

# Human Cancers Overexpress Genes that are Specific to a Variety of Normal Human Tissues

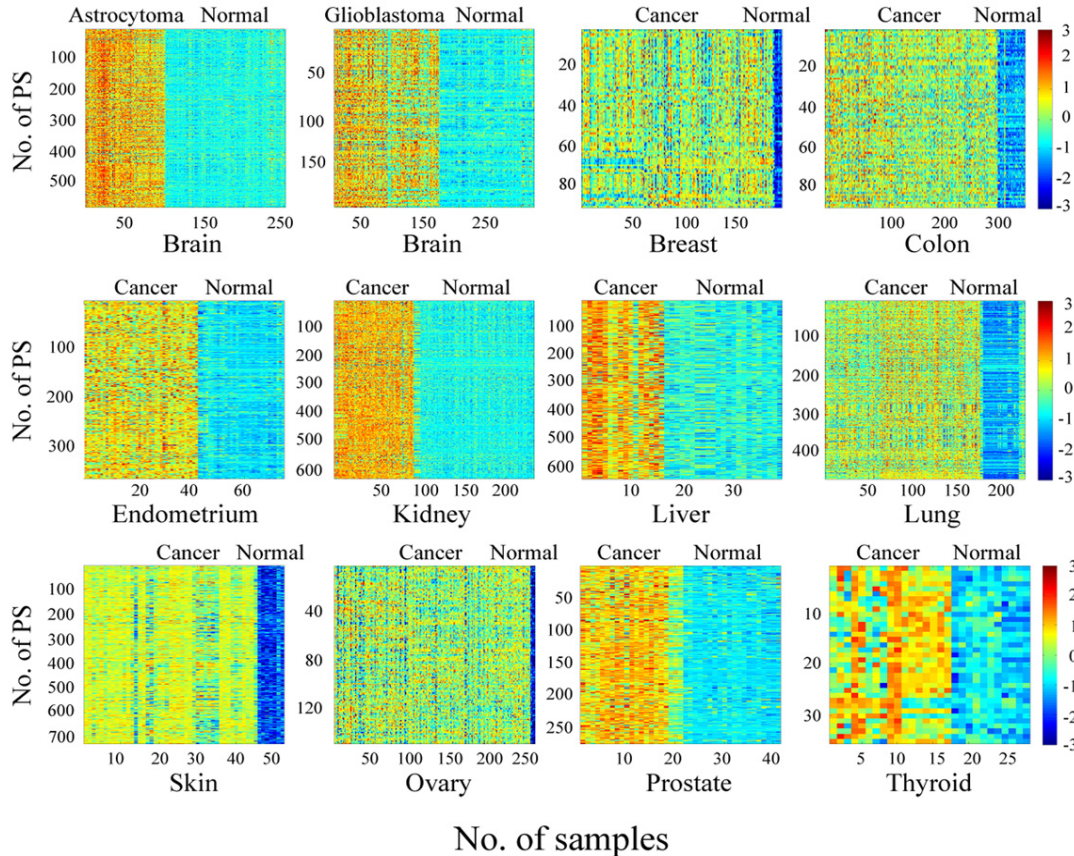
The genetic and epigenetic changes that lead to cancer development are associated with aberrant gene expression including overexpression of genes compared to the normal tissue from which the cancers originated (reviewed in Lotem J and Sachs L, 2006). In collaboration with Eytan Domany and Dvir Netaneli we have previously shown that some of the genes that are highly expressed in mouse and human leukemia cell lines and in leukemic cells from patients were preferentially expressed in various normal tissues including testis, brain, kidney, lung, liver and others (Lotem et al, 2005). In collaboration with Eytan Domany and Jacob-Bock Axelsen we have now analyzed gene expression in different normal human tissues and different types of solid cancers derived from these tissues. The cancers analyzed include brain (astrocytoma and glioblastoma),

breast, colon, endometrium, kidney, liver, lung, ovary, prostate, skin and thyroid cancers. Comparing gene expression in each normal tissue to 12 other normal tissues, we identified 4917 tissue-selective genes that were selectively expressed in different normal tissues. We also identified 2929 genes that are overexpressed at least 4-fold in the cancers compared to the normal tissue from which these cancers were derived (Fig. 1).

