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| Supplementary Item & Number | Title or Caption |
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**Supplementary information for:**

# ARID1B is a specific vulnerability in *ARID1A*-mutant cancers

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**Supplementary Figure 1**

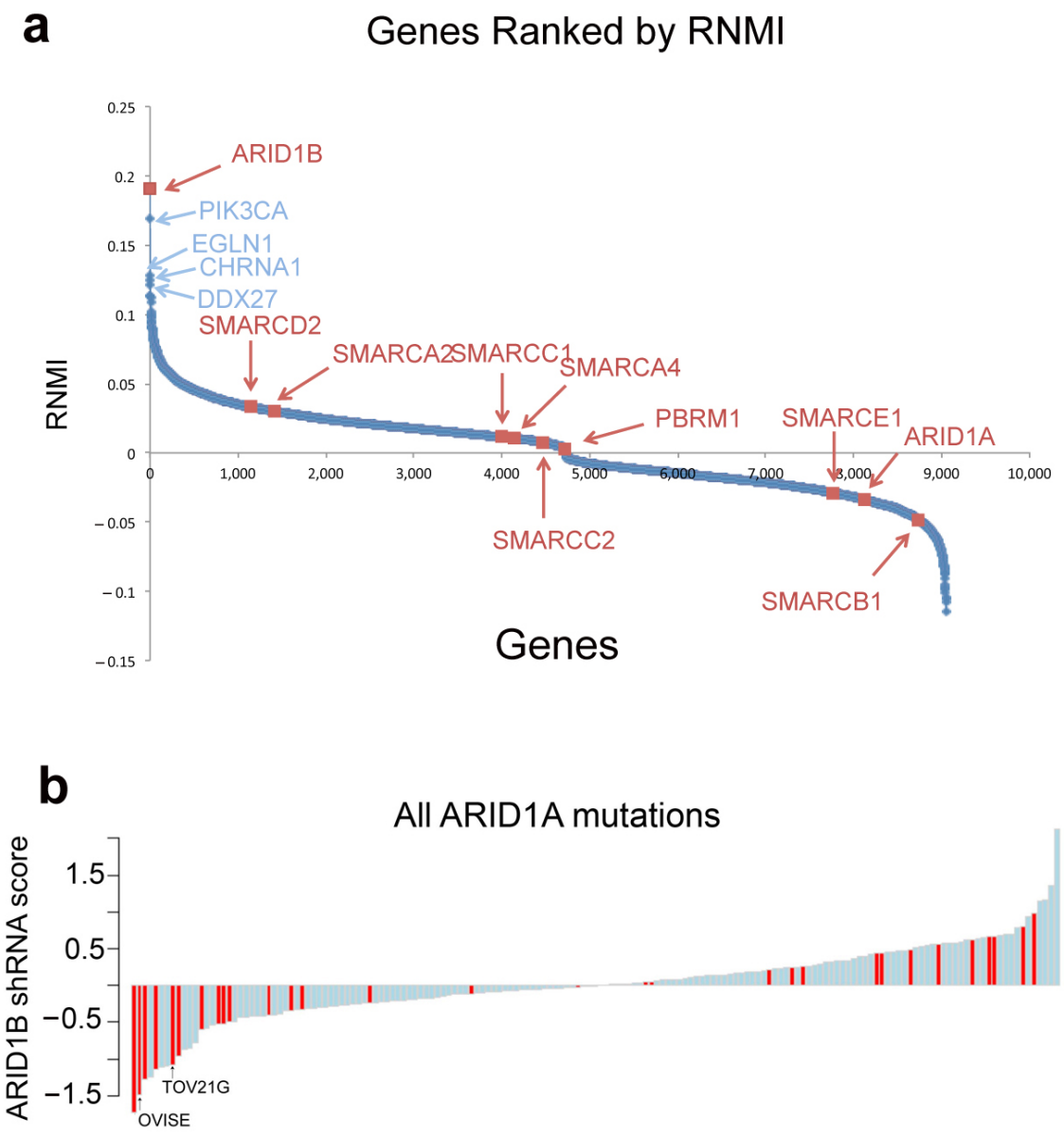


**Figure S1. Specifics of *ARID1A* class comparison**
**a:** Rank list of vulnerabilities identified by screen of Achilles platform cell lines with *ARID1A* class comparison. Position of SWI/SNF subunits are indicated on curve.
**b:** Effects of ARID1B shRNAs across cell lines in Achilles screen. Cell lines used for validation studies are indicated with arrows

