Supplementary online material

The Effect of Translocation-Induced Nuclear Re-organization on Gene Expression

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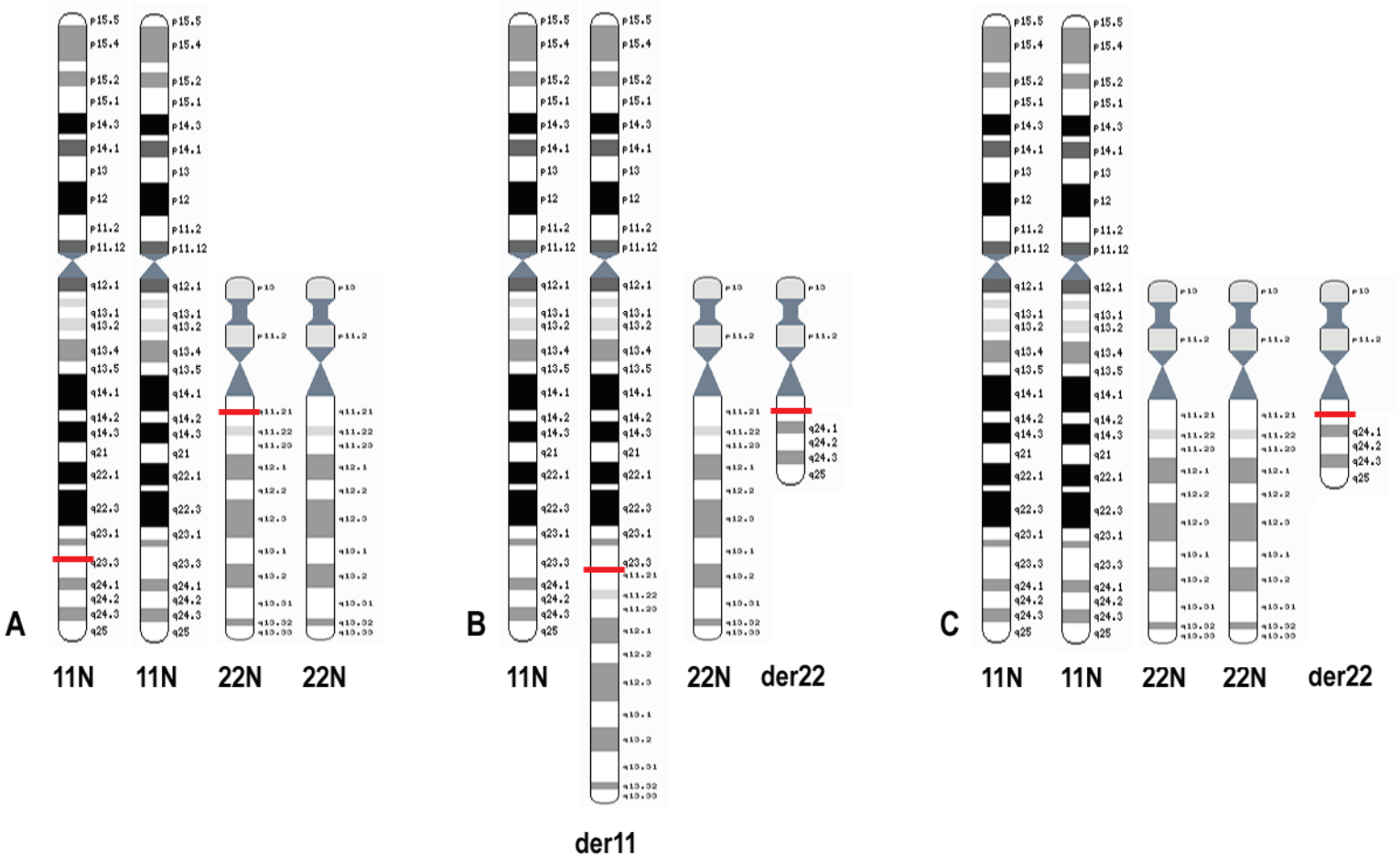
Supplementary Figure S1: Partial ideograms of the translocation chromosomes

