Supplementary Table 1. Overview of the different transduction/transplantation groups

Experiment	Group	Cumulative MOI	Prestim	1.TD			Recovery	2.TD			Transplantation (cells per mouse)
				IG/ml	Cells/ml	MOI		IG/ml	Cells/ml	MOI	
A	**G1**	100	24h	$1x10^8$	$1x10^6$	MOI 100 (24h)	-	-	-	-	$0.5x10^6$
	G2	300		$1.5x10^8$	$1x10^6$	MOI 150 (24h)	-	$1.5x10^8$	$1x10^6$	MOI 150 (24h)	$0.6x10^6$
	XCGD-ctrl	-		-	-	-	-	-	-	-	$1x10^6$
	Wt healthy donor-ctrl	-		-	-	-	-	-	-	-	$0.9x10^6$
B	**G3**	200	36h	$2x10^8$	$2x10^6$	MOI 100 (12h)	12h	$2x10^8$	$2x10^6$	MOI 100 (12h)	$5x10^6$
	XCGD-ctrl	-		-	-	-	-	-	-	-	$5x10^6$
	Wt healthy donor-ctrl	-		-	-	-	-	-	-	-	$3x10^6$
C	**G4**	200	24h	$1x10^8$	$1x10^6$	100	-	$1x10^8$	$1x10^6$	100	0.4-1.0 x 10^6
	XCGD-ctrl	-		-	-	-		-	-	-	
	G5	200		$1x10^8$	$1x10^6$	100		$1x10^8$	$1x10^6$	100	
	XCGD-ctrl	-		-	-	-		-	-	-	

Supplementary Table 2. Transduction efficiencies, gp91phox expression and DHR activity after myeloid differentiation of transduced CD34$^+$ cells *in vitro*

Experiment	Group	%gp91+ d4	VCN 10d post TD	mean VCN 10d	%gp91+ of CD11b$^+$ d21-24	DHR+ of CD11b$^+$	mean DHR+	error
A	**G1**	nd	0.35	0.35	nd	42.6	45.6	2.7
						47.5		
						46.8		
	G2	nd	0.96	0.96	nd	49.9	51.3	1.8
						50.8		
						53.3		
	wt	nd	-	-	nd	93.9	93.7	0.3
						93.5		
	X-CGD	nd	-	-	nd	1.9	1.9	
B	**G3**	25.7	0.45	0.57	22.8	59.9	55.6	6.9
			0.53		24.2	49.2		
			0.37		23.2	60.5		
		34.4	0.54		24.5	61.5		
			0.39		25	47.1		
			1.14		25.5			
	wt	0.8	-	-	85.8	97	96.9	0.1
					82.4	96.8		
	X-CGD	0.1	-	-	0.8	0	0.1	0.1
					1	0.1		
C*	**G4**	52	1		19	19		
	X-CGD	10	0.01		5	1		
	G5	33	0.39		11	20		
	X-CGD	0.1	ND		2.4	0		

* In Exp. C the percentage of CD34 cells expressing the transgene was determined 3 days after transduction. Average vector copy number was determined 8 days post transduction for P1 and 13 days post transduction for P2.

Supplementary Table 3. Lineage distribution of human cells in engrafted animals.

Experiment A											
		engraftment	lineage distribution of hCD45$^+$ cells							% gp91$^+$ of hCD45$^+$ and	
			% of hCD45$^+$			% of human CD45$^+$ CD33$^+$ cells					
Tx-Group	Mouse Nr.	% hCD45$^+$	CD19$^+$	CD33$^+$	unknown	CD14$^+$ CD15$^-$	CD14$^+$CD15$^+$	CD14$^-$ CD15$^-$	CD14$^-$ CD15$^+$	CD19$^+$	CD33$^+$
G1	#1	24.8	34.0	22.8	43.2	19.4	23.7	34.0	22.8	15.0	37.9
	#2	21.5	33.1	28.4	38.5	14.8	23.7	33.1	28.4	13.9	29.3
	#3	6.0	27.2	22.8	50.0	14.9	35.1	27.2	22.8	3.8	22.1
	#4	7.8	26.8	14.2	59.0	27.0	31.9	26.8	14.2	16.3	43.8
	#5	23.1	29.9	20.8	49.3	25.5	23.8	29.9	20.8	21.8	45.9
	#6	34.8	30.1	15.1	54.8	26.4	28.4	30.1	15.1	21.7	46.9
G2	#7	12.8	41.4	25.7	32.9	12.1	20.8	41.4	25.7	6.1	49.3
	#8	1.8	42.4	20.3	37.3	16.6	20.7	42.4	20.3	3.8	48.7
	#9	2.8	36.0	26.4	37.6	14.9	22.7	36.0	26.4	8.5	26.4
	#10	18.1	32.1	16.4	51.5	22.3	29.2	32.1	16.4	22.9	70.0
	#11	9.1	36.2	15.5	48.3	22.6	25.7	36.2	15.5	18.3	49.3
	#12	8.3	33.1	13.6	53.3	27.3	26.0	33.1	13.6	11.3	32.4
X-CGD	#13	13.4	31.9	32.4	35.7	14.1	21.6	31.9	32.4	0.2	0.8
X-CGD	#14	41.2	28.6	14.3	57.1	30.0	27.1	28.6	14.3	0.1	1.1
Wt	#15	3.4	27.5	17.4	55.1	14.6	40.6	27.5	17.4	8.4	85.8
Wt	#16	9.4	41.1	15.0	43.9	12.5	31.3	41.1	15.0	5.5	71.6
Wt	#17	36.5	30.4	29.5	40.1	11.3	28.9	30.4	29.5	5.0	88.0
Wt	#18	45.6	29.4	16.0	54.6	22.6	32.0	29.4	16.0	4.7	81.5