**Supplementary Figure 2**

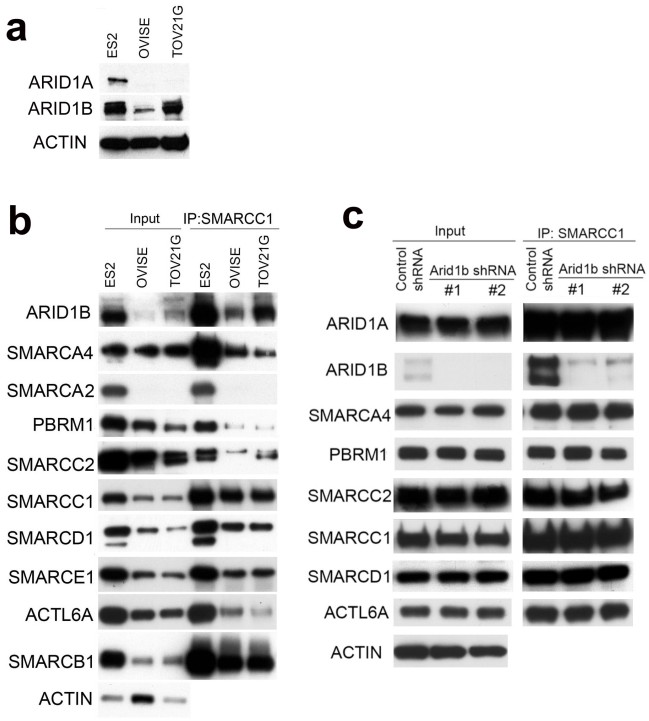


**Figure S2: A residual SWI/SNF complex is present in *ARID1A*-mutant cancer cells**
**a.** Expression levels of ARID1A, ARID1B in ES-2, OVISE and TOV21G cells.
**b.** Immunoblots of nuclear extracts (Input) and immunoprecipitation with the core SWI/SNF subunit SMARCC1 in wildtype (ES-2) and *ARID1A*-mutant (OVISE and TOV21G cell lines).
**c.** Co-immunoprecipitation of SWI/SNF complex by SMARCC1 from the nuclear extract of 293T cells upon control shRNA or two independent ARID1B shRNAs treatment