The overlap between these two gene groups identified 1340 tissue-selective genes that are overexpressed in cancers (Table 1).

Different types of cancers, including different brain cancers arising from the same lineage, showed differences in the tissue-selective genes they overexpressed. All types of cancer

overexpressed genes that are selectively expressed in normal tissues different from the tissue in which the cancer originated. Melanomas overexpressed the highest number of brain-selective genes and this may contribute to melanoma metastasis to the brain. Of all the genes with tissue-selective expression, those selectively expressed in testis showed the highest frequency of



**Fig. 1.** Overexpressed probe sets (PS) in different human solid cancers. The expression level of all PS in all samples of different types of human solid cancers were compared to the expression level in all samples of the normal tissues in which these cancers originated. Those PS whose expression level in a given type of cancer was at least 4-fold higher than in the corresponding normal tissue were scored as overexpressed.

Overexpressed PS in cancers*	Number of tissue-selective PS*													
	Blood (624)	Brain (634)	Breast (313)	Colon (244)	Endomet. (162)	Kidney (449)	Liver (578)	Lung (878)	Ovary (106)	Prostate (514)	Skin (210)	Testis (272)	Thyroid (424)	
Brain (Astrocytoma)	(575)	42	<b>5</b>	22	8	20	10	31	89	13	87	15	23	32
(Glioblastoma)	(195)	18	<b>6</b>	6	6	19	4	18	26	8	28	10	8	7
Breast	(90)	4	0	<b>0</b>	6	7	3	4	1	2	2	0	17	2
Colon	(89)	6	2	17	<b>1</b>	20	3	6	14	3	30	9	0	3
Endomet.	(361)	17	16	26	15	<b>0</b>	13	19	91	4	46	13	11	22
Kidney	(633)	69	26	25	12	30	<b>2</b>	52	134	7	73	19	10	39
Liver	(637)	34	20	48	48	47	16	<b>0</b>	71	23	81	36	19	25
Lung	(465)	9	13	40	55	20	20	28	<b>0</b>	6	38	50	21	14
Ovary	(149)	3	0	6	13	5	7	1	7	<b>0</b>	5	4	16	6
Prostate	(275)	12	7	12	13	3	10	14	46	2	<b>2</b>	5	0	9
Skin (Melanoma)	(728)	17	45	14	2	9	7	10	31	5	5	<b>3</b>	11	7
Thyroid	(35)	2	5	2	0	1	0	6	6	1	2	2	1	<b>0</b>

**Table 1.** \*The number of tissue-selective PS, and the number of PS overexpressed in different human solid cancers are outlined in red and blue letters in parentheses, respectively. The values outlined in bold pink letters are the numbers of cancer overexpressed PS whose expression profile in normal tissues is selective for the tissue in which the cancers originated. The values in plain letters are the number of cancer overexpressed PS whose expression profile in normal tissues is selective for tissues that are different from the tissue in which the cancers originated. Endomet., endometrium.

genes that are overexpressed in at least 2 types of cancer. However, colon and prostate cancers did not overexpress any testis-selective gene. Nearly all the genes with tissue-selective expression that are overexpressed in cancers showed selective expression in tissues different from the cancers' tissue of origin. Cancers aberrantly expressing such genes may acquire phenotypic alterations that contribute to cancer cell viability, growth and metastasis.

#### Selected publications

Lotem, J., Netanel, D., Domany, E., and Sachs, L. (2005) Human cancers over express genes that are specific to a variety of normal human tissues. Proc. Natl. Acad. Sci. USA., 102, 18556-18561.

Lotem J., and Sachs, L. (2006) Epigenetics and the plasticity of differentiation in normal and

cancer stem cells. Oncogene, 25, 7663-7672.

Axelsen, J-B., Lotem, J., Sachs, L., and Domany, E. (2007) Genes overexpressed in different human solid cancers exhibit different tissue-specific expression profiles. Proc. Natl. Acad. Sci. USA., 104, 13122-13127.

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