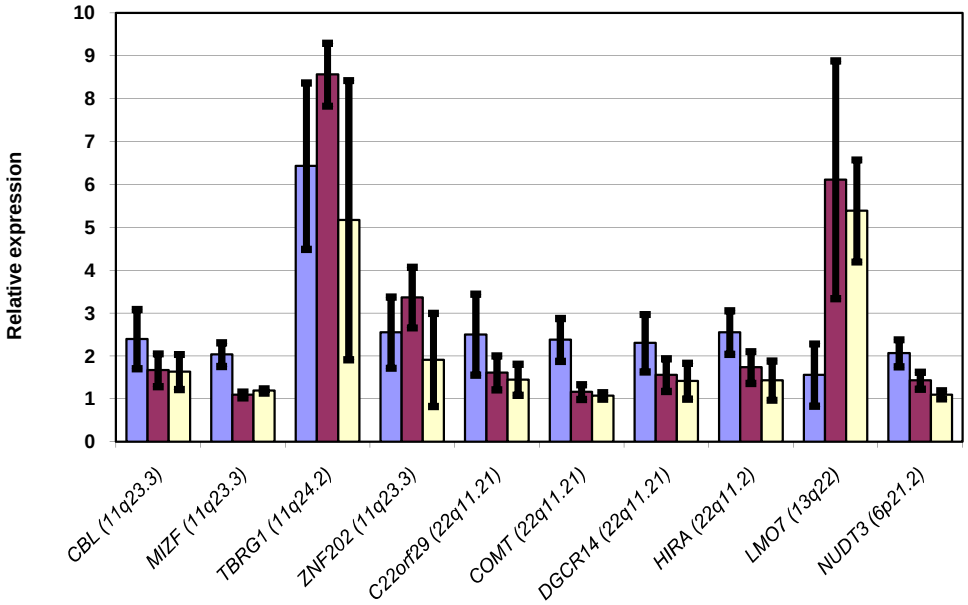
Partial ideograms of chromosomes 11 and 22 in a normal individual showing the two copies of each chromosome **(A)**, a balanced t(11;22)(q23;q11) translocation carrier **(B)**, showing the normal 11 (11N), the normal 22 (22N), the derivative 11 (der11) and the derivative 22 (der22) chromosomes and an Emanuel syndrome patient partially trisomic for chromosomes 11 and 22 with two normal chromosome 11s, two normal chromosome 22s and a derivative 22 (der22) **(C)**. Red lines mark the location of the breakpoints of the translocation.