**Supplementary Figure 3**

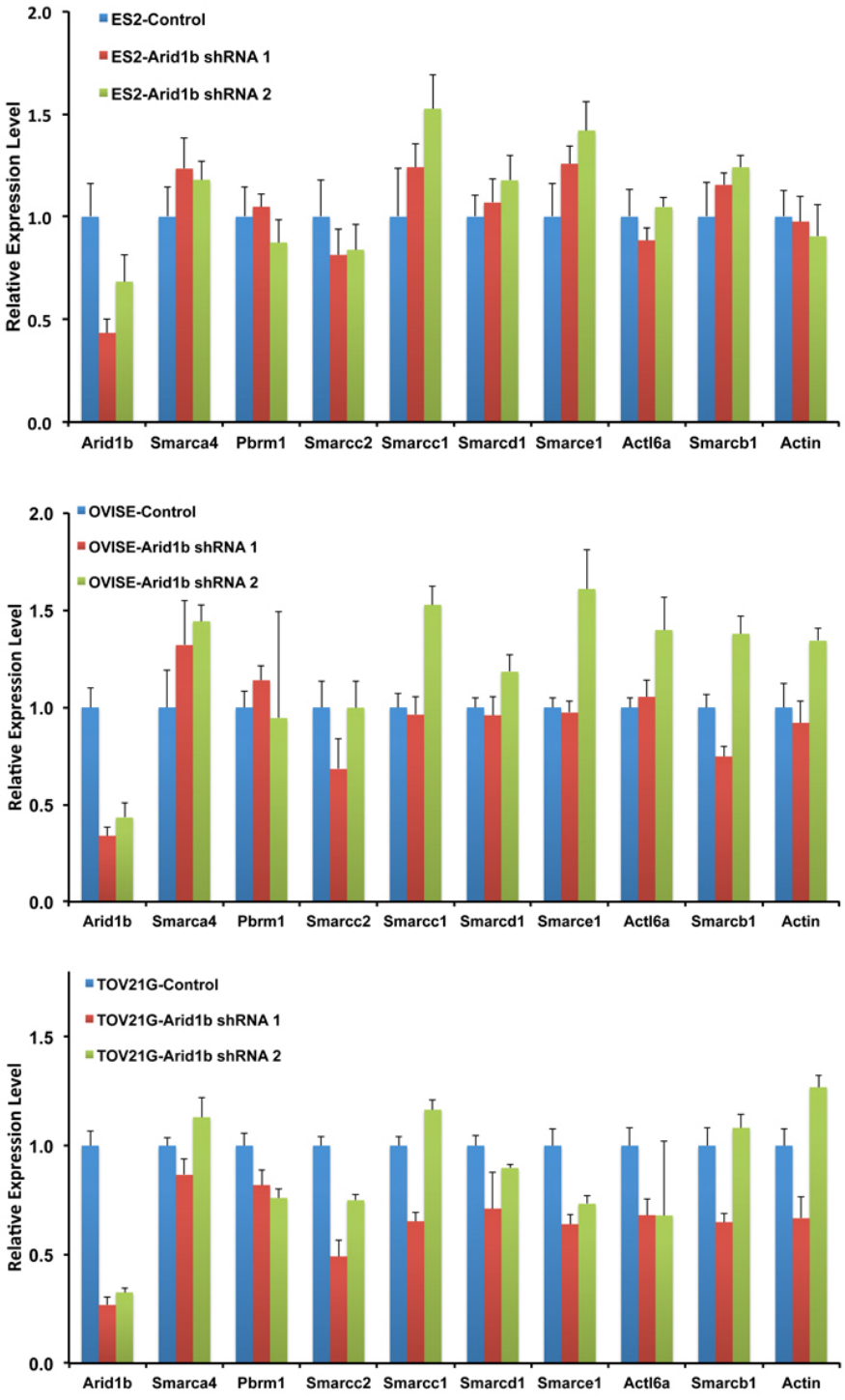


**Figure S3: mRNA levels of SWI/SNF complex subunits**
RT-qPCR analysis of the expression of indicated SWI/SNF complex subunits in ES-2, OVISE and TOV21G cells with either control shRNA or two independent ARID1B shRNAs treatment.

