

Correction

Correction: Human fetal neuroblast and neuroblastoma transcriptome analysis confirms neuroblast origin and highlights neuroblastoma candidate genes

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We wish to report some corrections to our study [1], none of which alters the interpretation of the data or the conclusions drawn. After publication, we noticed that one of the microarray hybridizations (on sample NB11) was performed on the same patient's material as another hybridization (sample NB4; see Table 1; a corrected version of Table 5 [1]). As this error leads to an incorrect subclassification of the patients into the 'favourable' and 'unfavourable' neuroblastoma subgroups, we would like to exclude this data point from the differential expression analysis of favorable versus unfavorable neuroblastoma given under the heading 'Differential expression analysis of favorable and unfavorable neuroblastoma' in the Results section of [1]. Careful reanalysis after exclusion of NB11 did not lead to important changes in the generated gene lists and conclusions; the changes are given in the corrected paragraph and Table 2 (a corrected version of Table 4 [1]), and the Additional data files 1 and 2 (corrected versions of Additional data files 2 and 3 [1]) available online with this article.

We also noticed that sample NB1 is stage 1 instead of stage 4S and that sample NB2 was not localized to the adrenals (see Table 1).

Results

Differential expression analysis of favorable and unfavorable neuroblastoma

So far, most published microarray studies on neuroblastomas mainly compared favorable with unfavorable neuroblastomas in order to identify prognostic markers or pathways that are involved in these clearly different neuroblastoma tumor types. In order to add value to such an analysis, we contrasted similar differentially expressed gene lists with the normal neuroblast expression profile (Additional data file 1). In a first step, we compared the differentially expressed genes between these two tumor types with published prognostic gene lists. We found that 23 of the 193 genes on our list were previously reported, including the well established markers *MYCN*, *NTRK1*, and *CD44* (see NBGS analysis in Additional data file 2). This overlap demonstrates the validity of the selected neuroblastoma panel and their expression profile. Subsequently, we looked for the corresponding gene expression levels of the differentially expressed genes in the normal counterpart cells, aiming to select neuroblastoma candidate genes. Of the 100 genes that are more highly expressed in favorable tumors (compared to unfavorable) 41 also have a significant differential expression (either higher or lower)

Table 1**Clinical and genetic data of carefully selected neuroblastoma samples that were included in this study**

Sample number	Lab number	% Tumor cells	Stage	MYCN amp	Ploidy	Adrenal localization	Age	Dead/alive	Overall survival (months)	Type
NB1	98T33	95	I	No	Tri	Yes	< 1 year	Alive	76.9	Favorable
NB2	99T84	90	I	No	Tri	No	< 1 year	Alive	71.8	Favorable
NB3	96T82	90	I	No	Tri	Yes	< 1 year	Alive	115.5	Favorable
NB4	99T129	90	I	No	Tri	Yes	< 1 year	Alive	71.7	Favorable
NB5	01T28	90	4	Yes	Di	Yes	> 1 year	Dead	5.6	Unfavorable
NB6	03T304	100	3*	No	Di	Abdominal	> 1 year	Alive	12.0	Unfavorable
NB7	03T236	90	4	No	ND	Yes	> 5 year	Dead	19.4	Unfavorable
NB8	00T54	70	I	No	Tri	Yes	< 1 year	Alive	62.6	Favorable
NB9	00T35	>95	4	Yes	Di	Yes	< 1 year	Dead	13.7	Unfavorable
NB10	99T125	80	3	No	Di	Yes	> 5 year	Alive	79.3	Unfavorable
NB11 = NB4	99T129	90	I	No	Tri	Yes	< 1 year	Alive	71.7	Favorable
NB12	02T192	100	4	Yes	Di	Abdominal	> 5 year	Dead	16.2	Unfavorable
NB13	D031	>95	4	No	Di	Abdominal	> 1 year	Dead	64.8	Unfavorable
NB14	E002	>80	4	No	ND	Abdominal	> 1 year	Alive	65.7	Unfavorable
NB15	E037	>80	4	No	ND	Abdominal	> 1 year	Alive	45.3	Unfavorable
NB16	E044	>80	4	No	ND	Yes	< 1 year	Alive	37.0	Unfavorable
NB17	E121	>80	4	Yes	ND	Abdominal	> 1 year	Dead	78.4	Unfavorable
NB18	04T121	60	3	Yes	Di	Yes	> 1 year	Dead	6	Unfavorable

Samples were subdivided into favorable or unfavorable type based on *MYCN* amplification, ploidy and age at diagnosis. *Neuroblastoma or nodular ganglioneuroblastoma. ND, not determined or unknown.

compared to neuroblasts, whereas 43 of the 93 genes that are more highly expressed in unfavorable tumors exhibit differential expression compared to the neuroblasts (Table 2).

From this analysis, a few putative positional tumor suppressor candidates emerge: *CDC42* on 1p36, *CACNA2D3* on 3p21 and *DLK1* on 14q. The latter two genes are of particular interest because they are highly expressed in neuroblasts and favorable neuroblastomas and their expression is significantly lower in unfavorable neuroblastomas. Among the genes that are more highly expressed in unfavorable neuroblastomas than in favorable ones and neuroblasts, the proven oncogenic transcription factor *MYCN* emerges (and putative downstream genes *KIFAP3*, *OPHN1*, *RGS7*, *ASCL1*, *ODC1*, *TWIST1* and *TYMS*, according to NBGS), as well as several other genes that have been identified or studied in the context of neuroblastoma such as *ALK* and *PRAME*, and positional candidates on 17q including *BIRC5* and *RNU2*.