Supplementary Figure S1



Supplementary Figure S2: Relative expression levels measured by quantitative PCR

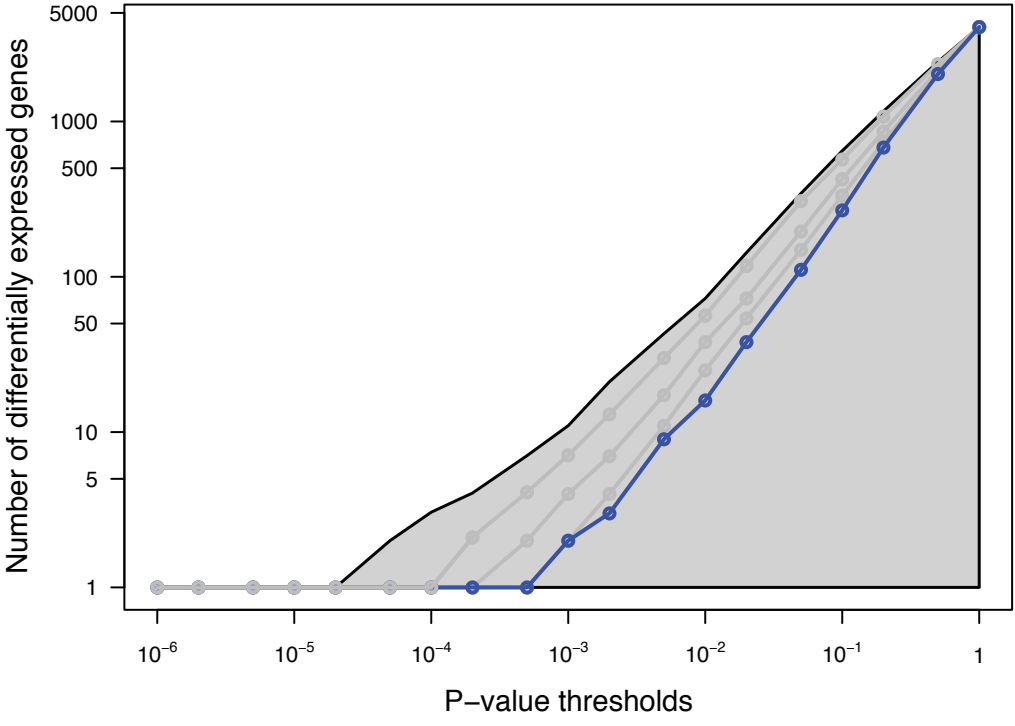
Averaged normalized relative expression levels of genes measured by quantitative PCR in cell lines from Emanuel syndrome patients (purple; average of n=4 different cell lines), t(11;22) carriers (burgundy; n=5) and controls (yellow; n=5). These genes were shown to present modified expression in Emanuel syndrome patients cells by expression arrays.


Relative expression
10
9
8
7
6
5
4
3
2
1
0
CBL (11q23.3)
MIZF (11q23.3)
TBRG1 (11q24.2)
ZNF202 (11q23.3)
C22orf29 (22q11.21)
COMT (22q11.21)
DGCR14 (22q11.21)
HIRA (22q11.2)
LMO7 (13q22)
NUDT3 (6p21.2)

Supplementary Figure S3: Numbers of differentially expressed transcripts between male and female individuals

Graph showing the number of differentially expressed transcripts between the male and female cohorts (blue line) identified with variable threshold values and mapping on the autosomal chromosomes. The gray lines and shaded area represent the 50%, 70%, 90% and 95% of the permutation distribution obtained by performing 1000 permutations (6 vs. 16; see the Results and Methods sections for details).

