

## Review PeerJ Manuscript # 2134v1.

### List of grammatical and/or spelling corrections to be made

Page	Line #	Change:
1	16	reprogrammed human → reprogram human
1	22	barriers of → barriers to
2	28	iPSCs → iPSC
2	31	iPSCs → iPSC
2	34	appraised → appraise
2	52	write out full name of ESC, this is the first use of the term.
3	56	embryo → embryos
3	56	characteristics → characteristic
3	57	termed as pluripotency → termed pluripotency.
3	60	ESCs was fraught → ESCs <u>is</u> fraught
3	62	were → are
3	63	will be → are
3	63	will limit a broader → will limit broader
3	64	bypass → bypasses
3	65	serves → serve
3	66	delete: (ESCs)
3	66	issue → issues
3	78	discovery → discoveries
3	84	viral vectors → viral vector
4	87	includes → include
4	90	influences → influence
4	96	change it's → the
4	111	change "We now hand" → "We next hand"
4	112	which one → those that
4	112	for the study → for this study
5	121	see if → ensure
5	121	on the study which was → on the study objectives which are
5	125	are → were
5	132	embryo are → embryo were
5	138	induced → induce
5	139	fibroblast was → fibroblasts <b>were</b>
5	141	is to be → is
5	142	would be → are
5	143	in somatic → in normal somatic
5	143	and this cells are → which are
5	146	factors → factor
6	163	is → was
6	164	fibroblast → fibroblasts
6	165	levels → level
6	166	genes → gene expression
6	169	fibroblast → fibroblasts

6	172	iPSCs → iPSC
6	172	is → are
6	174	iPSCs → iPSC
6	178	cleared → overcome
6	178	iPSCs → iPSC
7	181	tumor → tumors
7	181	of c-Myc → of the c-Myc
7	186	iPSCs → iPSC
7	191	Yamanaka → Yamanaka's
7	192	group → groups
7	210	act → acts
8	215	fibroblast → fibroblasts
8	215	proved → suggest
8	217	delete "us to"
8	217	mechanism → mechanisms
8	218	delete "on how"
8	218	increase → increasing
8	223	inhibit → inhibits
8	223	thus has → thus having
8	224	delete Thus
8	226	IPSCS → IPSC
8	228	delete "increase"
8	233	modified → modify
8	236	promote → promotes
8	238	keratinocyte → keratinocytes
8	239	promote → promotes
8	240	MEFs → MEF
9	250	enhanced → enhance
9	250-251	OSKM traditional → traditional OSKM
9	251	miRNA → miRNAs
9	252	and the amount → and amount
9	252	nearest → near
9	253	an effective → a more effective
9	254	method → methods
9	266	fragment → fragments
9	268	session → section
9	271	was → were
9	272	IPSCS → IPSC
9	272	are efficient → are an efficient
10	274	iPSC is → iPSC are
10	276	transgenes → transgene
10	281	Compared with → Like
10	284	type → types
10	284	iPSCs → iPSC
10	284	involve → involved

10	286	sites → events
10	288	allow for the → allowed the
10	291	systems) <sup>72,73</sup> → ) system <sup>72,73</sup>
10	291	delete
10	299	generate → generated
10	301	Transposons
10	303	mediate → mediates
11	306	scar → damage
11	307	includes → include
11	307	knowledge that → potential that the
11	308	contain → contains
11	308	meant → essential
11	309	the Sleeping → Sleeping
11	309	help → helped
11	310	these → many of the
11	310	compare → compared
11	311	are low → is low
11	314	system comes → systems come
11	315	system → systems
11	319	will → were
11	322	infection → infections
11	323	are → is
11	324	compare → compared
11	325	iPSCs → iPSC
11	326	They → These
11	332	provides an → provide another
11	333	DNA → DNAs
12	335	through the → using
12	336	not integrate → not involve integration
12	337	their → episomal vector
12	338	low → low, plasmids → plasmids,
12	338	the minicircle → minicircle DNA
12	340	to a lowered → to lowered
12	346	iPSCs → iPSC
12	350	iPSCs → iPSC usage → use
12	350	the → a settings → setting
12	360	quality → high quality
12	360	application → application
12	361	mechanism → mechanisms
12	365	discover → discovered
12	365	iPSCs → iPSC
13	373	loses its → lose
13	373	play → plays
13	375	complex → complexes
13	376	derive stem cells to ESC → derived stem cells to the ESC
13	376	complex and → complexes and

