

Table S1. Immunoreactivity of selected epithelial and stromal markers of paired primary tumor and metastasis biopsies, sampled with less than 1.9 years in-between (below study median time)

	Primary tumor	Metastases	Rs (n)
<u>Epithelial markers</u>			
ERG (pos./total)	15/40	11/40*	0.80***
Ki67 (%), n=49	15 (10; 23)	19 (11; 26)	0.49***
PSA (score), n=49	8 (6; 9)	6 (3; 10)	0.54***
AR (score), n=44	12 (8; 12)	8 (4; 12)**	0.12
<u>Stromal markers</u>			
Ki67 (%), n=36	2.0 (1.1; 3.3)	6.0 (2.5; 7.1)***	0.33*
AR (%), n=32	17 (8.0; 25)	2.2 (1.8; 4.0)***	0.35*
SMA density (%), n=23	15 (12; 17)	5.2 (3.1; 8.4)***	0.075
SDF-1 density (%), n=25	3.3 (2.1; 4.1)	4.7 (3.6; 6.1)**	0.038
PDGFR β density (%), n=18	6.6 (6.0; 13)	11 (8.5; 13)	0.053
ERG, endothelium density (%), n=35	1.0 (0.66; 1.5)	1.0 (0.76; 1.3)	0.012

Marker values are median and 25th and 75th percentiles, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. ERG, ETS-related gene; Ki67, marker for proliferation; PSA, prostate specific antigen; AR, androgen receptor; SMA, smooth muscle actin; SDF-1, stroma derived factor 1; PDGFR β , platelet-derived growth factor receptor β .

Table S2. Immunoreactivity of selected epithelial and stromal markers of paired primary tumor and metastasis biopsies, sampled with more than 1.9 years in-between (above study median time)

	Primary tumor	Metastases	Rs (n)
<u>Epithelial markers</u>			
ERG (pos./total)	15/40	10/40	0.63***
Ki67 (%), n=49	12 (7.0; 17)	14 (7.9; 24)	0.22
PSA (score), n=49	8 (6; 12)	6 (4; 9)*	0.13
AR (score), n=48	12 (9; 12)	8 (4; 12)***	0.31*
<u>Stromal markers</u>			
Ki67 (%), n=39	1.0 (0.50; 2.3)	4.0 (3.0; 7.0)***	-0.15
AR (%), n=36	19 (13; 34)	3.1 (1.5; 5.4)***	0.19
SMA density (%), n=27	16 (13; 18)	5.8 (4.3; 7.9)***	0.072
SDF-1 density (%), n=26	3.1 (1.9; 3.9)	4.1 (2.6; 5.6)	-0.50**
PDGFR β density (%), n=19	9.0 (3.7; 12)	9.6 (7.0; 12)	0.40
ERG, endothelium density (%), n=34	0.88 (0.66; 1.4)	1.0 (0.55; 1.4)	-0.20

Marker values are median and 25th and 75th percentiles, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. ERG, ETS-related gene; Ki67, marker for proliferation; PSA, prostate specific antigen; AR, androgen receptor; SMA, smooth muscle actin; SDF-1, stroma derived factor 1; PDGFR β , platelet-derived growth factor receptor β .