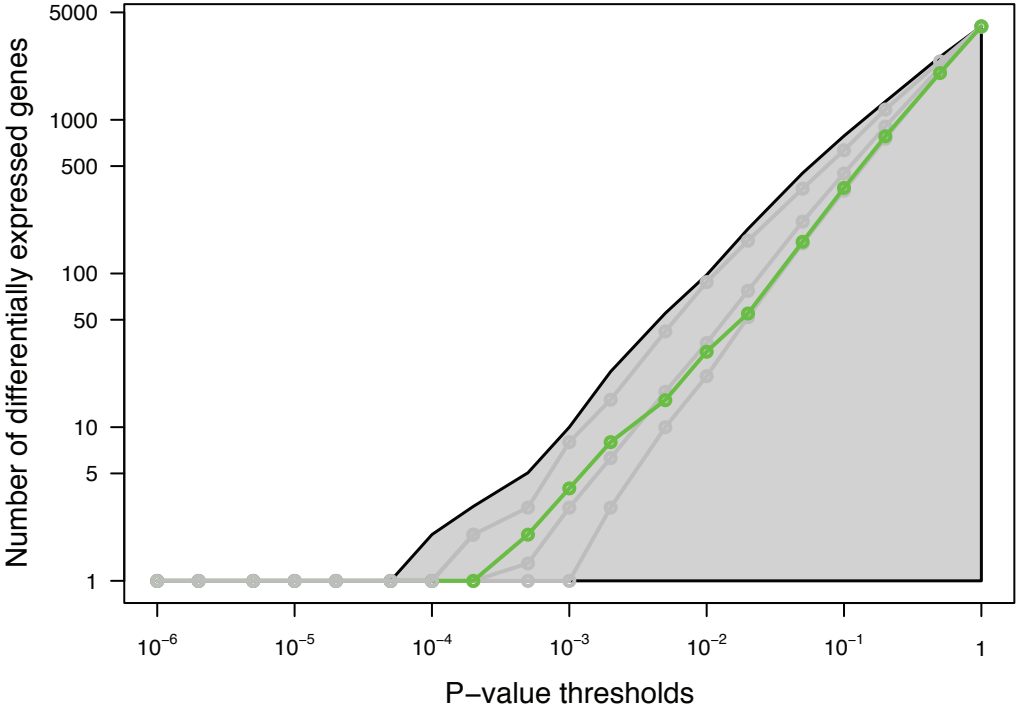
Supplementary Figure S3



Supplementary Figure S4: Numbers of differentially expressed transcripts between young and old individuals

Graph showing the number of differentially expressed transcripts between the male and female cohorts (green line) identified with variable threshold values and mapping on the autosomal chromosomes. The gray lines and shaded area represent the 50%, 70%, 90% and 95% of the permutation distribution obtained by performing 1000 permutations (9 vs. 13; see the Results and Methods sections for details).

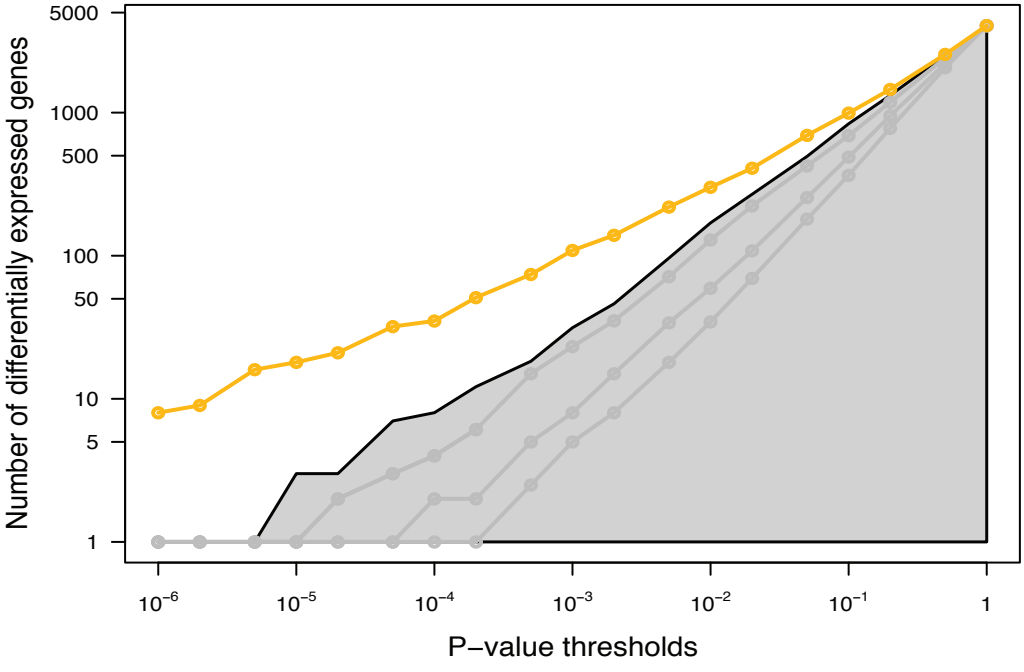
Supplementary Figure S4



Supplementary Figure S5: Numbers of differentially expressed transcripts between unbalanced and full-genome complement individuals