**Supplementary Figure 4**

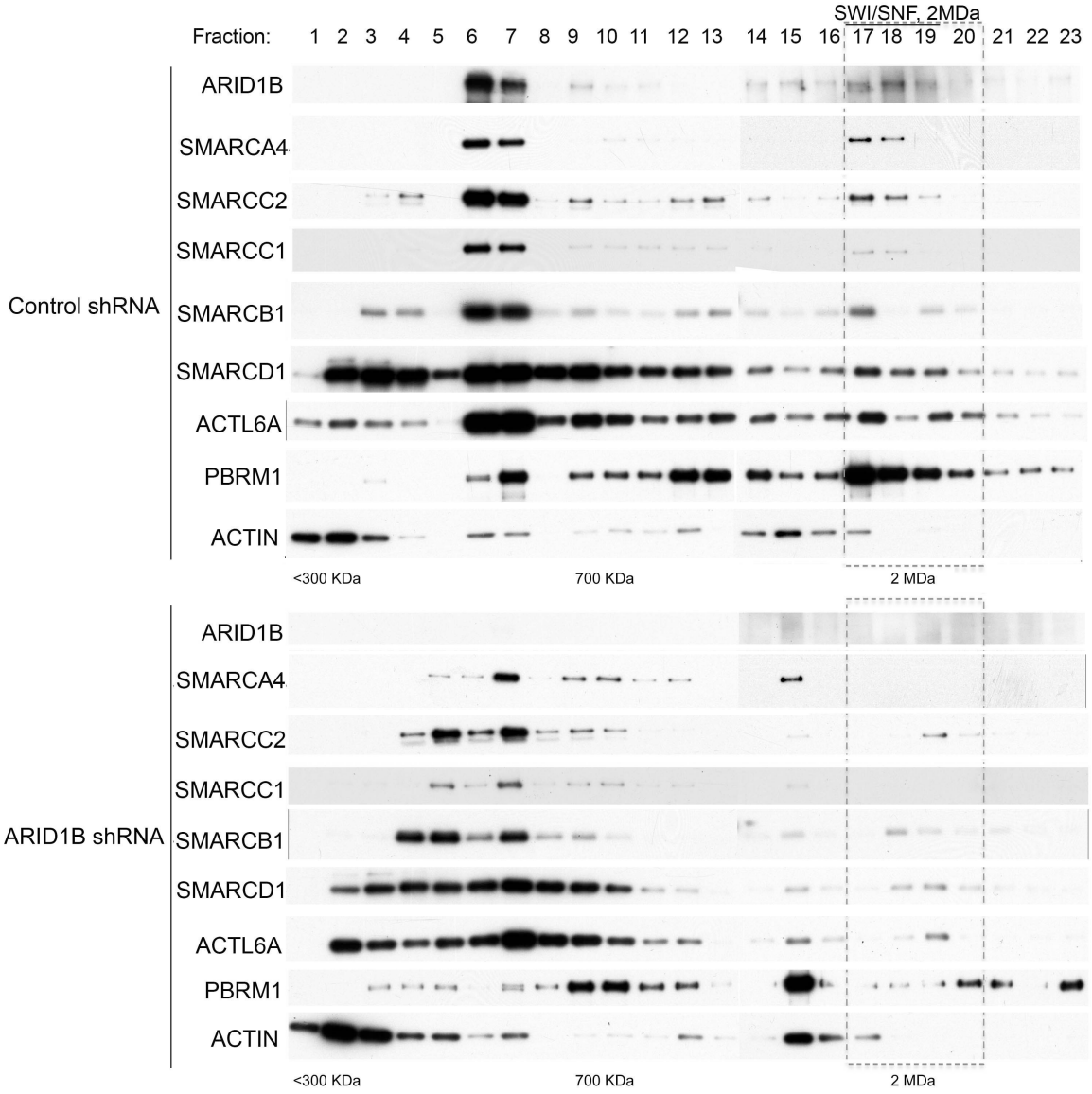


**Figure S4: Sucrose sedimentation assay of SWI/SNF complex in OVISE cells**
Sucrose sedimentation (20-50%) assay of SWI/SNF complex from OVISE cells treated with either control shRNA or ARID1B shRNA