Suppl. Table 3 cont.

Experiment B											
		engraft-ment	lineage distribution of hCD45^{+} cells							% gp91^{+} of hCD45^{+} and	
			% of hCD45^{+}			% of human CD45^{+} CD33^{+} cells					
Tx-Group	**Mouse Nr.**	**% hCD45^{+}**	**CD19^{+}**	**CD33^{+}**	**unknown**	**CD14^{+} CD15^{-}**	**CD14^{+}CD15^{+}**	**CD14^{-} CD15^{-}**	**CD14^{-} CD15^{+}**	**CD19^{+}**	**CD33^{+}**
	#19	57.8	85.9	5.3	8.8	13.5	14.5	25.8	46.2	10.1	48.5
G3	**#20**	0.1	-	-	-	-	-	-	-	-	-
	#21	62.1	86.6	5.8	7.6	15.2	15.9	24.9	43.9	20.2	55.3
	#22	Dead	-	-	-	-	-	-	-	-	-
	#23	67.2	87.1	3.6	9.3	12.9	15.5	26.9	44.6	12.1	48.4
	#24	56.7	88.8	3.8	7.4	16.6	12.5	29.6	41.3	7.5	45.6
	#25	64.5	90.3	3.3	6.4	12.8	14.1	26.0	47.0	16.6	57.0
	#26	54.6	84.9	3.8	11.3	12.5	11.6	26.6	49.3	11.4	44.9
X-CGD	**#27**	54.4	83.3	9.2	7.5	13.9	16.7	21.4	48.0	0.1	1.0
X-CGD	**#28**	37.1	87.8	4.2	8.0	10.8	31.8	16.3	41.1	0.4	1.9
Wt	**#29**	68.1	80.2	5.8	14.0	11.2	9.9	34.5	44.4	7.2	89.1
Wt	**#30**	40.7	81.1	5.4	13.5	6.1	20.4	25.9	47.6	4.8	92.6

Experiment C				
		engraft-ment	of hCD45	% gp91^{+} of hCD45^{+} and
Tx-Group	**Mouse Nr.**	**% hCD45^{+}**	**% CD13^{+}**	**CD13^{+}**
G4	#1	42.0	8.0	42.0
	#2	28.0	9	41
	#3	63.0	7.0	58.0
G5	#1	67.0	8.5	40.0
	#2	75.0	6.0	38.0
	#3	64.0	7.0	44.0
X-CGD (G4)		8.0	2.3	17.0
X-CGD (G5)		3.0	0.2	ND

Supplementary Table 4. Biopotency of G1XCGD-transduced myeloid cells after *in vitro* differentiation of hCD34+ cells obtained from the bone marrow of transplanted animals.

