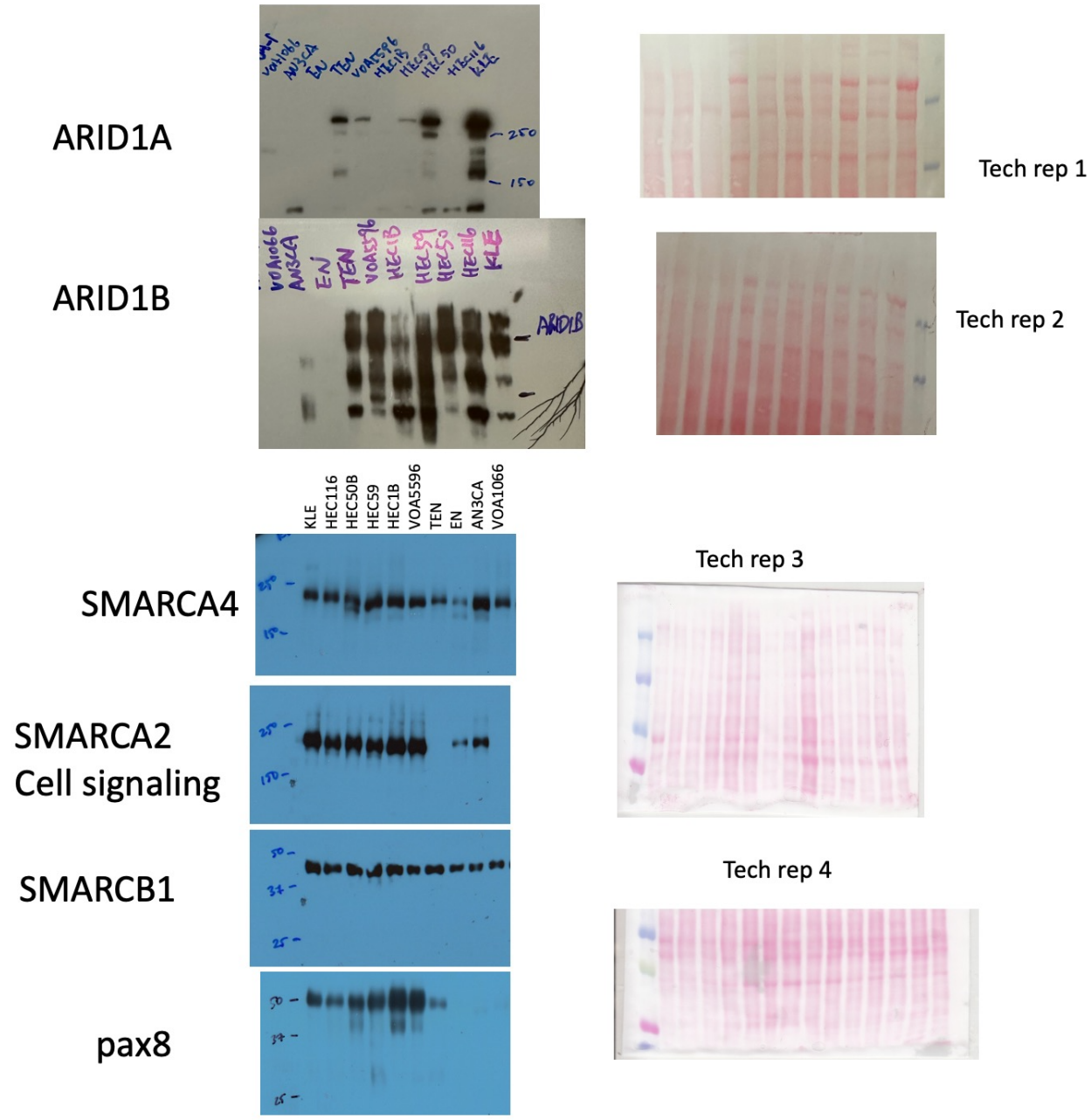


**Figure S4. Expression of p53, ARID1A and ARID1B in MMRd EC cell lines and their derived mouse xenografted tumors. a)** H&E staining and immunostaining of VOA12371, HOUA-I and VOA14590H cell line xenografted tumors. b) Immunoblotting of p53 expression in MMRd EC cell lines.