**Supplementary Figure 5**

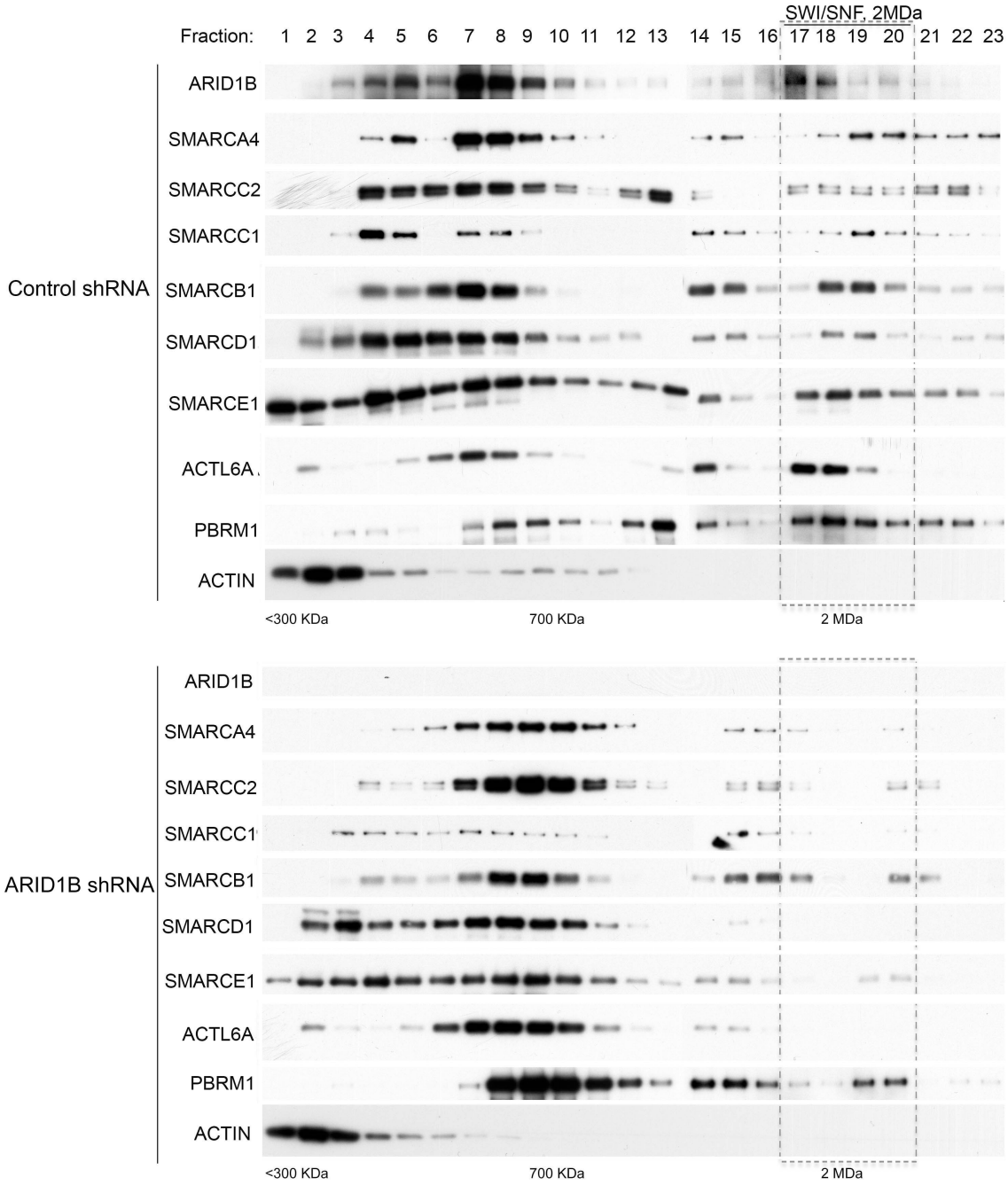


**Figure S5: Sucrose sedimentation assay of SWI/SNF complex in TOV21G cells**
Sucrose sedimentation (20-50%) assay of SWI/SNF complex from TOV21G cells treated with either control shRNA or ARID1B shRNA

