Electronic Supplementary Material (ESI) for Molecular BioSystems. This journal is © The Royal Society of Chemistry 2015

number	Table S1 Er	riched biolo	gical pro	cess to	erms of gene	ontology	. ·		
Consistion Regulation Regulation Regulation Regulation Parallel genes in score Parallel genes in score Parallel genes in proteinant Parallel genes in proteinant Parallel genes in proteinant Parallel genes in proteinant Parallel genes in proteinant B1384-54 10 10 10 10 10 10 10 10 10 10 10 10 10 10 1			Numbe	Fur	nctional Cluster		Number		Regulated
Control No Indicators Indicators Control states Control states Control states Control states Produce	Comparison	Pogulation	r or regulat			- Gene ontology class	ot regulated	Enrichment	genes in
Biology 1 Biology 4 0 (1) Up 1 1 2 0 0 - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - -	companion	Regulation	ed	ID	Enrichment	Gene ontology class	genes in	P-value	Functional
B19A-5-14 Nr. B19A-5-4 41 Up 2 -			genes	10	score		GO class		Cluster
Bisses Op 2 n n n n n n Bisses Down 11 - n -									
Vi. B1946-5 Down 11 -	B19A6-S-14	Up	2						
11 Down 11 12 1 <th1< th=""> 1 <th1< th=""> 1 1 <th1< td="" th<=""><td>vs. B19A6-S-</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></th1<></th1<></th1<>	vs. B19A6-S-								
Up 12 sterial metabolic process 5 0.0012	41	Down	11						
Image: constraint of the second sec		Up	12						
1 1.79 teroi metabolic process 4 0.000 Abcat, one tabolic process 3 0.0140 Abcat, c, abcab, c, ab									
1 1.79 cholesterol metabolic process 4 0.009 Abca1, etch, etch	·					sterol metabolic process	5	0.0012	
1 1.79 3 0.0140 Medal,					1.79				
1 1.79 steroi biosynthetic process 3 0.0140 Athin.1, C.A. 1 1.79 steroid biosynthetic process 5 0.0170 Ppapa.2, Ppapa.1 1 <t< td=""><td></td><td></td><td></td><td></td><td>cholesterol metabolic process</td><td>4</td><td>0.0090</td><td rowspan="5">Abca1, Nsdhl, Aldh1a1, Cat, Ppap2a, Hmgcs1,</td></t<>						cholesterol metabolic process	4	0.0090	Abca1, Nsdhl, Aldh1a1, Cat, Ppap2a, Hmgcs1,
1 1.79 steroid metabolic process 5 0.0170 Pap25, Pap25, Steroid metabolic process 3 0.0700 SSd 1 1.79 steroid metabolic process 3 0.0700 SSd 1 1.00 100 0.0180 100				1		sterol biosynthetic process	3	0.0140	
8 0.0170 Ppap2.4. Ppage.4. Ppage.4. Ppage.4. 1 0.0700 Ppap2.4. Ppage.4. Ppage.4. 1 0.0300 5.553 1 0.0300 0.0300 1 0.0300 6.653 1 0.0300 6.654 1 0.0300 6.643 1 0.0300 6.6463 1 0.0440 A.amin.0. 1 0.0550 Piaz.2.									