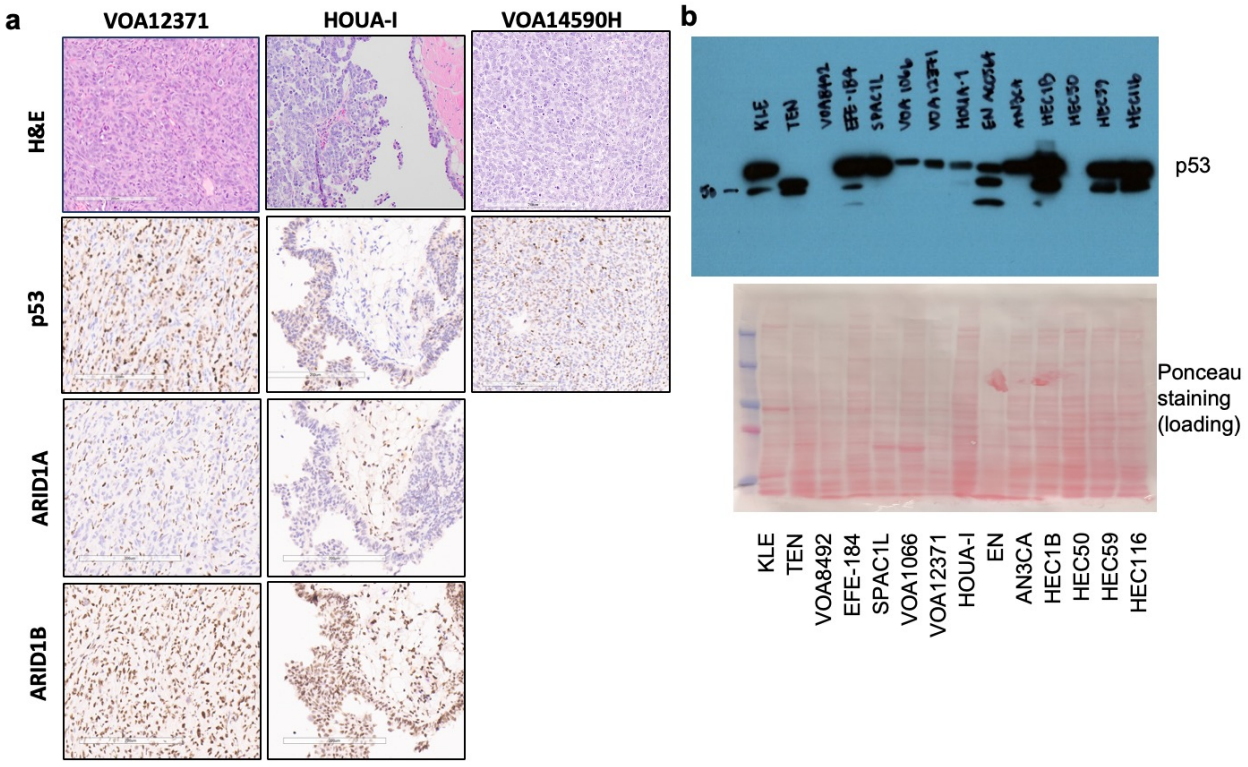


**Figure S5. Histology of the primary tumors from which p53abn EC cell lines derived.**

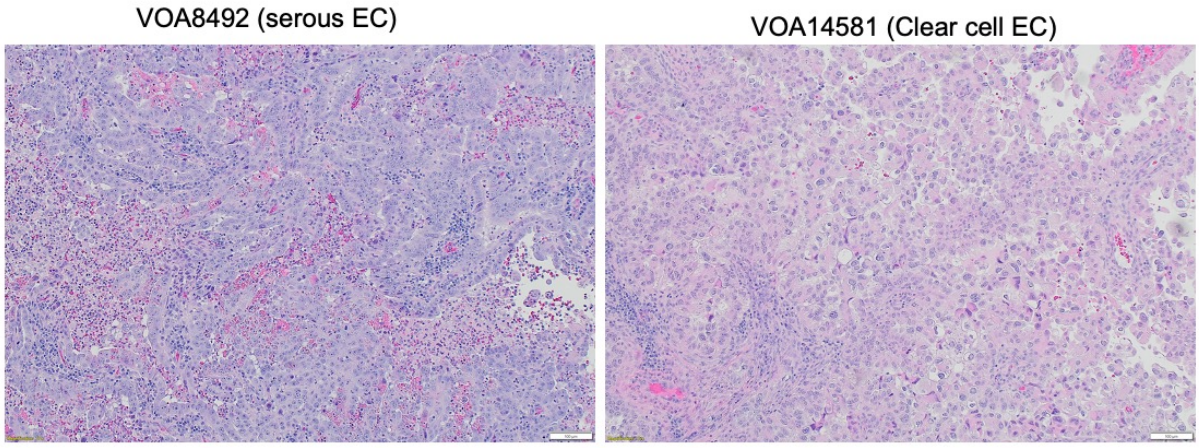


**Figure S6. Source data for Fig. 5b.**

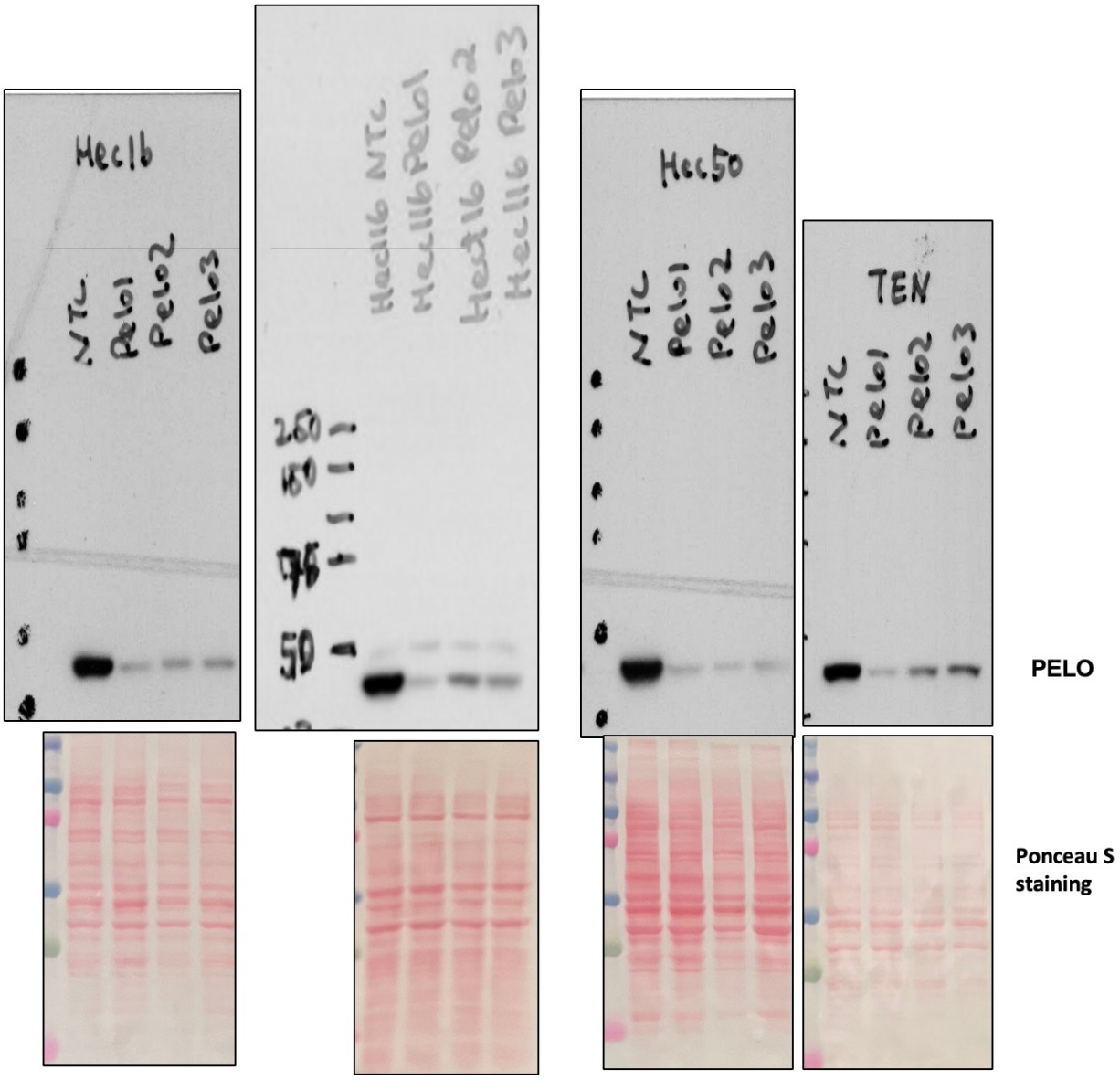