**Supplementary Figure 6**

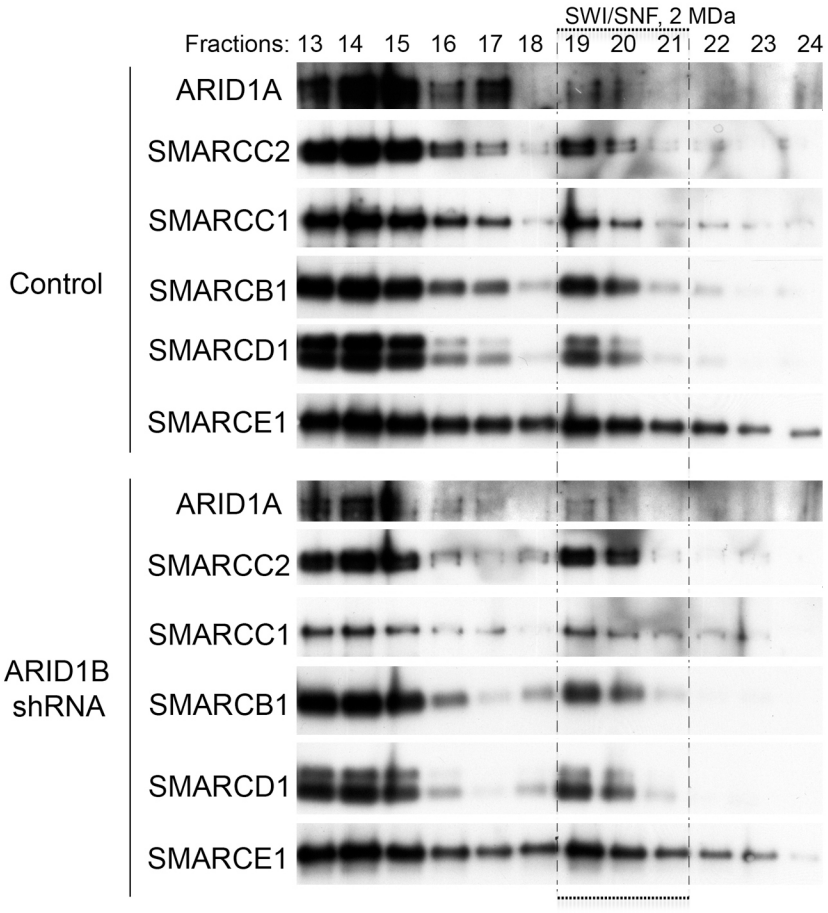


**Figure S6: Sucrose sedimentation assay of SWI/SNF complex in ES-2 cells**
Sucrose sedimentation (20-50%) assay of SWI/SNF complex from ES-2 cells treated with either control shRNA or ARID1B shRNA

