SUPPLEMENTARY DATA – Figure Legends

Supplementary Figure 1. **Pedigree from individual with *BAP1* c.121G>A (p.G41S) variant identified during evaluation for somatic *BAP1* mutations in ccRCC** A germline *BAP1* variant (c.121G>A; p.G41S) was identified in individual II:1 who presented with metastatic, unilateral, unifocal ccRCC at the age of 70 and died of the disease at age 74. The variant was confirmed in a second independent specimen. Three additional individuals in the family had RCC. Individual II:5, who was also affected with a parotid gland carcinoma died at age 84, II:6 at 75, and III:4 at 60. No samples for germline testing could be obtained, as the individuals were either deceased or unable to travel. Tumor samples were obtained from III:4, as well as III:8 (diagnosed with breast cancer at 55), III:17 (died of lung adenocarcinoma at 52), and III:18 (died of breast cancer at 45). Sequencing analyses for the *BAP1* c.121G>A variant found in the proband were performed as previously described in *Peña-Llopis et al. 2012* using tumor sections delineated by a pathologist from FFPE samples on 10 μm sections after DNA extraction using the QIAamp DNA FFPE Tissue Kit (Qiagen, Hilden, Germany). A sample from the proband was used as a positive control and all samples were negative for the presence of the variant.

Supplementary Figure 2. ***VHL* mutation in some but not all tumors from Family NCI-1326** *VHL* mutation status was evaluated by PCR and Sanger sequencing of exons 1-3 on DNA extracted from proband tumor 3 from 2012 surgery and tumor 1a and 1b (two independent regions from tumor 1) from 2008 surgery. *Upper sequence*: Example of wild-type *VHL* sequence (exon 2 is shown) from tumor 3. *Middle and lower sequences*: Forward and reverse sequences showing deletion of G (arrow) in exon 2 in two regions of tumor 1. Mutation (c.369delG; p.Thr124HisfsX35) creates a frameshift resulting in mutant sequence superimposed on wild-type sequence downstream (forward sequence) or upstream (reverse sequence) from site of G deletion and has previously been reported in ccRCC.

REFERENCES

Pena-Llopis S, Vega-Rubin-de-Celis S, Liao A, Leng N, Pavia-Jimenez A, Wang S, et al. BAP1 loss defines a new class of renal cell carcinoma. Nat Genet 2012;44:751-9.