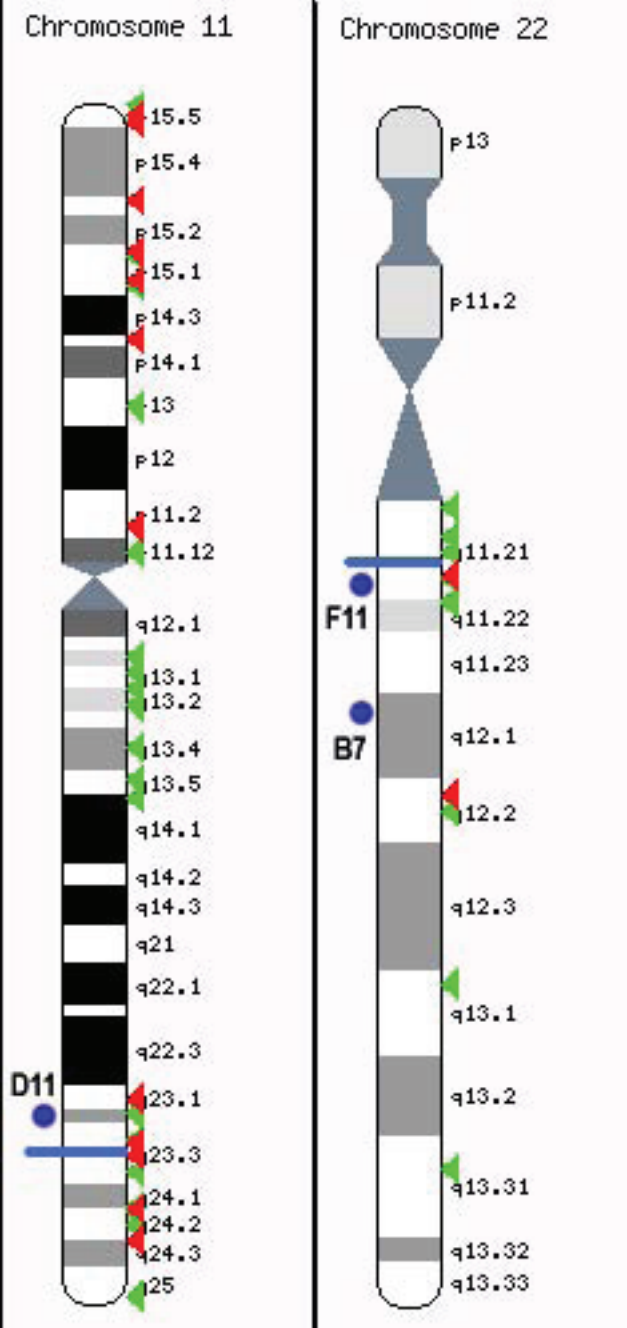
Graph showing the number of differentially expressed transcripts between unbalanced (Emanuel syndrome patients, with partial trisomy 11 and 22) versus full-genome complement cohorts (orange line) identified with variable threshold values and mapping on the autosomal chromosomes. The gray lines and shaded area represent the 50%, 70%, 90% and 95% of the permutation distribution obtained by performing 1000 permutations (4 vs. 22; see the Results and Methods sections for details).

Supplementary Figure S5



Supplementary Figure S6: Mapping of t(11;22) differentially expressed genes mapping on HSA11 and HSA22.

Ensembl Karyoview partial ideograms showing the chromosomal location of the 50 top differentially expressed genes between carriers of the balanced t(11;22) translocation and controls that map either to HSA11 (left panel) or to HSA22 (right panel). The blue lines indicate the translocation breakpoints. Green arrowheads mark the genes showing an increase in expression in cell lines from translocation carriers, whilst red arrowheads depict those showing a decrease. A complete list of these genes and their rankings is presented in Table S5. The mapping of the three chromosome HSA11 or HSA22 genes for which nuclear positioning was assessed by FISH (see text for details) are marked by a blue disk (the fourth, D5, is on chromosome 9q21.32 and is not shown).


