Table S1 – List of gene mutations in patients from the C1A ACC subgroup. Data from Zheng et al., 2016.

| Sample ID | Patient ID | CTNNB1: AMP HOMDEL MUT FUSION; | APC: AMP HOMDEL MUT FUSION; | MEN1: AMP HOMDEL MUT FUSION; | ZNRF3: AMP HOMDEL MUT FUSION; | TP53: AMP HOMDEL MUT FUSION; | CDK4: AMP HOMDEL MUT FUSION; | CDKN2A: AMP HOMDEL MUT FUSION; | RB1: AMP HOMDEL MUT FUSION; | MDM2: AMP HOMDEL MUT FUSION; | CCNE1: AMP HOMDEL MUT FUSION; |
|-----------|------------|--------------------------------|-----------------------------|-----------------------------|-------------------------------|--------------------------------|--------------------------------|--------------------------------|-------------------------------|--------------------------------|-----------------------------|
| TCGA-OR-A5J2-01 | TCGA-OR-A5J2 | MUT: Y30*; | MUT: H168Cfs*18; | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: |
| TCGA-OR-A5JY-01 | TCGA-OR-A5JY | MUT: S45P; | CNA: AMP; | CNA: AMP; | CNA: AMP; | CNA: AMP; | CNA: AMP; | CNA: AMP; | CNA: AMP; | CNA: AMP; | CNA: AMP; |
| TCGA-OR-A5LE-01 | TCGA-OR-A5LE | MUT: S45P; | MUT: H168Cfs*18; | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: |
| TCGA-OR-A5JJ-01 | TCGA-OR-A5JJ | MUT: S45F; | MUT: C275S; CNA: HOMDEL; | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: |
| TCGA-OR-A5LE-01 | TCGA-OR-A5LE | MUT: S45del; | CNA: AMP; | CNA: AMP; | CNA: AMP; | CNA: AMP; | CNA: AMP; | CNA: AMP; | CNA: AMP; | CNA: AMP; | CNA: AMP; |
| TCGA-OR-A5K9-01 | TCGA-OR-A5K9 | MUT: S45P,S52del; | CNA: HOMDEL; | CNA: AMP; | CNA: AMP; | CNA: AMP; | CNA: AMP; | CNA: AMP; | CNA: AMP; | CNA: AMP; | CNA: AMP; |
| TCGA-OR-A5K5-01 | TCGA-OR-A5K5 | MUT: G34V; | CNA: HOMDEL; | CNA: AMP; | CNA: AMP; | CNA: AMP; | CNA: AMP; | CNA: AMP; | CNA: AMP; | CNA: AMP; | CNA: AMP; |
| TCGA-OR-A5JS-01 | TCGA-OR-A5JS | MUT: G34R; | CNA: AMP; | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: |
| TCGA-OR-A5LJ-01 | TCGA-OR-A5LJ | MUT: G34E; | MUT: R521Rfs*15; | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: |
| TCGA-OR-A5JS-01 | TCGA-OR-A5JS | MUT: | R307W; | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: |
| TCGA-OR-A5J5-01 | TCGA-OR-A5J5 | MUT: | X267_splice; | CNA: HOMDEL; | CNA: HOMDEL; | CNA: HOMDEL; | CNA: HOMDEL; | CNA: HOMDEL; | CNA: HOMDEL; | CNA: HOMDEL; | CNA: HOMDEL; |
| TCGA-OR-A5JW-01 | TCGA-OR-A5JW | MUT: | X267_splice; | CNA: HOMDEL; | CNA: HOMDEL; | CNA: HOMDEL; | CNA: HOMDEL; | CNA: HOMDEL; | CNA: HOMDEL; | CNA: HOMDEL; | CNA: HOMDEL; |
| TCGA-OR-A5K0-01 | TCGA-OR-A5K0 | MUT: | X267_splice; | CNA: HOMDEL; | CNA: HOMDEL; | CNA: HOMDEL; | CNA: HOMDEL; | CNA: HOMDEL; | CNA: HOMDEL; | CNA: HOMDEL; | CNA: HOMDEL; |
| TCGA-OR-A5K5-01 | TCGA-OR-A5K5 | MUT: | X267_splice; | CNA: HOMDEL; | CNA: HOMDEL; | CNA: HOMDEL; | CNA: HOMDEL; | CNA: HOMDEL; | CNA: HOMDEL; | CNA: HOMDEL; | CNA: HOMDEL; |
| TCGA-OR-A5L3-01 | TCGA-OR-A5L3 | MUT: | X307_splice; | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: |
| TCGA-OR-A5L8-01 | TCGA-OR-A5L8 | MUT: | X307_splice; | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: |
| TCGA-OR-A5K6-01 | TCGA-OR-A5K6 | MUT: A389Efs*3; | MUT: E364Vfs*6; | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: | MUT: |
| TCGA-OR-A5J1-01 | TCGA-OR-A5J1 |
|-----------------|--------------|
| TCGA-OR-A5J8-01 | TCGA-OR-A5J8 |
| TCGA-OR-A5J9-01 | TCGA-OR-A5J9 |
| TCGA-OR-A5J6-01 | TCGA-OR-A5J6 |
| TCGA-OR-A5J0-01 | TCGA-OR-A5J0 |
| TCGA-OR-A5J2-01 | TCGA-OR-A5J2 |
| TCGA-OR-A5K0-01 | TCGA-OR-A5K0 |
| CNA: AMP; CNA: AMP; |
| MUT: T125=; |
| CNA: HOMDEL; |
| CNA: HOMDEL; |
| CNA: HOMDEL; |
| CNA: HOMDEL; |
| MUT: X125_splice; |
| MUT: E430Q; |
| CNA: HOMDEL; |
| CNA: HOMDEL; |
| MUT: Y234C; |
| MUT: E458*; |
| CNA: AMP; |
| CNA: AMP; |
| MUT: Y317*; |
| MUT: E339Afs*8; |
| CNA: AMP; |
| CNA: AMP; |
| MUT: Y317*; |
| CNA: HOMDEL; |
| MUT: E339Afs*8; |
| CNA: AMP; |
| CNA: AMP; |
| MUT: V394Sfs*4; |
| MUT: V394Sfs*4; |
| MUT: W270*; |
| MUT: E439*,X339_splice; |