**Figure S7. Immunoblotting confirmed the dual loss of ARID1A/B in EFO-27 cells.**

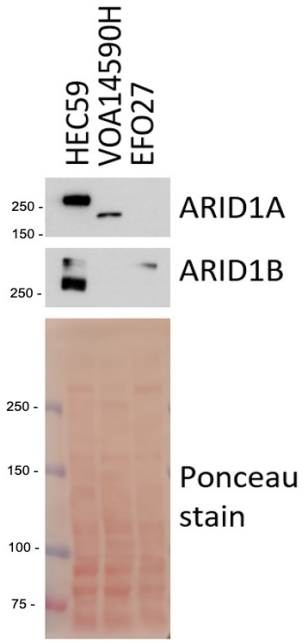


**Figure S8. Seahorse assay analyzing the oxygen consumption rate in VOA1066 cells. (A)** Oxygen consumption rates (OCR) measured with the Seahorse Mito Stress test for VOA1066 cells treated with and without IACS-010759 (2 nM for 1 hour). (B) Bar graphs show relative basal respiration and ATP-linked respiration in (**A**).

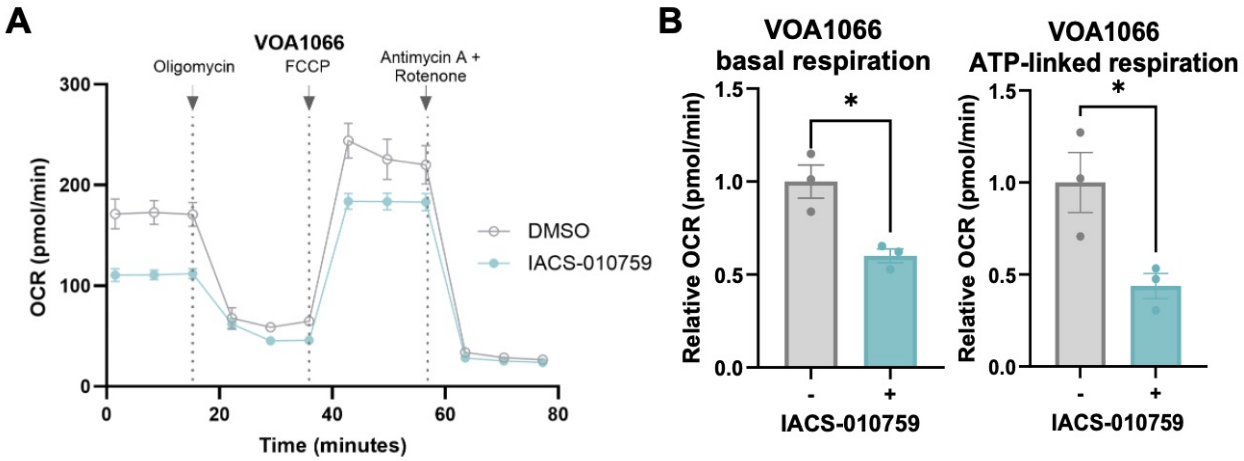
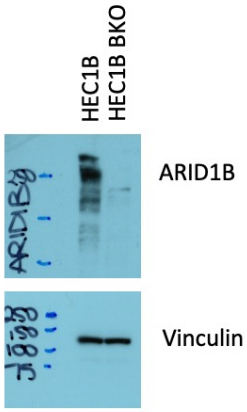