13	376	is → are
13	382	loop → loops
13	383	location → localization
13	384	much → better
13	386	an → several
13	387	loop → loops
13	392	hundreds of other ESCs → hundred other ESC
13	393	maintain a → maintain the
14	397	ESCs → ESC
14	398	genes are → genes are essentially
14	403	loop → loops
14	403	will need → need
14	420	PSCs → iPSCs (**See comment above)
14	421	their → the
14	424	epigenetic → the epigenetic
15	430	Model of → A model of the
15	430	phonotypes → phenotype
15	431	assumed → assume
15	436	DNA are → DNA is
15	441	iPSCs → iPSC
15	442	at C5 → at the C5
15	444	PSCs → iPSCs (**See comment above)
15	444	de nove → the
15	451	iPSCs → iPSC
15	459	on → of
15	460	→ Transcription of these genes is repressed by the..
16	463	only → exclusively
16	464	represent → represents
16	467	allow an access → allows access
16	467	on their → to their
16	471	binds → bind
16	471	protein coding → protein-coding
16	473	promotes → promote
16	488	associate → associates
16	490	it → c-Myc
17	494	effect → effects    iPSCs → iPSC
17	495	increase → increases
17	499	expressions → expression
17	505	indicate → indicates
17	511	induce → induces
17	518	how exactly → exactly how
17	519	of the → in the
18	535	that is → explains
18	539	of the → of

18	542	resuscitation → restoration
18	542	lead → leads
18	543	reactivations → reactivation
18	544	EITHER: loops continue OR: loop continues
18	544	self-maintained → self-maintain
18	545	to a completion → to completion
18	553	As was mentioned → As mentioned above
18	557	elites → elite
19	560	Although, → Although    population → populations
19	560	contains → contain
19	562	but majority → but the majority
19	578	limited-range expression levels → limited-level expression of
19	579	stoichiometry → stoichiometric
19	580	for a → to
19	581	even a rare → even rare,
19	583	create a → result in
19	586	such as, → such as the choice of;
20	591	enhance → enhances
20	601	factors combination, → factor combinations,
20	602	A study reveals → One study revealed
20	604	ESCs population → ESC populations
20	609	as compared → when compared
20	610	The table 3 → Table 3
20	610	iPSCs → iPSC
20	610	as compared with → when compared to
20	611	iPSCs → iPSC
20	618	iPSCs → iPSC
21	625	models → model
21	625	offers → offer
21	629	ensured → ensures                      use → used
21	630	those → many
21	632	iPSCs → iPSC
21	652	drugs → drug
22	653	studies → studies and are
22	654	use → used
22	657	iPSCs offers → iPSCs offer
22	657	advantage → advantages
22	658	does → do
22	659	saves → save
22	660	animals → animals, differences → differences,
22	679	Jaenisch → Jaenisch's
23	694	has → have
23	696	present → presents
23	697	information → analysis

23	701	so → much
23	706	the → with the
23	706	genome → genomes
23	711	enabled → able
23	712	to the → in
24	721	similar → a similar
24	731	which is → which are
24	734	directed → is directed
24	736	off-targets → off-target
25	765	have → has
25	765	successes → success
25	767	heterogeneity → heterogeneous
25	771	are → is
25	780	marks → marked
26	785	infancy stage → infancy OR infant stage.
26	786	has → have
26	787	I → We

#### Some additional comments and suggestions:

2	40	replace: <u>birth</u> by <u>development</u>
3	58	remove: <u>that will be</u> → ...factors necessary .....
4	92	remove: repetition of “of reprogramming.” and rewrite phase as “have significantly improved its efficiency.”
4	95	change: “provide a summary” → “summarize”

The sentence Pg:10-302 to Pg:11-305 does not make sense. I would suggest you stop the phrase at the parenthesis on 10 303 and completely change 11-304 to something like “Co-transfection of a donor plasmid (the transposon) with a helper plasmid expressing the transposase enzyme leads to efficient integration of the transposon.”

11	328-329	Additionally, because they constitutively replicate, these vectors ...
12-13	396-397	This sentence does not make sense. “... Oct4/Sox2 are essential for iPSC generation, c-Myc and Klf4 were essential factors...” ← for what? I think it should read: “They discovered Oct4, Sox2, Klf4 and c-Myc were essential for iPSC generation while nanog was dispensable.”
13	386	May read better as “both their own genes and those of each other,”
10	273-274	I suggest moving the phrase “They can integrate ....mutagenesis.” to line 278 before “Certainly ... transgene.” But do this only after you have made other corrections or the line numbers will become wrong.