| TCGA-OR-A5J3-01 | TCGA-OR-A5J3 |
|-----------------|--------------|
| TCGA-OR-A5J7-01 | TCGA-OR-A5J7 |
| TCGA-OR-A5J8-01 | TCGA-OR-A5J8 |
| TCGA-OR-A5J9-01 | TCGA-OR-A5J9 |
| TCGA-OR-A5JB-01 | TCGA-OR-A5JB |
| TCGA-OR-A5JE-01 | TCGA-OR-A5JE |
| TCGA-OR-A5JF-01 | TCGA-OR-A5JF |
| TCGA-OR-A5JG-01 | TCGA-OR-A5JG |
| TCGA-OR-A5JP-01 | TCGA-OR-A5JP |
| TCGA-OR-A5KT-01 | TCGA-OR-A5KT |
| TCGA-OR-A5KW-01 | TCGA-OR-A5KW |
| TCGA-OR-A5KZ-01 | TCGA-OR-A5KZ |
| TCGA-OR-A5L8-01 | TCGA-OR-A5L8 |
| TCGA-OR-A5LD-01 | TCGA-OR-A5LD |
| TCGA-OR-A5L0-01 | TCGA-OR-A5L0 |
| TCGA-OR-A5LS-01 | TCGA-OR-A5LS |
| TCGA-OU-A5PI-01 | TCGA-OU-A5PI |
| TCGA-P6-A5OF-01 | TCGA-P6-A5OF |
| TCGA-OR-A5J3-01 | TCGA-OR-A5J3 |
| TCGA-OR-A5J7-01 | TCGA-OR-A5J7 |
| TCGA-OR-A5K0-01 | TCGA-OR-A5K0 |
| TCGA-OR-A5KV-01 | TCGA-OR-A5KV |
| TCGA-OR-A5KX-01 | TCGA-OR-A5KX |
Table S2 – Frequency of patients with genetic alterations in Wnt/β-catenin and p53/Rb pathways in the C1A subgroup from Assié et al., 2014.