Additional data files

Additional data files 1 and 2 containing the corrected data available online with this article.

References

- De Preter K, Vandesompele J, Heimann P, Yigit N, Beckman S, Schramm A, Eggert A, Stallings RL, Benoit Y, Renard M, et al.: **Human fetal neuroblast and neuroblastoma transcriptome analysis confirms neuroblast origin and highlights neuroblastoma candidate genes.** *Genome Biol* 2006, **7**:R84.

(Continues on the next page)

Table 2

Genes that are differentially expressed in favorable vs unfavorable neuroblastoma

Favorable NB > unfavorable NB		NBGS	Favorable NB < unfavorable NB		NBGS
neuroblast < favorable NB			neuroblast < favorable NB, neuroblast < unfavorable NB		
<i>AKAP7</i>	6q	-	<i>FABP6</i>	5q	-
<i>ARL4C</i>	2q	-	<i>IGLJ3</i>	22q	1
<i>ASPN</i>	9q	-	<i>NEFL</i>	8p	-
<i>BCL2</i>	18q	1	<i>NPY</i>	7p	-
<i>CALB1</i>	8q	-	<hr/>		
<i>CAMK2B</i>	22q	2	neuroblast < unfavorable NB		
<i>CD24</i>	6q	-	<hr/>		
<i>CDC42</i>	1p	1	<i>ALK</i>	2p	-
<i>DDAH1</i>	1p	-	<i>ASCL1</i>	12q	1
<i>DNAPTP6</i>	2q	-	<i>BCL11A</i>	2p	-
<i>EPB41L3</i>	18p	1	<i>BIRC5</i>	17q	3
<i>FAM70A</i>	Xq	-	<i>C3</i>	19p	-
<i>KIFAP3</i>	1q	1	<i>CALCB</i>	11p	-
<i>OPHN1</i>	Xq	-	<i>CCL18</i>	17q	-
<i>PPAN</i>	19p	-	<i>CCL21</i>	9p	-
<i>PRKCB1</i>	16p	1	<i>CCNB1</i>	5q	1
<i>REEP1</i>	2p	-	<i>CD74</i>	5q	-
<i>RGS7</i>	1q	2	<i>CRH</i>	8q	-
<i>RNF11</i>	1p	-	<i>CSPG3</i>	19p	-
<i>SCD5</i>	4q	2	<i>CXCR4</i>	2q	2
<i>SERINC1</i>	6q	1	<i>DYNCL11</i>	7q	-
<i>ST6GALNAC5</i>	1p	-	<i>F12</i>	5q	-
<i>SV2C</i>	5q	-	<i>GFRA2</i>	8p	-
<hr/>			<i>IGHA1</i>	14q	2
neuroblast > favorable NB, neuroblast > unfavorable NB			<i>IGHG3</i>	14q	-
<hr/>			<i>IGHM</i>	14q	-
<i>CACNA2D3</i>	3p	-	<i>IGKC</i>	2p	1
<i>DLK1</i>	14q	2	<i>IGLC1</i>	22q	-
<i>HBG1</i>	11p	-	<i>IGLC2</i>	22q	-
<i>HBG2</i>	11p	-	<i>LMO3</i>	12p	1
<hr/>			<i>MMP9</i>	20q	1
neuroblast > unfavorable NB			<i>MYCN</i>	2p	9
<hr/>			<i>NEFH</i>	22q	-
<i>ALDH3A2</i>	17p	1	<i>ODC1</i>	2p	3
<i>DBH</i>	9q	1	<i>OGDHL</i>	10q	-
<i>DLC1</i>	8p	-	<i>P2RX5</i>	17p	-
<i>EYA1</i>	8q	-	<i>PRAME</i>	22q	1
<i>GCH1</i>	14q	1	<i>RPS4Y1</i>	Yp	1
<i>HBA1</i>	16p	-	<i>SERPINF1</i>	17p	-
<i>HBA2</i>	16p	-	<i>SIX3</i>	2p	-
<i>NTRK1</i>	1q	4	<i>SST</i>	3q	1
<i>PTPRD</i>	9p	-	<i>TNFRSF10B</i>	8p	2
<i>PTPRK</i>	6q	-	<i>TWIST1</i>	7p	1
<i>SFRP1</i>	8p	1	<i>XAGE1</i>	Xp	-
<i>SLC18A1</i>	8p	-	<hr/>		
<i>TFAP2B</i>	6p	-	neuroblast > favorable NB		
<i>TLN2</i>	15q	1	<hr/>		
<hr/>			<i>RNU2</i>	17q	-
<hr/>			neuroblast > favorable NB, neuroblast > unfavorable NB		
<hr/>			<hr/>		
<hr/>			<i>C11orf43</i>	11p	-

Genes that are differentially expressed compared with neuroblasts among the differentially expressed genes in favorable neuroblastoma (NB) vs unfavorable NB, with an indication of the number of neuroblastoma microarray studies in which these genes were found through NBGS analysis. NBGS, Neuroblastoma Gene Server.