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 versus 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 diagnostic 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)
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: \textit{CDC42} on 1p36, \textit{CACNA2D3} on 3p21 and \textit{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 \textit{MYCN} emerges (and putative downstream genes \textit{KIFAP3}, \textit{OPHN1}, \textit{RGS7}, \textit{ASCL1}, \textit{ODC1}, \textit{TWIST1} and \textit{TYMS}, according to NBGS), as well as several other genes that have been identified or studied in the context of neuroblastoma such as \textit{ALK} and \textit{PRAME}, and positional candidates on 17q including \textit{BIRC5} and \textit{RNU2}.

### Additional data files

Additional data files 1 and 2 containing the corrected data available online with this article.
### 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 < unfavorable NB, neuroblast < unfavorable NB |
| AKAP7 6q                      |      | FABP6 5q                     |      |
| ARL4C 2q                      |      | IGLJ3 22q                    | 1    |
| ASPN 9q                       |      | NEFL 8p                      |      |
| BCL2 18q 1                    |      | NPY 7p                       |      |
| CALB1 8q                      |      |                              |      |
| CAMK2B 22q 2                  |      |                              |      |
| CD24 6q                       |      |                              |      |
| CDC42 1p                      |      | ALK 2p                       |      |
| DDAH1 1p                      |      | ASCL1 12q                    | 1    |
| DMAPT6 2q                     |      | BCL11A 2p                    |      |
| EPB41L3 18p 1                 |      | BIRC5 17q                    | 3    |
| FAM70A Xq                     |      | C3 19q                       |      |
| KIFAP3 1q 1                   |      | CALCB 11p                    |      |
| OPHN1 Xq                     |      | CCL18 17q                    |      |
| PPAN 19p                      |      | CCL2 9p                      |      |
| PRKCB1 16p 1                  |      | CCNB1 5q                     | 1    |
| REPI 2p                       |      | CD74 5q                      |      |
| RGS7 1q 2                    |      | CRH 8q                       |      |
| RNF11 1p                      |      | CSPG3 19p                    |      |
| SCD5 4q 2                    |      | CSCR4 2q                     | 2    |
| SERINC1 6q 1                  |      | DYNC1C1 7q                   |      |
| ST6GALNAC5 1p                 |      |                              |      |
| SV2C 5q                       |      |                              |      |
| neuroblast > favorable NB, neuroblast > unfavorable NB |
| CACNA2D3 3p                   |      | IGKC 2p                      | 1    |
| DLK1 14q 2                    |      | IGLC1 22q                    |      |
| HBG1 11p                      |      | IGLC2 22q                    |      |
| HBG2 11p                      |      | LMO3 12p                     | 1    |
| neuroblast > unfavorable NB   |      | MMP9 20q                     | 1    |
| MLYCN 2p 9                    |      | NEFH 22q                     |      |
| ALDH3A2 17p 1                 |      | ODC1 2p 3                    |      |
| DBH 9q 1                      |      | OGDML 10q                    |      |
| DLC1 8p                       |      | PRKX 17p                     |      |
| EYA1 8q 1                     |      | PRAME 22q                    | 1    |
| GCH1 14q 1                    |      | RPS4Y1 1p                    | 1    |
| HBA1 16p                      |      | SERPINF1 17p                 |      |
| HBA2 16p                      |      | SIX3 2p                      |      |
| NTRK1 1q 4                    |      | SST 3q                       | 1    |
| PTPRD 9p                      |      | TNSFR5F10B 8p 2              |      |
| PTPRK 6q                      |      | TWIST1 7p                    | 1    |
| SRF1 8p 1                     |      | XAGE1 Xp                     | -    |
| SLIC1BA1 8p                   |      |                              |      |
| TFAP2B 6p                     |      |                              |      |
| TNL2 15q 1                    |      |                              |      |
| neuroblast > favorable NB     |      |                              |      |
| RNU2 17q                      |      |                              |      |
| neuroblast > favorable NB, neuroblast > unfavorable NB |
| C1orf43 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.