| Genetic alterations                                      | Frequency of patients |
|---------------------------------------------------------|-----------------------|
| Wnt/β-catenin pathway alterations                       | 5/21 (24%)            |
| p53/Rb pathway alterations                              | 4/21 (19%)            |
| Wnt/β-catenin and p53/Rb pathway alterations            | 8/21 (38%)            |
| Absence of Wnt/β-catenin or p53/Rb pathway alterations  | 4/21 (19%)            |

Table S3 – Adrenal Weight by Age

|                 | Control | PCreAS/+ | BCrAS/+ | BPCrAS/+ |
|-----------------|---------|----------|---------|----------|
| 1-5 months      | 3.1±0.7 | 3.3±0.7  | 2.8±0.5 | 3.6±1.5  |
| (n=34)          | (n=26)  | (n=7)    | (n=24)  |          |
| 6-12 months     | 2.8±1.1 | 2.9±0.8  | 9.1±6.3*| 189.2±229.9**|
| (n=5)           | (n=13)  | (n=16)   | (n=18)  |          |

Average Adrenal Weight (mg) Mean±SEM; *P<0.05, **P<0.01; Kruskal–Wallis
Table S4 – Age, Sex and Average Adrenal Weight of the BPCre^{As⁻}\textsuperscript{+} mice with no tumor (n=26)

| Animal ID | Age (month) | Sex | Adrenal Weight (mg) | Weiss Score | Ki-67 (%) | Metastasis |
|-----------|-------------|-----|---------------------|-------------|-----------|------------|
| 1083996-7 | 1           | F   | 2.2                 | -           | -         | -          |
| 1083993-1 | 1           | F   | 1.4                 | -           | -         | -          |
| 1084025-6 | 1           | F   | 2.9                 | -           | -         | -          |
| 1084084-5 | 1           | F   | 2.75                | -           | -         | -          |
| 1084084-8 | 1           | F   | 2.6                 | -           | -         | -          |
| 1084045b-1| 1           | F   | 3                   | -           | -         | -          |
| 1084101-5 | 1           | F   | 3.1                 | -           | -         | -          |
| 1084022-2 | 1           | F   | 2.25                | -           | -         | -          |
| 1084022-5 | 1           | F   | 1.75                | -           | -         | -          |
| 377-2     | 3           | F   | 3.45                | -           | -         | -          |
| 378-4     | 3           | F   | 2.5                 | -           | -         | -          |
| 1084045-6 | 3           | F   | 3.95                | -           | -         | -          |
| 1803992A-3| 3           | F   | 4                   | -           | -         | -          |
| 1084094-1b| 3           | F   | 3.75                | -           | -         | -          |
| 1084071-3 | 3           | F   | 3.55                | -           | -         | -          |
| 1084071-4 | 3           | F   | 3.85                | -           | -         | -          |
| 1084045A-4| 3           | M   | 3.5                 | -           | -         | -          |
| 1084056-7 | 3           | M   | 3.6                 | -           | -         | -          |
| 389-1     | 6           | M   | 2.25                | -           | -         | -          |
| 395-2     | 5.5         | M   | 7.15                | -           | -         | -          |
| 393-3b    | 5           | F   | 4.55                | -           | -         | -          |
| 393-4     | 5           | F   | 4.2                 | -           | -         | -          |
| 389-2b    | 5           | M   | 2.6                 | -           | -         | -          |
| 389-2c    | 5           | M   | 5.25                | -           | -         | -          |
| 395-4     | 5           | M   | 4.35                | -           | -         | -          |
| 385-5     | 7           | M   | 1.85                | -           | -         | -          |
Table S5 – Age Distribution, Sex, Average Adrenal Weight, Weiss Score, Percent Ki-67 and Metastasis of the tumors observed in the BPCre<sup>As/+</sup> mice (n=16)

