Supplementary Methods

All analyses were carried out on human embryonic stem cells at the undifferentiated stage.

Human ES cell culture

SA01 (XY, passages 21-83, Cellartis AB, Sweden), H9 (XX, passages 34-76, WiCell Research Institue Madison, WI, USA), H1 (XY, passages 24-64, WiCell Research Institue Madison, WI, USA), VUB01[1] (XY, passages 80-150 AZ-VUB, Belgium) and VUB05-HD[1] (XY, passage 34-105, AZ-VUB, Belgium, derived from an embryo carrying a mutant huntingtin gene) embryonic stem cell lines have been cultured for variable number of passages. Manual dissection was systematically used to passage the cells rather than enzymatic methods. The hES cells were cultured in DMEM/F12 glutamax supplemented with 20% knockout serum replacement, 1 mM nonessential amino acids, 1% penicillin/streptomycin, 0.55 mM 2-mercaptoethanol and 5 ng/ml recombinant human FGF2 (all from Invitrogen, Cergy Pontoise, France). Cultures were fed daily and passaged every 5-7 days.

Assessment of copy number variation

Genomic DNA was isolated from hESC using the Wizard® Genomic DNA Purification Kit (Promega, Charbonnieres, France**)**. IntegraChip genome-wide BAC arrays of 5,245 BAC clones (526-kb median spacing) were hybridized with genomic DNA by the manufacturer, IntegraGen Company (Evry, France) as previously described [2]. Copy number analysis was performed with GenoCensus software (IntegraGen) which includes block Loess normalization. HumanHap300 Chip (Illumina Inc. San Diego, USA) containing 318,237 SNPs were hybridized with genomic DNA. Genotyping was performed by Integragen Company (Evry, France) as per the manufacturer's protocol (Illumina Inc.) using 750 ng of genomic DNA[3 4].

Fluorescence in situ hybridization

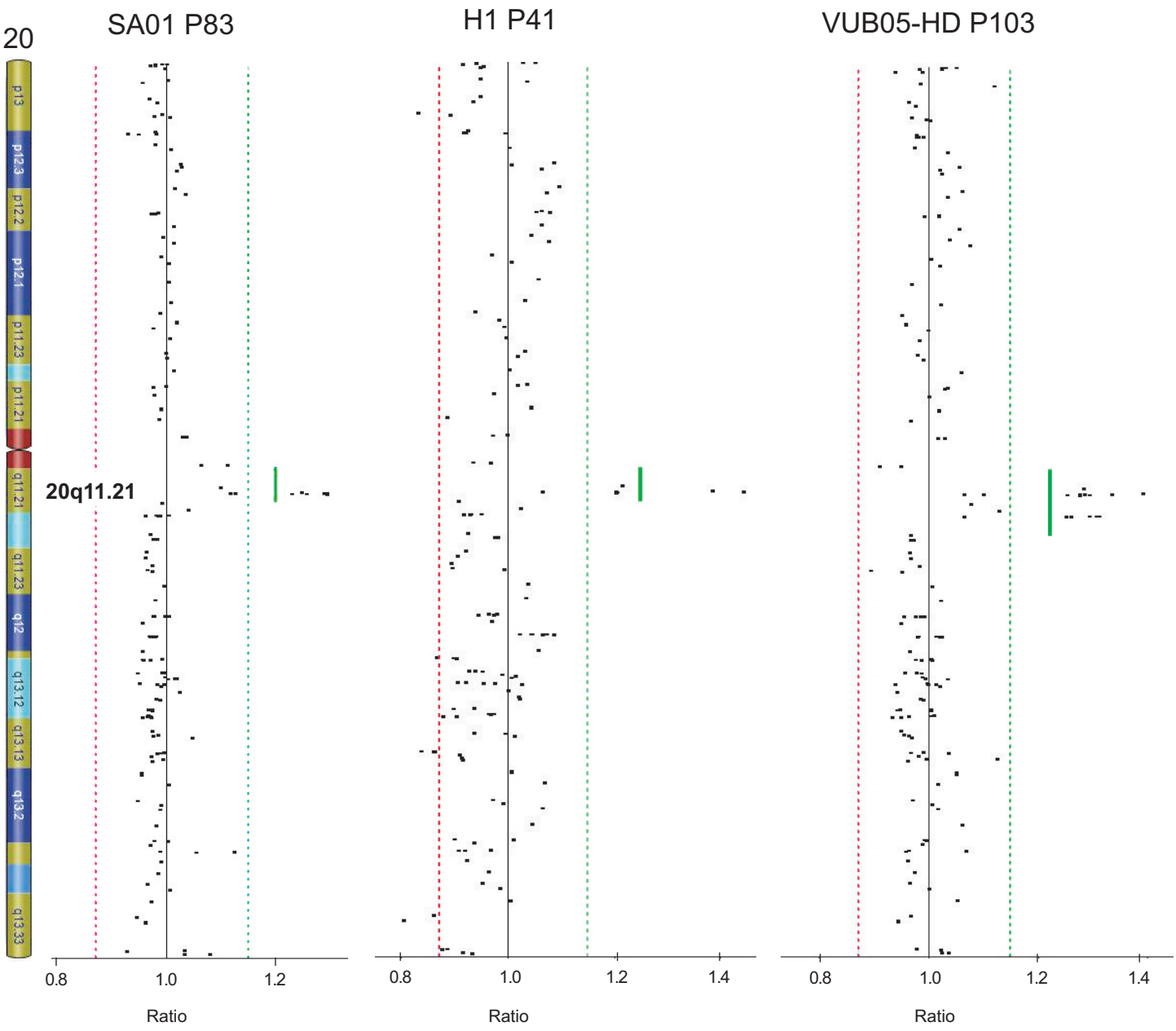
FISH analyses were performed on metaphase spreads and interphase nuclei from cultured embryonic stem cells. We used 3 BAC probes specific for 20q11.21 chromosomal region [RP5-836N17, RP5-857M17, RP5-1018D12]. BAC probes were nick-translated with fluorescein-12-dUTP or tetramethyl-rhodamine-6-dUTP (Roche, Meylan, France).