**Figure S9. Source data for Fig. 6g.**



Supplementary Tables

Table S1. Molecular features of EC cell lines

Table S2. STR profiles of 4 in-house developed EC cell lines

**Table S1. Molecular features of endometrial cancer cell lines. POLE mutation, microsatellite stability and p53 mutation status as well as mutation burden were included.**

| Cell line | ProMisE Classification | Microsatellite Status | Depmap TMB (mut/Mb) | Ploidy (WES)[2] | Adjusted Depmap TMB (mut/Mb)[3] | p53 Status | p53 mutation | POLE Status | POLE Endonuclease domain mutuation | MMR gene mutation Status |
|---|---|---|---|---|---|---|---|---|---|---|
| AN3CA | MMRd | MSI[2] | 52.65789474 | 2.196 | 47.958 | abn | p.R213Q | wt | wt | mutant |
| COLO684 | MMRd | MSI[2] | 18.31578947 | 2.304 | 15.899 | wt | n/a | wt | wt | mutant |
| EFE184 | p53_abn | MSS[1] | 3.710526316 | 3.386 | 2.192 | abn | patho/likely patho -p.R282W | wt | wt | wt |
| EMTOKA | p53_abn | n/a | 3.052631579 | n/a | 3.053 | abn | OncoKB likely patho -K132N | wt | wt | wt |
| EN | MMRd | MSI[2] | 133.6578947 | 2.024 | 132.073 | abn | p.R273H | wt | wt | mutant |
| HEC1 | MMRd | MSI[2] | 72.65789474 | 3.491 | 41.626 | abn | p.R248Q | wt | wt | mutant |
| HEC108 | MMRd | MSI[1] | 200.6052632 | 4.286 | 93.610 | abn | p.P151H - OncoKB likely patho | wt | wt | mutant |
| HEC116 | MMRd | n/a | 61.18421053 | n/a | 61.184 | abn | R248Q | wt | wt | wt |
| HEC151 | MMRd | MSI[1] | 59.86842105 | 1.945 | 61.561 | wt | n/a | wt | wt | mutant |
| HEC1A | MMRd | MSI[1] | 65.28947368 | n/a | 65.289 | abn | R248Q | wt | wt | mutant |
| HEC1B | MMRd | MSI[1] | 57.34210526 | n/a | 57.342 | abn | R248Q (In-house Western blot data shows abn staining) | wt | wt | mutant |
| HEC251 | POLE | MSS[1] | 200.0789474 | 2.064 | 193.875 | abn | S241Y, R213* | EDM | P286R | mutant |
| HEC265 | MMRd | MSI[1] | 45.97368421 | 1.946 | 47.249 | wt | n/a | wt | wt | mutant |
| HEC50B | p53_abn | MSS[1] | 11.65789474 | 2.238 | 10.418 | abn | CN Gain, DEL | wt | wt | wt |
| HEC59 | MMRd | MSI[1] | 141.3947368 | 3.846 | 73.528 | abn | p.R273H | wt | wt | mutant |
| HEC6 | MMRd | MSI[1] | 87.73684211 | 3.491 | 50.265 | abn | p.R273H | wt | wt | mutant |
| HHUA | MMRd | n/a | 47.44736842 | n/a | 47.447 | wt | n/a | wt | wt | mutant |
| HOUAI | MMRd | n/a | 19.18421053 | n/a | 19.184 | wt | n/a | wt | wt | wt |
| HTMMT | p53_abn | n/a | 4.210526316 | n/a | 4.211 | abn | p.R273H | wt | wt | wt |
| ISHIKAWAHERAKLIO02ER | MMRd | MSI[1] | 56.86842105 | n/a | 56.868 | abn | M246V | wt | wt | wt |
| JHUEM1 | MMRd | MSI[1] | 38.31578947 | n/a | 38.316 | wt | n/a | wt | wt | mutant |
| JHUEM2 | MMRd | MSI[1] | 19.18421053 | 2.126 | 18.047 | wt | n/a | wt | wt | mutant |
| JHUEM3 | p53_abn | MSS[1] | 2.315789474 | 2.119 | 2.186 | abn | Q167* | wt | wt | wt |
| JHUEM7 | POLE | MSS[1] | 145.9210526 | 1.945 | 150.047 | abn | uncertain - c.861G>T_p.E287D, OncoKB - likely patho E287D | EDM | P286R | wt |
| KLE | p53_abn | MSS[2] | 2.157894737 | 2.765 | 1.561 | abn | p.R175H, CNA loss | wt | wt | wt |
| MFE280 | p53_abn | MSS[2] | 3.526315789 | 2.518 | 2.801 | abn | likely patho - c.919+1G>C, depmap dbsnpID is patho/likely patho | wt | wt | wt |
| MFE296 | MMRd | MSI[2] | 18.76315789 | 3.699 | 10.145 | abn | R306*,Y220C | wt | wt | mutant |
| MFE319 | MMRd | MSI[2] | 107.2894737 | 1.999 | 107.343 | abn | R273C,Y220C | wt | wt | mutant |
| RL952 | MMRd | MSI[2] | 46.73684211 | 2.045 | 45.708 | abn | V73fs*50, DM: p.V218del | wt | wt | mutant |
| SNGM | MMRd | MSI[2] | 46.10526316 | 2.002 | 46.059 | wt | n/a | wt | wt | mutant |
| SNU1077 | p53_abn | MSS[1] | 3.473684211 | 3.757 | 1.849 | abn | uncertain/patho - I195S, OncoKB considered likely oncogenic | wt | wt | wt |
| SNU685 | p53_abn | MSS[1] | 3.236842105 | 4.279 | 1.513 | abn | likely patho c.919+1G>T, DM: just says "SNP" | wt | wt | wt |
| TEN | p53_abn | MSS[1] | 4.289473684 | 3.478 | 2.467 | abn | R342*, CNA loss | wt | wt | wt |
| VOA1066 | NSMP | n/a | n/a | n/a | 7.526 | wt | | wt | wt | wt |
| VOA12371 | MMRd | n/a | n/a | n/a | 105.935 | wt | | wt | wt | mutant |
| VOA14581 | p53_abn | n/a | n/a | n/a | 13.079 | abn | R210X | wt | wt | wt |
| VOA14590 | MMRd | n/a | n/a | n/a | 126.823 | wt[4] | D186fs | wt | wt | mutant |
| VOA8492 | p53_abn | n/a | n/a | n/a | 7.447 | abn | CN loss | wt | wt | wt |
| SPAC1L | p53_abn | n/a | n/a | n/a | 20.711 | abn | R141H | wt | wt | mutant |