| Animal ID | Age (month) | Sex | Adrenal Weight (mg) | Weiss Score | Ki-67 (%) | Metastasis |
|-----------|-------------|-----|---------------------|-------------|-----------|------------|
| 1         | 3.5         | F   | 5.1                 | 2           | -         | No         |
| 2         | 3.8         | F   | 3.55                | 3           | -         | No         |
| 3         | 5.9         | F   | 7.8                 | 1           | 0.05      | No         |
| 4         | 6.5         | M   | 21.3                | 2           | 26        | No         |
| 5         | 6.5         | F   | 113.5               | 4           | 30        | No         |
| 6         | 6.8         | M   | 23.0                | 5           | 16.6      | No         |
| 7         | 7.1         | F   | 9                   | 1           | 38.53     | No         |
| 8         | 7.1         | F   | 339                 | 6           | 12.5      | Yes        |
| 9         | 7.2         | M   | 3.9                 | 1           | 7.15      | No         |
| 10        | 8.0         | F   | 97.9                | 5           | 8.91      | No         |
| 11        | 8.4         | M   | 5.3                 | 1           | 16        | No         |
| 12        | 9.3         | M   | 258.4               | 6           | 27.3      | No         |
| 13        | 9.4         | M   | 80.4                | 3           | 10.6      | No         |
| 14        | 9.4         | M   | 423.5               | 6           | 14.5      | Yes        |
| 15        | 10.4        | F   | 643.5               | 7           | 14.7      | Yes        |
| 16        | 12.0        | F   | 800                 | 7           | 45.45     | Yes        |

Table S6 – Age Distribution of tumors in BPCre<sup>As/+</sup> mice

| Age (Month) | Weiss<3 ACA | Weiss >3 ACC | Weiss Score None | Total | Tumor: ACA or ACC |
|-------------|-------------|--------------|------------------|-------|-------------------|
| <3          | 0           | 0            | 11 (100%)        | 11    | 0 (0%)            |
| 3-4.5       | 1 (11%)     | 1 (11%)      | 7 (78%)          | 9     | 2 (22%)           |
| 5-7.5       | 4 (27%)     | 3 (20%)      | 8 (53%)          | 15    | 7 (47%)           |
| >7.5        | 1 (14%)     | 6 (86%)      | 0 (0%)           | 7     | 7 (100%)          |
Table S7 – Complete list of probes used in the qPCR experiments.

| Probe   | Assay ID               |
|---------|------------------------|
| Axin2   | Mm00443610_m1          |
| Lef1    | Mm00550265_m1          |
| Cyp11b2 | Mm01204955_g1          |
| Cyp11b1 | Mm01204952_m1          |
| Trp53   | Mm01731290_g1          |
| Cdkn1a  | Mm00432448_m1          |
| Ezh2    | Mm00468464_m1          |
| Actb    | Mm02619580_g1          |
| Rn18s   | Mm03928990_g1          |

Table S8 – Antibodies

| Protein target | Source                     | Dilution | Application |
|----------------|----------------------------|----------|-------------|
| Beta-catenin   | Abcam [12F7] (ab22656)     | 1:400    | IHC         |
| SF-1           | Abcam (ab65815)            | 1:300    | IHC         |
| Ki-67          | [SP6] (ab16667)            | 1:300    | IHC         |
| Beta-catenin   | BD 610153                  | 1:300    | IF          |