Chromosome 11
p15.5
p15.4
p15.2
p15.1
p14.3
p14.1
p13
p12
p11.2
q11.12
q12.1
q13.1
q13.2
q13.4
q13.5
q14.1
q14.2
q14.3
q21
q22.1
q22.3
D11
q23.1
q23.3
q24.1
q24.2
q24.3
q25
Chromosome 22
p13
p11.2
q11.21
F11
q11.22
q11.23
B7
q12.1
q12.2
q12.3
q13.1
q13.2
q13.31
q13.32
q13.33

Supplementary Table S1: List of lymphoblastoid cell lines

Table S1: List of Lymphoblastoid cell lines

Cell line	Karyotype	Sex	Age (years)	Source	Cohort
FY1197	46,XX,t(11;22)(q23;q11)pat	F	22	ECACC	balanced
GM06229	46,XX,t(11;22)(q23;q11)	F	23	Coriell	balanced
GM06275	46,XX,t(11;22)(q23;q11)	F	29	Coriell	balanced
DD1990	46,XX,t(11;22)(q23;q11)	F	38	ECACC	balanced
25/93E	46,XX,t(11;22)(q23;q11)	F	66	Elisabeth Blennow, Karolinska Institute	balanced
27/93E	46,XX,t(11;22)(q23;q11)	F	50	Elisabeth Blennow, Karolinska Institute	balanced
65/92E	46,XX,t(11;22)(q23;q11)	F	49	Elisabeth Blennow, Karolinska Institute	balanced
CC0210	46,XY,t(11;22)(q23;q11)pat	M	17	ECACC	balanced
FY1199	46,XY,t(11;22)(q23;q11)	M	60	ECACC	balanced
GM06228	47,XX,+der(22)t(11;22)(q23;q11)	F	9 months	Coriell	unbalanced
DD1618	47,XX,+der(22)t(11;22)(q23;q11)	F	31	ECACC	unbalanced
BO2188	47,XY,+der(22)t(11;22)(q23;q11)	M	4 days	ECACC	unbalanced
GM14258	47,XY,+der(22)t(11;22)(q23;q11)	M	14	Coriell	unbalanced
GM12139	Control (46,XX)	F	17	Corriel	control
GM07053	Control (46,XX)	F	24	Corriel	control
GM12151	Control (46,XX)	F	26	Corriel	control
GM07014	Control (46,XX)	F	39	Corriel	control
GM07002	Control (46,XX)	F	63	Corriel	control
GM10863	Control (46,XX)	F	43	Corriel	control
GM06991	Control (46,XX)	F	42	Corriel	control
GM07353	Control (46,XY)	M	20	Corriel	control
GM07017	Control (46,XY)	M	61	Corriel	control
GM13072	Control (46,XX)	F	4	Corriel	control
GM11983	Control (46,XX)	F	29	Corriel	control
GM11878	Control (46,XY)	M	6	Corriel	control
GM07535	Control (46,XY)	M	15	Corriel	control

Supplementary Table S2: Mapping of top-25 transcripts differentially expressed between Emanuel syndrome patients and controls

Table showing the proportion of transcripts mapping to different chromosomes, as well as the expected and observed number of transcripts within the top 25 differentially expressed genes between Emanuel patients (unbalanced) and controls that map to those chromosomes.

Table S2: Mapping of the top-25 transcripts differentially expressed between Emanuel syndrome patients and controls

Chromosome	Nb transcripts	Prop.	Expected	Found	Prop.	*P* value
HSA1	4572	8.36	2.09	1	4	0.72
HSA11	2574	4.71	1.18	5	20	0.01
HSA21	599	1.1	0.27	0	0	1
HSA22	1107	2.02	0.51	5	20	0.00029