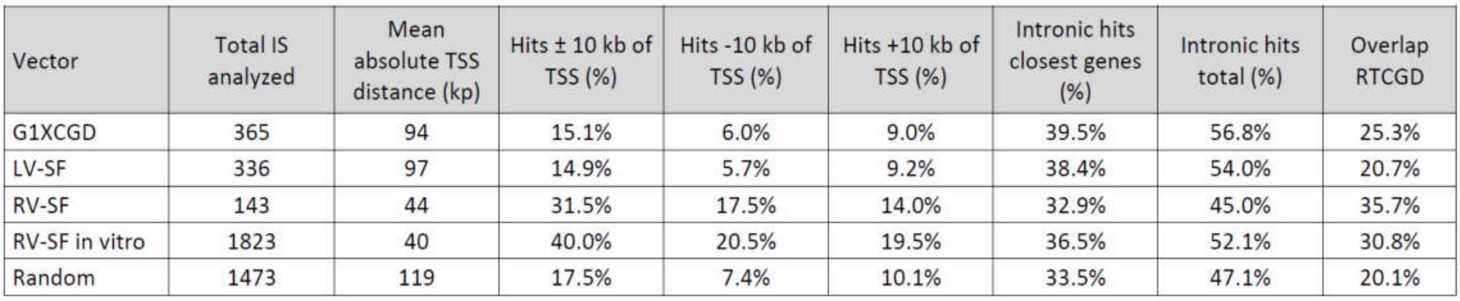
Experiment A													
		VCN in total human BM cells isolated from tpl. mice			VCN in hCD34+ cells after isolation from total hBM cells			% of gp91phox$^+$ and DHR$^+$ cells after *in vitro* differentiation of hCD34$^+$ cells purified from BM of tpl. mice					
Tx-Group	Mouse Nr.	VCN	mean VCN	error	VCN hCD34$^+$	Mean	error	% gp91$^+$ out of CD11b$^+$	mean % gp91$^+$	error	% DHR$^+$ out of CD11b$^+$	mean % DHR$^+$	error
G1	#1	0.62	0.56	0.145052	0.2794	0.33745	0.082095	15.9	16.0	0.1	26.5	27.6	1.6
	#2	0.38											
	#3	0.38											
	#4	0.69			0.3955			16.0			28.7		
	#5	0.58											
	#6	0.70											
G2	#7	1.46	1.69	0.427352	0.5583	0.55985	0.002192	10.2	16.6	9.1	32.2	38.2	8.5
	#8	1.42											
	#9	1.20											
	#10	2.22			0.5614			23.0			44.2		
	#11	2.20											
	#12	1.61											
X-CGD	#13							1.4	1.5	0.1	0.3	0.3	0.1
X-CGD	#14							1.5			0.2		
Wt	#15							84.5	85.3	1.1	88.5	90.8	3.3
Wt	#16												
Wt	#17							86			93.1		
Wt	#18												

Experiment B													
		VCN in total human BM cells isolated from tpl. mice			VCN in hCD34$^+$ cells after isolation from total hBM cells			% of gp91phox$^+$ and DHR$^+$ cells after *in vitro* differentiation of hCD34$^+$ cells purified from BM of tpl. mice					
Tx-Group	Mouse Nr.	VCN human BM cells	mean VCN hBM	error	VCN hCD34$^+$	Means	error	% gp91$^+$ out of CD11b$^+$	mean % gp91$^+$	error	% DHR$^+$ out of CD11b$^+$	mean % DHR$^+$	error
G3	#19	0.32	0.48	0.43	0.33	0.39	0.06	11.8	9.8	1.9	24.4	32.4	6.4
	#20	-						11.0			23.0		
	#21	0.26			0.47			8.2			39.2		
	#22	-						7.1			37.1		
	#23	0.15			0.36			9.2			33.3		
	#24	0.19						8.1			28.4		
	#25	1.39			0.41			12.4			35.0		
	#26	0.28						10.8			39.1		
X-CGD	#27							1.2	0.9	0.4	0.1	0.4	0.4
X-CGD	#28							0.6			0.7		
Wt	#29							61.0	57.2	5.4	93.7	95.5	2.5
Wt	#30							53.4			97.2		

Suppl. Table 4 cont.

Experiment C			
Tx-Group	**Mouse Nr.**	**% DHR$^+$ out of CD16$^+$**	**VCN**
G4	#1	19.0	0.2
	#2	42.0	1.1
	#3	46.0	1.0
G5	#1	24.0	0.4
	#2	16.0	0.1
	#3	7.0	0.1
X-CGD		2.0	

Supplementary Table 5



Vector	Total IS analyzed	Mean absolute TSS distance (kp)	Hits ± 10 kb of TSS (%)	Hits -10 kb of TSS (%)	Hits +10 kb of TSS (%)	Intronic hits closest genes (%)	Intronic hits total (%)	Overlap RTCGD
G1XCGD	365	94	15.1%	6.0%	9.0%	39.5%	56.8%	25.3%
LV-SF	336	97	14.9%	5.7%	9.2%	38.4%	54.0%	20.7%
RV-SF	143	44	31.5%	17.5%	14.0%	32.9%	45.0%	35.7%
RV-SF in vitro	1823	40	40.0%	20.5%	19.5%	36.5%	52.1%	30.8%
Random	1473	119	17.5%	7.4%	10.1%	33.5%	47.1%	20.1%

Supplementary Table 5. Insertion site distribution and cancer gene database overlaps. We show the number of insertion sites (IS) analyzed, the mean absolute distance of insertion relative to the TSS, the hits within 10 kb of the TSS (upstream and downstream), the percent of intronic hits regarding the gene with the closest TSS, the percent intronic hits relative to all IS (even if the TSS of another gene was closer) and the percent overlap in different cancer gene databases. The groups G1XCGD, LV-SF and RV-SF are compared to in vitro data of the mutagenic vector RV-SF or a random *in silico* control.