Supplemental data information

Supplemental Table 1. Fifty patients involved in the *PDE11A* study.

Supplemental Table 2. Primers used to generate mutant expression vectors of *PDE11A*.

Legend: All the forward and reverse primers are complementary to each other and contain the mutant base (**bold**) mismatched to the wild type in the middle of the sequence.

Supplemental table 3. *In silico* modeling of the effect of *PDE11A* missense substitution on the protein function.

Legend: * greater score indicates higher probability to impair the protein function; the factors taken into account for the calculation of the score are:
(1) difference in the thermo-physical properties of the wt and mutant protein, and
(2) evolutionary preservation of the residue in the corresponding position.

Supplemental Table 4: Allele frequency distribution of sequence variations in *PDE11A* in PCa patients compared to patients with testicular germ cell tumors (TGCT) and adrenocortical tumors (ADT).

Legend:* Newly identified in the PCa patients only variations.
NA=Not Applicable.
χ^2 is calculated after Yates correction for continuity (Yates correction was applied for all calculations having number<10 in any cell of the contingency table).

Supplemental Table 1. Fifty patients involved in the *PDE11A* study.

Sample	Age	Familiar History	Gleason Score	previous PSA	last PSA	Staging
1 DT	64	0	6	7.89	0.040	pT2b
2 DT	56	0	6	8.30	0.020	pT3a
3 DT	61	0	8	9.20	0.079	pT2b
4 DT	61	0	8	5.00	0.010	pT3a
5 DT	67	0	6	9.50	0.100	pT2b
6 DT	66	0	6	13.80	0.007	-
7 DT	56	0	6	10.60	0.050	pT3a
8 DT	61	0	6	4.20	0.169	pT3b
9 DT	64	0	6	5.70	0.050	pT3b
10 DT	78	-	6	-	-	pT2a
11 DT	71	0	6	8.95	0.010	pT3a
12 DT	56	0	7	21.90	0.300	pT2b
13 DT	50	1	7	18.16	3.500	pT2b
14 DT	57	0	7	4.60	0.030	pT2b
15 DT	72	0	7	7.32	0.040	pT4a
16 DT	64	0	7	25.90	0.010	pT3a
17 DT	77	0	7	7.20	0.110	pT2b
18 DT	58	1	7	2.40	0.075	pT2b
19 DT	69	0	7	20.30	0.010	pT2b
20 DT	55	0	7	14.00	0.918	pT2b
21 DT	48	0	7	7.60	0.050	pT2a
22 DT	62	0	7	5.74	0.050	pT3a
23 DT	58	1	7	8.60	0.062	pT3a
24 DT	61	0	7	17.80	0.030	pT3a
25 DT	54	0	7	7.30	0.050	pT3a
26 DT	60	0	7	4.22	0.010	pT3a
27 DT	64	1	7	7.50	0.008	pT3a
28 DT	71	0	7	7.10	0.179	pT3a
29 DT	65	0	7	16.50	0.080	pT3a
30 DT	62	0	7	5.11	0.040	pT2a
31 DT	55	0	7	22.10	0.003	pT2b
32 DT	72	0	7	6.80	0.053	pT3a
33 DT	60	0	7	5.20	0.019	pT3b
34 DT	61	0	7	5.70	0.020	pT3a
35 DT	79	0	7	8.63	0.100	pT2b
36 DT	62	0	7	20.28	0.320	pT2b
37 DT	73	2	7	21.87	0.040	pT3a
38 DT	60	0	7	32.05	0.310	pT2b
39 DT	68	0	7	6.21	0.060	pT3a
40 DT	-	0	7	-	-	pT4a
41 DT	74	0	7	5.25	0.020	pT3a
42 DT	65	0	7	13.94	0.586	pT2b
43 DT	64	0	7	9.20	0.090	pT2b
44 DT	56	0	7	9.60	0.085	pT3b
45 DT	70	0	7	10.30	0.008	pT2a
46 DT	66	0	7	33.61	0.170	pT3a
47 DT	63	0	7	3.93	0.010	-
48 DT	67	0	7	23.30	0.070	-
49 DT	74	0	7	6.30	0.003	-
50 DT	63	0	7	7.60	0.003	-

Supplemental Table 2. Primers used to generate mutant expression vectors of *PDE11A*.