Supplementary Table S3: Genes and quantitative PCR assays

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Gene	Accession nb.	category/mapping	Fwd. primer ID	Fwd. Primer sequence	Rev. primer ID	Rev. Primer sequence
CBL	NM_005188.2	11q23.3	CBL_F	CACCACCACCACCACCAC	CBL_R	CAGCTTTGGGTTCTGACACA
ZNF202	NM_003455.2	11q23.3	ZNF202_F	GCGTCCACACCAGGAAGA	ZNF202_R	TCTCCAGAGCTCCTCTCTGC
HINFP	NM_198971.1	11q23.3	MIZF_F	GCTACCACACCAAGCTGAAA	MIZF_R	CAGTGCTCCCACAGACACA
TBRG1	NM_032811.2	11q24.2	TBRG1_F	TTCCAAGACAGACACGGAAG	TBRG1_R	AATCGGGCCTCTAGGAATCT
LMO7	NM_005358.5	13q22	LMO7_F	TCGGTGGTTCCTGATCTTC	LMO7_R	CAGTAGGCGGTCCTGCTC
HIRA	NM_003325	22q11.2	HIRA_F	CTGGGTCCGGTTCACTACTC	HIRA_R	CCTGACACTCGGTGAAGAGG
DGCR14	NM_022719.2	22q11.21	DGCR14_F	ACTGGAGTGGTGGGCAAC	DGCR14_R	GTAGCGGCTCAGGAAGACAT
COMT	NM_000754.3	22q11.21	COMT_F	AGAAGGAGTGGGCCATGA	COMT_R	GCACAGCTGAGTAGCCACAG
C22orf29	NM_024627	22q11.21	C22orf29_F	GGAGCAGAAGAGCACAGCTA	C22orf29_R	GGTACCCAGCAGAAGTCCAC
NUDT3	NM_006703	6p21.2	NUDT3_F	AGCTCAAGTCGAACCAGACC	NUDT3_R	ATGGCGACTACTGCTCACG
GusB	NM_000181	normalization	GusB_F	CCTGACTGACACCTCCAAGTATCCCAAGG	GusB_R	AGTCAAAATATGTGTTCTGGACAAAGTAA
DHSA	NM_004168.2	normalization	DHSA_F	CCTAAAGCACCTGAAGACGTTCGACCG	DHSA_R	AGGTCCGTGTTCCAGACCATT
TBP	NM_003194	normalization	TBP_F	CCGCAGCAAACCGCTTGGGA	TBP_R	CGTGGCTCTCTTATCCTCATGA

Supplementary Table S4: Mapping of top-25 transcripts differentially expressed between t(11;22) carriers and controls

Table showing the proportion of transcripts mapping to different chromosomes, as well as the expected and observed number of transcripts within the top 25 differentially expressed genes between carriers of the balanced t(11;22) translocation and controls that map to those chromosomes.

Table S4: Mapping of top-25 transcripts differentially expressed between t(11;22) carriers and controls

Chromosome	Nb transcripts	Prop.	Expected	Found	Prop.	*P* value
HSA1	4572	8.36	2.09	3	12	0.47
HSA11	2574	4.71	1.18	4	16	0.04
HSA21	599	1.1	0.27	0	0	1
HSA22	1107	2.02	0.51	0	0	1

Supplementary Table S5: List of genes and differentially expressed between t(11;22) carriers and controls and mapping to HSA11 or HSA22

Table listing the top-50 most differentially expressed genes between carriers of the balanced t(11;22) translocation (B) and controls (C) that map to HSA11 or HSA22, as well as their ranking in the complete list of differentially expressed genes.