Supplementary table, figures legends

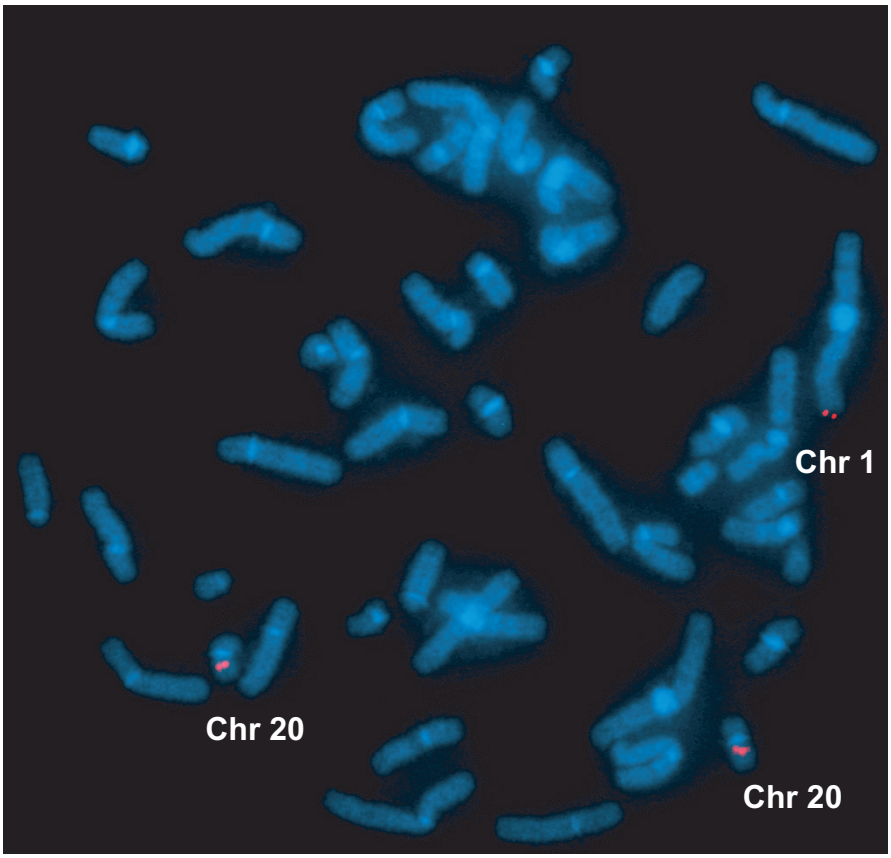
Supplementary Table 1:

FISH results using BACs specific of the 20q11.21 region in interphase nuclei in the different embryonic stem cells lines.

Line	Passage	2 signals	3 signals	number of cells analysed	% cells with 3 signals
SA01	P21	200	0	200	0.0%
SA01	P24	198	2	200	1.0%
SA01	P37	200	0	200	0.0%
SA01	P56	67	83	150	55.3%
VUB05-HD	P34	100	0	100	0.0%
VUB05-HD	P98	200	0	200	0.0%
VUB05-HD	P105	64	86	150	57.3%
H9	P53	200	0	200	0.0%
H9	P55	198	2	200	1.0%
H9	P76	113	37	150	24.7%
H1	P24	229	71	300	23.7%
H1	P64	159	141	300	47.0%
VUB01	P80	85	1	86	1.1%
VUB01	P126	199	1	200	0.5%



Supplementary Figure 1: Genomic amplification at chromosome 20. a-CGH analysis using IntegraChip genome-wide BAC arrays of 5,245 BAC clones (526-kb median spacing). (Left panel) SA01 at passage 83 shows 2.5 Mb amplification ranging from 28,205,000 to 30,711,000 (middle panel) H1 at passage 41 shows 2.4 Mb amplification ranging from 28,267,000 to 30,711,000 (right panel) VUB05-HD at passage 103 shows 4.6 Mb amplification ranging from 28,267,000 to 32,921,000 (genome build 36).



Supplementary Figure 2: Insertion in H1 cells: Ins(1;20)(p36.3 ;q11.21).FISH analysis on metaphase (H1 at passage 64) showing an insertion of the 20q11.21 region into the telomeric chromosomal region of the short arm of chromosome 1 (1p36.3)

References

1. Mateizel, I. et al. Derivation of human embryonic stem cell lines from embryos obtained after IVF and after PGD for monogenic disorders. *Hum Reprod* **21**, 503-511 (2006).
2. Struski, S. et al. Confirmation of a novel recurrent association: BCR-ABL t(9;22) and t(19;21). *Cancer Genet Cytogenet* **179**, 127-131 (2007).
3. Peiffer, D.A. et al. High-resolution genomic profiling of chromosomal aberrations using Infinium whole-genome genotyping. *Genome Res* **16**, 1136-1148 (2006).
4. Simon-Sanchez, J. et al. Genome-wide SNP assay reveals structural genomic variation, extended homozygosity and cell-line induced alterations in normal individuals. *Hum Mol Genet* **16**, 1-14 (2007).