***PDE11A* missense variation**	**Forward primer (5’ – 3’)**	**Reverse primer (5’ – 3’)**
c.604C>T / p.R202C	TGAG**T**GTCAGTTCTTTCTGGAATTG	CAATTCCAGAAAGAACTGAC**A**CTCA
c.1973A>G / p.Y658C	CT**G**TCGGATGGTTCTATACCACAA	TTGTGGTATAGAACCATCCGA**C**AG
c.2518G>A / p.E840K	CAGTGAGTTCTTC**A**AACAAGGAGAT	ATCTCCTTGTT**T**GAAGAACTCACTG

Supplemental Table 3. *In silico* modeling of the effect of *PDE11A* missense substitution on the protein function.

DNA change	Protein change	Domain	In silico modeling	
			Prediction	Score*
c.607C>T	p.R202C	cAMP binding A	Likely benign	0.021
c.1973A>G	p.Y658C	Catalytic Domain	Probably damaging	2.846
c.2518G>A	p.E840K	Catalytic Domain	Likely benign	1.309

Supplemental Table 4: Allele frequency distribution of sequence variations in *PDE11A* in PCa patients compared to patients with testicular germ cell tumors (TGCT) and adrenocortical tumors (ADT).

Sequence change	**Mutation type**	**PCa patients (100 alleles)**	**TGCT patients (128 alleles)**	**ADT patients (234 alleles)**	**PCa vs TGCT**		**PCa vs ADT**	
					χ^2	**P**	χ^2	**P**
p.R52T	missense	0 (0.00)	1 (0.008)	0 (0.000)	0.02	0.89	0.09	0.76
c.171Tdel FS41X	frame-shift stop-codon	1 (0.01)	0 (0.000)	0 (0.000)	0.02	0.89	NA	NA
p.R202C*	missense	1 (0.01)	0 (0.000)	0 (0.000)	0.02	0.89	NA	NA
p.F205L	missense	0 (0.00)	0 (0.000)	1 (0.004)	NA	NA	0.09	0.76
p.F258Y	missense	0 (0.00)	1 (0.008)	0 (0.000)	0.02	0.89	0.09	0.76
p.G291R	missense	0 (0.00)	1 (0.008)	0 (0.000)	0.02	0.89	0.09	0.76
p.R307X	nonsense	0 (0.00)	1 (0.008)	1 (0.004)	0.02	0.89	0.09	0.76
p.A349T	missense	0 (0.00)	0 (0.000)	2 (0.009)	NA	NA	0.09	0.76
c.1655_1657indel FS15X	frame-shift stop-codon	0 (0.00)	0 (0.000)	0 (0.000)	NA	NA	NA	NA
p.D609N	missense	0 (0.00)	0 (0.000)	1 (0.004)	NA	NA	0.09	0.76
p.Y658C*	missense	1 (0.01)	0 (0.000)	0 (0.000)	0.02	0.89	NA	NA
p.H664G	missense	0 (0.00)	0 (0.000)	1 (0.004)	NA	NA	0.09	0.76
p.Y727C	missense	5 (0.05)	3 (0.023)	4 (0.017)	0.52	0.47	0.00	1
p.R804H	missense	3 (0.03)	3 (0.023)	8 (0.034)	0.02	0.89	0.06	0.81
p.V820M	missense	0 (0.00)	1 (0.008)	0 (0.000)	0.02	0.89	0.09	0.76
p.E840K*	missense	2 (0.02)	0 (0.000)	0 (0.000)	0.79	0.37	NA	NA
p.R867G	missense	1 (0.01)	3 (0.023)	5 (0.021)	0.07	0.79	0.06	
p.M878V	missense	2 (0.02)	2 (0.016)	1 (0.004)	0.07	0.79	0.09	0.76
Total		**16 (0.160)**	**16 (0.125)**	**24 (0.103)**	**0.57**	**0.45**	**2.19**	**0.14**