Note:

[1] Chen *et al.* 2019

[2] Cell Model Passports

[3] The TMB for cell lines with ploidy data available from Cell Model Passports are adjusted based on the ploidy

**Table S2. STR profiles of 4 in-house developed EC cell lines**

| Cell Line | VOA8492 | VOA12371 | VOA14581 | VOA14590H |
|---|---|---|---|---|
| **D3S1358** | 17 | 15, 16, 17 | 14, 15 | 14, 15 |
| **TH01** | 32.2, 33.2 | 29, 31, 32 | 29 | 27, 28, 30, 31 |
| **D21S11** | 14 | 12, 15 | 13, 15 | 13 |
| **D18S51** | 8, 11 | 12, 16 | 12, 16 | 11, 12 |
| **Penta E** | 13, 16 | 9, 10 | 9, 12 | 9, 13 |
| **D5S818** | 11, 15 | 10, 14, 16 | 13, 14 | 13, 14 |
| **D13S317** | 23, 24 | 19, 24 | 20, 25 | 18, 21 |
| **D7S820** | 9, 12 | 11, 12 | 11, 12 | 11, 12, 13 |
| **D16S539** | 13 | 10, 11, 12 | 11, 12 | 12 |
| **CSF1PO** | 9, 11 | 10, 11 | 10, 11 | 8, 10 |
| **Penta D** | 11 | 9, 11 | 11 | 12, 13 |
| **vWA** | 14, 17 | 16, 17 | 14, 18 | 15, 19 |
| **D8S1179** | 9.3 | 6, 9 | 7 | 9.3 |
| **TPOX** | X | X | X | X |
| **FGA** | 11 | 12, 13 | 11, 12 | 10, 11 |
| **AMEL** | 8 | 8 | 8 | 8, 11 |
| **Mouse** | NA | NA | NA | NA |

Supplementary Data

Suppl. Data 1. List of somatic nucleotide variants (SNVs) of 60 copy-number high primary endometrial cancers from TCGA

Suppl. Data 2. List of CNVs of 60 copy-number high primary endometrial cancers from TCGA.

Suppl. Data 3. Comparison of gene effect scores between p53abn and MMRd EC cell lines. Genome-wide CRISPR screen data was downloaded from the DepMap database.

Suppl. Data 4. List of ARID1A and ARID1B mutations in all CCLE cell lines. Data was downloaded from the DepMap database.

Suppl. Data 5. Comparison of gene effect scores between ARID1A/B-dual deficient cancer cell lines and all ARID1A/B-intact EC cell lines. Genome-wide CRISPR screen data was downloaded from the DepMap database.