Table S3. Correlations														
				Primary tumor epithelium					Primary tumor stroma					
		Age diagnosis	PSA serum diagnosis	ISUP	Ki67	PSA	AR	ERG	Ki67	AR	SMA	SDF1	PDGFRB	ERG endo
Age diagnosis	Correlation Coefficient	1	0.078	0.071	-0.102	0.113	0.179	-0.015	-0.009	0.029	-0.169	0.092	-0.049	0.165
	N	97	95	97	97	97	96	85	94	96	68	66	60	83
PSA serum diagnosis	Correlation Coefficient	0.078	1	0.085	-0.179	0.199	0.187	-0.205	-0.038	0.041	-0.176	0.059	0.329*	0.213
	N	95	96	96	96	96	95	85	93	95	68	67	60	83
Primary tumor epithelium														
ISUP	Correlation Coefficient	0.071	0.085	1	0.224*	-0.085	0.005	-0.331**	0.226*	-0.154	-0.337**	0.211	0.122	0.261*
	N	97	96	98	98	98	97	86	95	97	69	67	61	84
Ki67	Correlation Coefficient	-0.102	-0.179	0.224*	1	-0.404***	0.09	-0.001	0.530***	-0.337***	-0.235	0.313**	-0.142	-0.002
	N	97	96	98	98	98	97	86	95	97	69	67	61	84
PSA	Correlation Coefficient	0.113	0.199	-0.085	-0.404***	1	0.096	0.001	-0.385***	0.345***	0.024	-0.008	0.163	0.203
	N	97	96	98	98	98	97	86	95	97	69	67	61	84
AR	Correlation Coefficient	0.179	0.187	0.005	0.09	0.096	1	0.084	-0.062	0.200*	-0.238*	0.199	0.068	0.122
	N	96	95	97	97	97	97	86	94	97	69	67	61	84
ERG	Correlation Coefficient	-0.015	-0.205	-0.331**	-0.001	0.001	0.084	1	-0.064	0.063	-0.109	-0.005	-0.144	-0.294**
	N	85	85	86	86	86	86	86	84	86	67	66	60	83
Primary tumor stroma														
Ki67	Correlation Coefficient	-0.009	-0.038	0.226*	0.530***	-0.385***	-0.062	-0.064	1	-0.277**	-0.245*	0.2	-0.339**	0.076
	N	94	93	95	95	95	94	84	95	94	67	66	59	82
AR	Correlation Coefficient	0.029	0.041	-0.154	-0.337***	0.345***	0.200*	0.063	-0.277**	1	0.06	0.013	0.232	-0.084
	N	96	95	97	97	97	97	86	94	97	69	67	61	84
SMA	Correlation Coefficient	-0.169	-0.176	-0.337**	-0.235	0.024	-0.238*	-0.109	-0.245*	0.06	1	-0.035	0.002	-0.164
	N	68	68	69	69	69	69	67	67	69	69	62	57	68
SDF1	Correlation Coefficient	0.092	0.059	0.211	0.313**	-0.008	0.199	-0.005	0.2	0.013	-0.035	1	0.153	0.312*
	N	66	67	67	67	67	67	66	66	67	62	67	54	66
PDGFRB	Correlation Coefficient	-0.049	0.329*	0.122	-0.142	0.163	0.068	-0.144	-0.339**	0.232	0.002	0.153	1	0.197
	N	60	60	61	61	61	61	60	59	61	57	54	61	61
ERG endo	Correlation Coefficient	0.165	0.213	0.261*	-0.002	0.203	0.122	-0.294**	0.076	-0.084	-0.164	0.312*	0.197	1
	N	83	83	84	84	84	84	83	82	84	68	66	61	84

		Metastasis tumor epithelium				Metastasis stroma						Metastatic subtype (%)		
		Ki67	PSA	AR	ERG	Ki67	AR	SMA	SDF1	PDGFRB	ERG endo	MetA	MetB	MetC
Age diagnosis	Correlation Coefficient	-0.075	0.082	0.083	0.002	-0.22	0.105	-0.086	0.04	0.02	-0.042	0.059	-0.118	0.165
	N	97	97	93	91	78	69	72	76	60	82	69	69	69
PSA serum diagnosis	Correlation Coefficient	-0.236*	0.354***	-0.081	-0.177	-0.15	-0.015	-0.179	-0.098	0.121	-0.073	0.365**	-0.313**	-0.068
	N	96	96	92	90	76	68	70	75	59	80	68	68	68
Primary tumor epithelium														
ISUP	Correlation Coefficient	-0.143	0.033	0.149	-0.397***	0.019	0.243*	-0.174	-0.168	-0.115	-0.009	0.022	-0.129	0.136
	N	98	98	93	92	78	69	72	76	60	82	70	70	70
Ki67	Correlation Coefficient	0.376***	-0.342***	0.08	-0.006	0.306**	-0.192	0.244*	-0.211	-0.086	0.294**	-0.473**	0.267*	0.15
	N	98	98	93	92	78	69	72	76	60	82	70	70	70
PSA	Correlation Coefficient	-0.235*	0.373***	0.105	0.019	-0.331**	0.113	-0.081	0.15	0.157	-0.219*	0.307**	-0.225	-0.013
	N	98	98	93	92	78	69	72	76	60	82	70	70	70
AR	Correlation Coefficient	-0.042	0.136	0.218*	0.062	-0.051	0.143	0.155	-0.215	0.017	-0.088	0.128	-0.043	0.001
	N	97	97	92	91	77	68	71	75	59	81	70	70	70
ERG	Correlation Coefficient	0.068	-0.06	-0.004	0.712***	-0.260*	-0.06	-0.071	0.051	0.067	-0.114	0.086	0.021	-0.128
	N	86	86	82	80	71	63	61	66	52	71	64	64	64
Primary tumor stroma														
Ki67	Correlation Coefficient	0.147	-0.154	0.082	-0.066	0.074	-0.004	0.122	-0.073	-0.145	0.359**	-0.129	0.255*	-0.214
	N	95	95	90	89	75	66	69	73	58	79	68	68	68
AR	Correlation Coefficient	-0.08	0.222*	0.089	0.098	-0.11	0.265*	-0.208	0.156	-0.066	-0.301*	0.265*	-0.248*	0.005
	N	97	97	92	91	77	68	71	75	59	81	70	70	70
SMA	Correlation Coefficient	-0.18	-0.124	-0.03	-0.09	0.08	-0.129	0.097	0.041	-0.046	0.000	-0.037	0.092	0.038
	N	69	69	65	64	56	47	50	52	40	56	51	51	51
SDF1	Correlation Coefficient	0.038	-0.016	0.167	-0.021	-0.035	-0.007	0.107	-0.268	-0.16	-0.032	-0.106	-0.012	0.08
	N	67	67	64	61	54	45	47	51	39	53	48	48	48
PDGFRB	Correlation Coefficient	0.094	0.157	0.219	0.018	-0.011	-0.113	-0.2	-0.166	0.265	-0.013	-0.095	0.027	0.277
	N	61	61	57	56	50	41	44	45	37	35	48	44	44
ERG endo	Correlation Coefficient	-0.127	0.163	0.151	-0.342**	-0.050	0.224	-0.048	-0.091	0.167	-0.094	0.110	-0.152	0.096
	N	84	84	80	79	69	61	60	63	51	69	63	63	63