**Supplementary Figure 7**

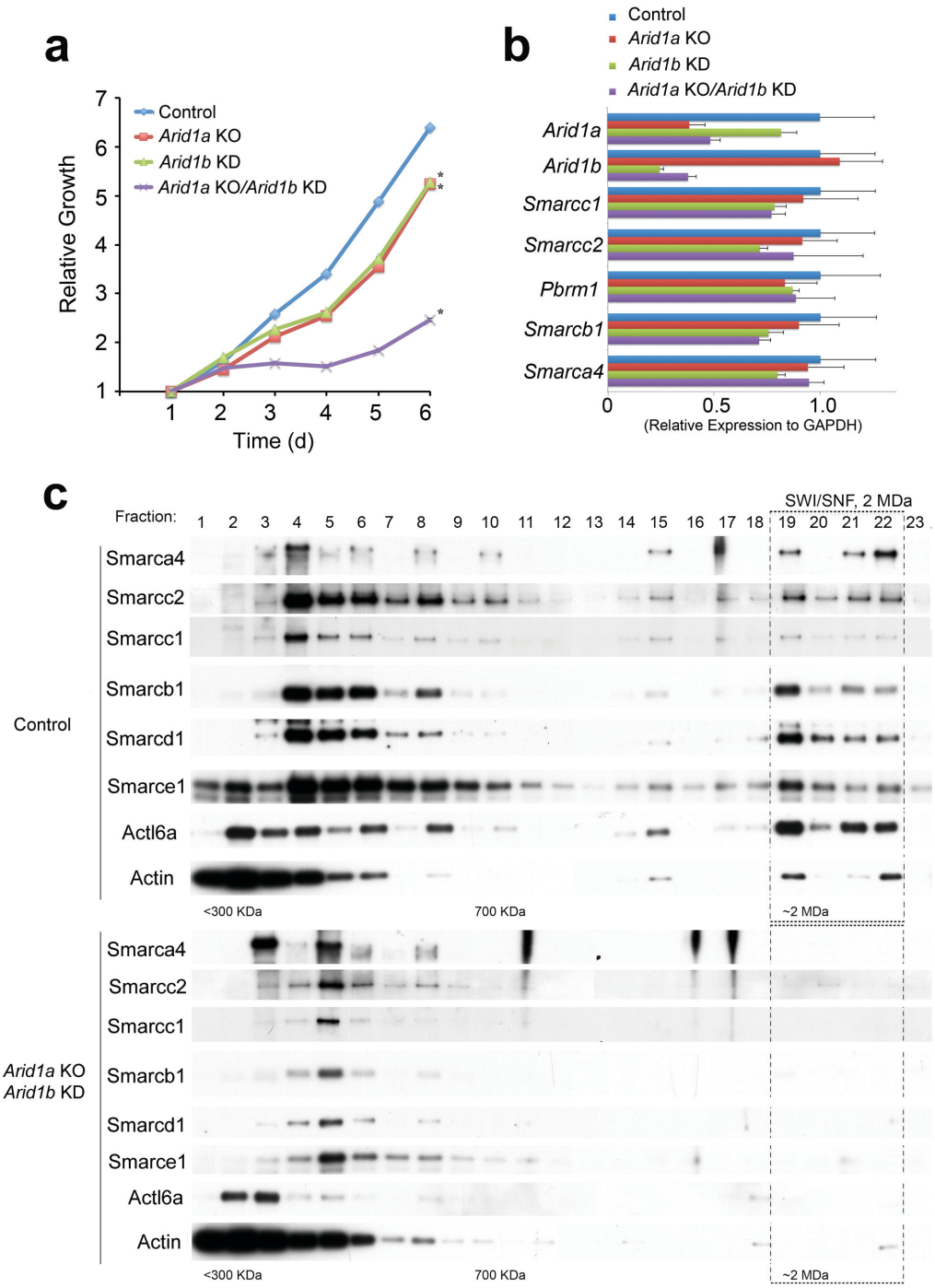


**Figure S7: *Arid1a* loss creates a dependency on Arid1b-containing SWI/SNF complex in primary cells**

**a.** MTT proliferation assay of control MEFs, *Arid1a* knockout (KO) MEFs, *Arid1b* knockdown (KD) MEFs, or combined *Arid1a* KO and *Arid1b* KD MEFs. * $p<0.05$. Data are expressed as means ± S.D.