Rank in Top 11/22 list	Affymetrix ID	Gene Symbol	Chromosomal Location	Mapping	Rank in C vs B list
1	231837_at	*USP28*	chr11q23	HSA11 to der 11	**8**
2	241610_x_at	*PACS1*	chr11q13.1	HSA11 to der 11	**9**
3	230306_at	*VPS26B*	chr11q25	HSA11 to der22	**20**
4	210102_at	*VWA5A*	chr11q23	HSA11 to der22	**16**
5	1552678_a_at	*USP28*	chr11q23	HSA11 to der 11	**29**
6	1554360_at	*FCHSD2*	chr11q13.4	HSA11 to der 11	**70**
7	244418_at	*RTN3*	chr11q13	HSA11 to der 11	**78**
8	212516_at	*ARAP1*	chr11q13.4	HSA11 to der 11	**92**
9	235010_at	*LOC729013*	chr11p15.3	HSA11 to der 11	**105**
10	226285_at	*CAPRIN1*	chr11p13	HSA11 to der 11	**126**
11	222599_s_at	*NAV2*	chr11p15.1	HSA11 to der 11	**159**
12	216171_at	*EEF1G*	chr11q12.3	HSA11 to der 11	**188**
13	222807_at	*C11orf30*	chr11q13.5	HSA11 to der 11	**195**
14	242106_at	*MAPK1*	chr22q11.2	HSA22 to der 11	**150**
15	215241_at	*ANO3*	chr11p14.2	HSA11 to der 11	**355**
16	228142_at	*UQCR10*	chr22cen-q12.3	HSA22 to der 11	**308**
17	235865_at	*CELF1*	chr11p11	HSA11 to der 11	**264**
18	218114_at	*GGA1*	chr22q13.31	HSA22 to der 11	**335**
19	635_s_at	*PPP2R5B*	chr11q12-q13	HSA11 to der 11	**372**
20	220998_s_at	*UNC93B1*	chr11q13	HSA11 to der 11	**367**
21	207180_s_at	*HTATIP2*	chr11p15.1	HSA11 to der 11	**384**
22	217185_s_at	*ZNF259 / LOC442240*	chr11q23.3	HSA11 to der 11	**255**
23	212421_at	*C22orf9*	chr22q13.31	HSA22 to der 11	**269**
24	223172_s_at	*MTP18*	chr22q	HSA22 to der 11	**241**
25	221845_s_at	*CLPB*	chr11q13.4	HSA11 to der 11	**389**
26	227925_at	*LOC644563 / C6orf51 / FLJ39051*	chr11q24.2	HSA11 to der22	**295**
27	204156_at	*SIK3*	chr11q23.3	HSA11 to der22	**533**
28	208745_at	*ATP5L*	chr11q23.3	HSA11 to der22	**438**
29	208291_s_at	*TH*	chr11p15.5	HSA11 to der 11	**621**
30	229965_at	*PIK4CA*	chr22q11.21	HSA22 to der 11	**578**
31	200084_at	*C11orf58*	chr11p15.1	HSA11 to der 11	**557**
32	227086_at	*HIRA*	chr22q11.2	HSA22 to der 22	**615**
33	218327_s_at	*SNAP29*	chr22q11.21	HSA22 to der 11	**624**
34	214381_at	*LOC441601*	chr11p11.12	HSA11 to der 11	**597**
35	225744_at	*ZDHHC8*	chr22q11.21	HSA22 to der 22	**563**
36	1558613_at	*OAF*	chr11q23.3	HSA11 to der22	**535**
37	220470_at	*BET1L*	chr11p15.5	HSA11 to der 11	**519**

38	213897_s_at	*MRPL23*	chr11p15.5-p15.4	HSA11 to der 11	**502**
39	1566958_at	*GAB2*	chr11q14.1	HSA11 to der 11	**444**
40	1569022_a_at	*PIK3C2A*	chr11p15.5-p14	HSA11 to der 11	**426**
41	211725_s_at	*BID*	chr22q11.1	HSA22 to der 22	**600**
42	206580_s_at	*EFEMP2*	chr11q13	HSA11 to der 11	**499**
43	1566959_at	*GAB2*	chr11q14.1	HSA11 to der 11	**579**
44	212203_x_at	*IFITM3*	chr11p15.5	HSA11 to der 11	**634**
45	1562283_at	*MAPK1*	chr22q11.2	HSA22 to der 11	**657**
46	208810_at	*DNAJB6 / LOC387820*	chr11q24.2	HSA11 to der22	**679**
47	222268_x_at	*LOC649768 / MUC5B*	chr11p15.5	HSA11 to der 11	**825**
48	235062_at	*LOC120379*	chr11q23.1	HSA11 to der 11	**779**
49	1568939_at	*OR8B3*	chr11q24.2	HSA11 to der22	**904**
50	236059_at	*C11orf61*	chr11q24.2	HSA11 to der22	**1010**