Supplementary Online Content

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eTable 1. *BAP1* mutations seen in multiple families and associated phenotype in affected family members.
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This supplementary material has been provided by the authors to give readers additional information about their work.

Supplementary Information: The BAP1 Cancer Syndrome: A Report of 8 New Families and Review of Genotypic and Phenotypic Features

Supplemental Table 1. *BAP1* mutations seen in multiple families and associated phenotype in affected family members.

Mutation	**Papers**	**Associated Phenotype in Tested Patients**
c.1717delC, p.L573fs*3	Testa et al, 2011 Cebulla et al, 2015 Carbone et al, 2015 (three families) Ohar et al, 2016 (two families) Our Family 3	Mesothelioma(64), UM(58) UM(18) CM(32), mesothelioma(55,60,51,52,67, 70), bone(71), BCC(67,71), RCC(70), UM(71), breast(50) Mesothelioma (asbestos exposed) in both families BDT(10)
c.1153C>T, p.R385X	Njauw et al, 2012 Betti et al, 2016	BDT, UM(51,55, 57, 59), breast(x2), lung(57, x2), CM(36, 60), cholangiocarcinoma CM(53,57), meningioma(37), mesothelioma(53)
c.2050C>T, p.Q684X	Testa et al, 2011 Pilarski et al, 2014	Mesothelioma(50,59, 63), BCC, SCC, UM, pancreatic cancer UM(41), mesothelioma, epithelial malignancy of unknown origin(42)
c.588G>A, p.W196X	Popova et al, 2013 de la Fouchardiere, 2015	CM(47) Papillary thyroid cancer(41), leptomeningeal melanoma(40)
c.1938T>A, p.Y646X	Cheung et al, 2015 Carbone et al, 2015	Mesothelioma (x2), BCC (x2), meningioma, CM(x2), BDTs Mesothelioma
c.1882_1885delTCAC, p.S628fs*8	Testa et al, 2011 Pilarski et al, 2014 Ohar et al, 2016	UM, mesothelioma CM, UM, colorectal cancer, RCC (x2), breast cancer UM, mesothelioma (asbestos exposed)

<u>Supplemental Table 2.</u> Patients with multiple melanomas. As seen in the table, most patients with multiple melanomas had truncating or missense mutations in the UCH domain of the BAP1 protein.

Paper	**Mutation**	**Domain Affected**	**Mutation Type**	**Phenotype**
Gerami et al, 2016	c.592G>T, p.E198X	UCH	Nonsense	7 CM first seen at age 43
Njauw et al, 2012	c.706_707insG, p.D236Gfs*7	UCH	Frameshift	7 CM starting at age 31; at least 10 BDTs
Betti et al, 2016	c.1153C>T, p.Arg385X	none	Nonsense	CM at 53, 57, meningioma at 37, mesothelioma at 53
Aoude et al, 2015	c.361G>C, p.G121R	UCH	Missense	CM at 25 and 72
Aoude et al, 2015	c.448C>T, p.R150C	UCH	Missense	CM at 32 and 57, breast cancer at 57
Popova et al, 2013	c.37+1delG	UCH	Splice site	CM at 29,31,34; RCC at 36
Popova et al, 2013	c.660-11T>A	UCH	Splice site	CM at 47 and 52
Wadt et al, 2012	c.1708C>G, p.L570V	none	Missense	CM at 27 (x2), another CM at 33

Supplemental Table 3. Patients with mesothelioma and *BAP1* mutations (ages provided where available).