**b.** mRNA levels of the SWI/SNF complex subunits upon individual loss of *Arid1a*, ARID1B or both.

**c.** Sucrose sedimentation (20-50%) assay of SWI/SNF complex from MEFs with indicated treatment.

**Supplementary Table 1**

| | ARID1A | | | ARID1B | | |
|---|---|---|---|---|---|---|
| **Cell Line** | **Protein Change** | **Mutation Classification** | **Homozygous or Heterozygous?** | **Protein Change** | **Mutation Classification** | **Homozygous or Heterozygous?** |
| 23132/87 | p.C2081fs | frame shift deletion | heterozygous | | WT | |
| A2780 | p.Q1430* | nonsense | heterozygous | p.R869fs | frame shift insertion | homozygous |
| | p.R1721fs | frame shift deletion | heterozygous | | | |
| BL41 | p.A1648fs | frame shift insertion | heterozygous | | WT | |
| DV90 | p.G1848fs | frame shift deletion | heterozygous | | WT | |
| EFO27 | p.G284fs | frame shift deletion | heterozygous | p.G663fs | frame shift deletion | heterozygous |
| | p.R1722* | nonsense | heterozygous | p.T1639fs | frame shift deletion | heterozygous |
| HCT15 | | WT | | p.G272* | nonsense | heterozygous |
| | | | | p.R1606* | nonsense | heterozygous |
| HEC108 | p.R1446* | nonsense | heterozygous | p.L1111fs | frame shift deletion | heterozygous |
| HEC251 | p.S2272* | nonsense | heterozygous | p.Y2100* | nonsense | heterozygous |
| HEC265 | p.1467fs | frame shift deletion | heterozygous | | WT | |
| HEC59 | p.Q428* | nonsense | heterozygous | p.T1568M | missense | heterozygous |
| HEC6 | p.G1848fs | frame shift deletion | homozygous | p.G1265fs | frame shift deletion | heterozygous |
| HS766T | p.Q538* | nonsense | heterozygous | | WT | |
| HS936T | | WT | | p.Q1657* | nonsense | heterozygous |
| IM95 | p.G1847fs | frame shift insertion | heterozygous | p.403fs | frame shift deletion | heterozygous |
| JHUEM2 | p.C1099fs | frame shift deletion | heterozygous | p.Q1792* | nonsense | heterozygous |
| | p.G1847fs | frame shift insertion | heterozygous | | | |
| JHUEM7 | p.R1989* | nonsense | heterozygous | p.R1784Q | missense | heterozygous |
| LNCAPCLONEFGC | p.G284fs | frame shift deletion | heterozygous | p.E2146* | nonsense | heterozygous |
| LOXIMVI | p.Q1212* | nonsense | heterozygous | | WT | |
| MFE296 | p.M274fs | frame shift deletion | heterozygous | p.K1155fs | frame shift deletion | heterozygous |
| | | | | p.Q1599* | nonsense | heterozygous |
| NAMALWA | p.G276* | nonsense | heterozygous | | WT | |
| NCIH1436 | p.S764fs | frame shift deletion | heterozygous | | WT | |
| NCIH2172 | p.F1720fs | frame shift deletion | homozygous | | WT | |
| NCIH2286 | p.G927* | nonsense | heterozygous | | WT | |
| NUGC3 | p.G1847fs | frame shift insertion | heterozygous | | WT | |
| OCILY19 | p.L818fs | frame shift deletion | heterozygous | | WT | |
| OCUM1 | p.I1130fs | frame shift deletion | homozygous | p.P865fs | frame shift deletion | heterozygous |
| OVMANA | p.Q1332* | nonsense | heterozygous | | WT | |
| | p.S2264* | nonsense | heterozygous | | | |
| RKO | p.P1114fs | frame shift deletion | heterozygous | | WT | |
| | p.G1848fs | frame shift deletion | heterozygous | | | |
| SKOV3 | p.Q586* | nonsense | heterozygous | | WT | |
| SNGM | p.G1848fs | frame shift deletion | heterozygous | p.S355fs | frame shift deletion | heterozygous |
| | p.P2139fs | frame shift deletion | heterozygous | | | |
| SNU1 | p.A1517fs | frame shift deletion | heterozygous | p.P1049fs | frame shift deletion | homozygous |
| | p.G1847fs | frame shift insertion | heterozygous | | | |
| SNU216 | p.Q1458* | nonsense | homozygous | | WT | |
| SNU324 | p.E1904fs | frame shift deletion | heterozygous | | WT | |
| SNU423 | p.G623* | nonsense | homozygous | p.D1708N | missense | heterozygous |
| SUDHL5 | p.G285* | nonsense | heterozygous | | WT | |
| TOV21G | p.Q548fs | frame shift insertion | heterozygous | p.L1957fs | frame shift insertion | heterozygous |
| | p.N756fs | frame shift deletion | heterozygous | | | |

**Table S1:** Co-occurring *ARID1A* and *ARID1B* mutations in cell lines. 38% of cell lines with *ARID1A* mutation also contain *ARID1B* mutation.

## Supplementary Discussion:

Of the cell lines in the Achilles screen, 18 contained inactivating mutations, four contained missense mutations, and eight had 3' UTR mutations. Of note, it is not known whether the missense mutations impair ARID1A function and act as drivers, or whether due to the high rate of mutations in some cancers, or acquired in cell culture, these mutations do not affect ARID1A function and are passenger mutations. The top panel of figure 1b shows the effect of ARID1B knockdown in all 30 Achilles cell lines carrying any ARID1A mutation (inactivating, misssense, or 3' UTR). The bottom panel shows the effect upon only those 18 cell lines that carry inactivating mutations. As can be seen by comparing the two, the lines with missense mutation appear unaffected by ARID1B knockdown. It is unknown whether this lack of dependence occurs because only inactivating ARID1A mutations result in dependence upon ARID1B or because the missense mutations are passenger mutations and would not be expected to result in dependence upon ARID1B.