		Metastasis tumor epithelium				Metastasis stroma						Metastatic subtype (%)		
		Ki67	PSA	AR	ERG	Ki67	AR	SMA	SDF1	PDGFRB	ERG endo	MetA	MetB	MetC
Metastasis tumor epithelium														
Ki67	Correlation Coefficient	1	-0.465***	0.149	0.169	0.538***	-0.319**	0.391***	-0.166	-0.052	0.419**	-0.394***	0.570***	-0.175
	N	98	98	93	92	78	69	72	76	60	82	70	70	70
PSA	Correlation Coefficient	-0.465***	1	0.118	-0.026	-0.335**	0.153	-0.166	0.054	0.076	-0.335**	0.367**	-0.346**	0.035
	N	98	98	93	92	78	69	72	76	60	82	70	70	70
AR	Correlation Coefficient	0.149	0.118	1	0.099	-0.028	-0.035	0.196	-0.215	0.086	-0.011	0.054	0.03	-0.044
	N	93	93	93	87	77	68	70	74	59	80	68	68	68
ERG	Correlation Coefficient	0.169	-0.026	0.099	1	-0.219	-0.058	-0.027	0.027	0.193	-0.177	0.115	-0.005	-0.094
	N	92	92	87	92	73	67	72	75	59	82	65	65	65
Metastasis stroma														
Ki67	Correlation Coefficient	0.538***	-0.335**	-0.028	-0.219	1	-0.245	0.503***	-0.253*	-0.059	0.409**	-0.373**	0.277*	-0.015
	N	78	78	77	73	78	62	63	63	49	70	62	62	62
AR	Correlation Coefficient	-0.319**	0.153	-0.035	-0.058	-0.245	1	-0.315*	0.144	-0.2	-0.162	0.340**	-0.400**	-0.004
	N	69	69	68	67	62	69	60	58	49	65	61	61	61
SMA	Correlation Coefficient	0.391***	-0.166	0.196	-0.027	0.503***	-0.315*	1	-0.226	0.138	0.333**	-0.373**	0.416**	-0.069
	N	72	72	70	72	63	60	72	63	53	71	58	58	58
SDF1	Correlation Coefficient	-0.166	0.054	-0.215	0.027	-0.253*	0.144	-0.226	1	0.450**	-0.210	0.223	-0.320*	0.044
	N	76	76	74	75	63	58	63	76	54	73	55	55	55
PDGFRB	Correlation Coefficient	-0.052	0.076	0.086	0.193	-0.059	-0.2	0.138	0.450***	1	-0.149	0.009	-0.018	0.093
	N	60	60	59	59	49	49	53	54	60	56	48	48	48
ERG endo	Correlation Coefficient	0.419**	-0.335**	-0.011	-0.177	0.409**	-0.162	0.333**	-0.210	-0.149	1	-0.415**	0.384**	-0.150
	N	82	82	80	82	70	65	71	73	56	82	63	63	63
Metastatic subtype (%)														
MetA	Correlation Coefficient	-0.394***	0.367**	0.054	0.115	-0.373**	0.340**	-0.373**	0.223	0.009	-0.415**	1	-0.518***	-0.506***
	N	70	70	68	65	62	61	58	55	48	63	70	70	70
MetB	Correlation Coefficient	0.570***	-0.346**	0.03	-0.005	0.277*	-0.400**	0.416**	-0.320*	-0.018	0.384**	-0.518***	1	-0.246*
	N	70	70	68	65	62	61	58	55	48	63	70	70	70
MetC	Correlation Coefficient	-0.175	0.035	-0.044	-0.094	-0.015	-0.004	-0.069	0.044	0.093	-0.150	-0.506***	-0.246*	1
	N	70	70	68	65	62	61	58	55	48	63	70	70	70

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.