Paper	Mutation	Effect on Protein	Phenotype
Ohar et al, 2016	c.1695insT, p.Glu566fs*1	Frameshift; truncating	Mesothelioma (asbestos exposed), RCC; breast cancer
Ohar et al, 2016	c.1717delC, p.Leu573fs*3	Frameshift; truncating	Mesothelioma (asbestos exposed)
Ohar et al, 2016	c.1882_1885delTCAC, p.Ser628fs*8	Frameshift; truncating	Mesothelioma (asbestos exposed), UM
Ohar et al, 2016	c.1717delC, p.Leu573fs*3	Frameshift; truncating	Mesothelioma (asbestos exposed)
Testa et al, 2011	c.2050C>T, p.Q684X	Truncating	Mesothelioma(50)
Testa et al, 2011	c.2050C>T, p.Q684X	Truncating	Mesothelioma(59), UM
Testa et al, 2011	c.2050C>T, p.Q684X	Truncating	Mesothelioma(63)
Wadt et al, 2015	c.1209_1210dupT; p.D404X	Truncating	Mesothelioma(62)
Wadt et al, 2015	c.1209_1210dupT; p.D404X	Truncating	Mesothelioma(46), Spitz nevus(32)
Wadt et al, 2015	c.1209_1210dupT; p.D404X	Truncating	Mesothelioma(51), BCC(50)
Wadt et al, 2015	c.823C>T, p.Q280*	Truncating	Mesothelioma(56), CM(55),
Popova et al, 2013	c.1654delG, p.Asp552Ilefs*19	Frameshift; truncating	Mesothelioma(41)
Popova et al, 2013	c.1654delG, p.Asp552Ilefsx19	Frameshift; truncating	UM(52); mesothelioma(59)
Popova et al, 2013	c.670dupC, p.H224Pfs*1	Frameshift; truncating	Mesothelioma(41)
Popova et al, 2013	c.1647delT; p.Val550Serfs*21	Frameshift; truncating	Mesothelioma(62)
Cheung et al, 2015	c.1938T>A, p.Y646X	Truncating	Mesothelioma,CM
Cheung et al, 2015	c.1938T>A, p.Y646X	Truncating	Mesothelioma, BCC, meningioma
Abdel-Rahman et al, 2011	c.799C>T, p.Q267X	Truncating	Mesothelioma
Testa et al, 2011	c.1832delC, p.Leu573fs*3	Frameshift; truncating	Mesothelioma(55,60), UM(48), CM(32)
Testa et al, 2011	c.2008-2011delTCAC, p.Ser628fs*8	Frameshift; truncating	mesothelioma(55), UM(53)
Wiesner et al, 2012	c.79delG, p.V27Cfs*45	Frameshift; truncating	Mesothelioma
Wiesner et al, 2012	c.79delG, p.V27Cfs*45	Frameshift; truncating	Mesothelioma
Wiesner et al, 2012	c.79delG, p.V27Cfs*45	Frameshift; truncating	Mesothelioma, BDTs
Ribeiro et al, 2013	c.758_759insA, p.Gln253fs*31	Frameshift; truncating	Mesothelioma(56), UM(56)
Ribeiro et al, 2013	c.758_759insA, p.Gln253fs*31	Frameshift; truncating	Mesothelioma(44)
Pilarski et al, 2014	c.2050C>T, p.Q684X	Truncating	Mesothelioma
Betti et al, 2015	c.46_47insA, p.Thr16fs*52	Frameshift; truncating	Mesothelioma(63); town in Italy with heavy asbestos exposure
Betti et al, 2015	c.46_47insA, p.Thr16fs*52	Frameshift; truncating	Mesothelioma(79); town in Italy with heavy asbestos exposure

Paper	Mutation	Effect on Protein	Phenotype
Betti et al, 2016	c.1153C>T, p.Arg385X	Truncating	Meningioma(37), mesothelioma(53), CM(53, 57)
Carbone et al, 2015	c.1938T>A, p.Y646X	Truncating	Mesothelioma
Carbone et al, 2015	c.1717_1717delC, p.Leu573fs*3	Frameshift; truncating	Mesothelioma(51)
Carbone et al, 2015	c.1717_1717delC, p.Leu573fs*3	Frameshift; truncating	Mesothelioma(52)

Supplemental Table 3 Continued

Paper	Mutation	Effect on Protein	Phenotype
Carbone et al, 2015	c.1717_1717delC, p.Leu573fs*3	Frameshift; truncating	BCC(61, 71), mesothelioma(67), RCC(70), UM(71)
Carbone et al, 2015	c.1717_1717delC, p.Leu573fs*3	Frameshift; truncating	Mesothelioma(55)
Rai et al, 2015	c.539T>C, p.L180P	Missense	Mesothelioma(71), CM(72), multiple BCCs beginning at 56
Rai et al, 2015	c.256-4_256-2del	Potential splice site; RT-pCR found two splice products, both affecting protein length	Mesothelioma
Ohar et al, 2016	c.1729+1G>A	Mini-gene expression assay showed mutation lead to an RNA message lacking exon 13; frameshift	Mesothelioma (asbestos exposed)
Ohar et al, 2016	c.1891+1G>A	Retention of a portion of intron 14; expected to lead to frameshift	Mesothelioma (asbestos exposed)
Testa et al, 2011	c.438-2A>G, p.P147fs*48	Frameshift; truncating	Mesothelioma(58)
Testa et al, 2011	c.438-2A>G, p.P147fs*48	Frameshift; truncating	Mesothelioma(50)
Testa et al, 2011	c.438-2A>G, p.P147fs*48	Frameshift; truncating	Mesothelioma(58)
Testa et al, 2011	c.438-2A>G, p.P147fs*48	Frameshift; truncating	Mesothelioma(44)
Testa et al, 2011	c.438-2A>G, p.P147fs*48	Frameshift; truncating	Mesothelioma(36)
Wadt et al, 2012	c.1708C>G, p.Leu570Val	Expected to lead to p.Leu570fs*40 due to aberrant splicing	Breast cancer (74), peritoneal mesothelial hyperplasia with atypia suspected to be peritoneal papillary mesothelioma(84)
Carbone et al, 2015	c.1717_1717delC, p.Leu573fs*3	Frameshift; truncating	Breast cancer(50), mesothelioma(70)
Klebe et al, 2015	c.518G>A, p.Tyr173Cys	Missense	UM (72), cholangiocarcinoma(72), mesothelioma(72)
Our Patient Family 5	exon 3 deletion	Truncating	Meningioma(36), CM(41), RCC and prostate cancer(51), mesothelioma(55), BDTx2(56)

Our Patient Family 8	c.79dupG	Frameshift; truncating	Mesothelioma(36)

Supplemental Table 4. Patients with germline *BAP1* mutations at or above the age of 56 without a diagnosis of mesothelioma.

Paper	Mutation	Effect on Protein	Phenotype
Testa et al, 2011	c.2050C>T, p.Q684X	Truncating	BCC; age unavailable but current age 68
Testa et al, 2011	c.2050C>T, p.Q684X	Truncating	SCC; age unavailable but current age 82
Testa et al, 2011	c.2050C>T, p.Q684X	Truncating	Pancreatic cancer; age not available but follow up until 73
Njauw et al, 2012	c.1899_1900ins5, p.Ala643Glyfs*5	Frameshift; truncating	UM(58)
Njauw et al, 2012	c.1153C>T, p.Arg385X	Truncating	UM(57), lung cancer(57), melanoma(60)
Njauw et al, 2012	c.1153C>T, p.Arg385X	Truncating	UM(59), lung cancer, DCIS
Njauw et al, 2012	c.706_707insG, p.Asp236Glyfs*7	Frameshift; truncating	UM(62), lung cancer(49)
Wiesner et al, 2011	c.1305delG, p.Gln436Asnfs*135	Frameshift; truncating	BAPomas, UM(72)
Wadt et al, 2015	c.1209_1210dupT, p.D404X	Truncating	CM(60)
Wadt et al, 2015	p.178C>T, p.R60X	Truncating	13 BCCs(65)
Wadt et al, 2015	p.178C>T, p.R60X	Truncating	UM(59)
Gupta et al, 2015	c.510_511insT, p.Val171Cysfs*12	Frameshift; truncating	colon cancer(53), prostate(63), RCC(63), UM
Carbone et al, 2015	c.1717_1717delC, p.Leu573fs*3	Frameshift; truncating	nasal carcinoma(56)
McDonnell et al, 2016	c.1777C>T, p.Q593X	Truncating	hepatocellular carcinoma(56)
Gossage et al, 2014	c.1946G>A, p.C649Y	Missense	RCC(56)
Gossage et al 2014	c.851A>G, p.E284G	Missense	RCC(72)
Maerker et al, 2014	c.299T>C, p.L100P	Missense	UM(56), cholangiocarcinoma(71)
Rai et al,2015	c.539T>C, p.L180P	Missense	Unaffected(59)
Rai et al, 2015	c.539T>C, p.L180P	Missense	UM(60), several BCC(61)
Aoude et al, 2015	c.361G>C, p.G121R	Missense	CM(25, 72)
Aoude et al, 2015	c.448C>T, p.R150C	Missense	CM(32, 57) breast(57)
Aoude et al, 2015	c.1337A>T, p.N446I	Missense	CM(53), lung cancer(65,68)
Testa et al, 2011	c.438-2A>G, p.P147fs*48	Frameshift due to splice acceptor mutation	RCC(57)
Popova et al, 2013	c.37+1delG	Splice site, unknown predicted effect on protein	UM(57)
Wadt et al, 2012	c.1708C>G, p.Leu570Val	Expected to lead to p.Leu570fs*40 due to aberrant splicing; truncating	UM(62)
Aoude et al, 2013	c.581-2A>G	Splice site; expected to be truncating	UM(57)

Aoude et al, 2013	c.581-2A>G	Splice site; expected to be truncating	UM(69)
Aoude et al, 2013	c.581-2A>G	Splice site; expected to be truncating	stomach cancer(69)
Turunen et al, 2016	c.67+1G>T	Predicted to lead to incorrect splicing; predicted loss of splice donor site with no splice site nearby; possibly leading to non-functional protein	bladder cancer(55), UM(57)