Image: 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1,						steroid metabolic process	5	0.0170	
Initial State of the biosynthetic process 3 0.0700 Sc5d Ilipid biosynthetic process 5 0.0970 Cd36, Initial construction of the biosynthetic process 9 0.0200 Cd36, Initial construction of the biosynthetic process 9 0.0320 Cd36, Initial construction of the biosynthetic process 9 0.0320 Cd36, Initial construction of the biosynthetic process 9 0.0320 Cd36, Initial construction of the biosynthetic process 9 0.0320 Cd36, Initial construction of the biosynthetic process 9 0.0320 Cd36, Initial construction of the biosynthetic process 8 0.0400 Adam10, Initial construction of the protein catabolic process 8 0.0400 Metap2, Initial construction of the protein catabolic process 7 0.0900 Ubra, Initial construction of the protein catabolic process 7 0.0900 Ubra, Initial construction of the protein catabolic process 7 0.0900 Ubra, Initial conodification of process 3							_		
Ibid biosynthetic process 5 0.0970 Index of the second s						steroid biosynthetic process	3	0.0700	Sc5d
B19A6-U-13 VS B19A6-U-3 39 Down 104 0.0180 Cd36, Cd36, Cellular macromolecule catabolic process 9 0.0200 Cd36, Ranbp2, Ranbp2, Protein catabolic process 9 0.0320 Edem3, Ranbp2, Ranbp2, Data 8 0.0440 Adam10, Cd37, Cd36, Ranbp2, Protein/sis involved in cellular protein catabolic process 8 0.0440 Adam10, Cd37, Cd36, Ranbp2, Protein/sis involved in cellular protein catabolic process 8 0.0440 Mmp19, Metap2, Pisa2, Ubiquitin dependent protein catabolic process 4 0.0550 Pisa2, Ubr2, Ubr3, Ubr3, Ubr3, Ubr3, Ubr3, Ubr3, Ubr3, Ubr3, Ubr3, Down 10 0.0460 Cf36, Cd36, Cd36, Ranbp2, Pisa2, Ubr3, Down 10 0.0400 Cf36, Cf36, Cf36, Cf36, Pisa2, Ubr3, Ubr3, Ubr3, Ubr3, Ubr3, Ubr3, Ubr3, Ubr3, Ubr3, Ubr3, Ubr3, Ubr3, Ubr3, Ubr3, Ubr3, Ubr3, Ubr3, Ubr3, Cf31, Dom,						lipid biosynthetic process	5	0.0970	
B19A6-U-13 0.0120 Cd36, cellular macromolecule catabolic process 9 0.0200 Cd36, Rahp2, Aahp2, Aahp2, B19A6-U-13 VS B19A6-U-13 2 1.33 cellular protein catabolic process 8 0.0440 Adamon, Aahp2, Aahp2, Aahp2, B19A6-U-13 39 Down 104 104 0.0550 Pia2, modification-dependent protein catabolic process 7 0.0900 Ubr2, Ubr3, Usp32 39 Down 104 1.32 modification-dependent protein catabolic process 7 0.0900 Ubr2, Usp32 30 Down 104 1.32 modification-dependent protein catabolic process 7 0.0900 Ubr3, Usp32 31 1.32 aminoglycan metabolic process 3 0.0400 Chst12, Dcn, Grs 3 1.32 aminoglycan metabolic process 3 0.0400 Chst12, Dcn, Grs 3 1.32 aminoglycan metabolic process 3 0.0400 Chst12, Dcn, Grs 4 1.2 RNA transport 3 0.0620 Rahp2, Rahp2, Rahp2, Nxf7 4 1.2 RNA transport 3 0.0620 Nxf7 8 <t< td=""><td></td><td></td><td rowspan="2"></td><td></td><td></td><td></td><td>-</td><td></td></t<>							-		
B19A6-U-13 VS B19A6-U-3 39 Down 104 A A A B A A						macromolecule catabolic process	10	0.0180	6436
 B19AG-U-13 VS B19AG-U-13 VS B19AG-14 VS B					1.33				
2 1.33 cellular macromolecule catabolic process 9 0.0320 Edem3, Rahbaz, Proteolysis involved in cellular protein catabolic process 8 0.0440 Adam10, Cast, C3, Proteolysis involved in cellular protein catabolic process 819A6-U-13 VS 819A6-U- 39 00wn 104 104 104 0.0550 Pja2, Pja2, Pja2, Pja2, Pja2, Pja2, modification-dependent protein catabolic process 7 0.0900 Ubr3, Ubr3, Ubr3, Ubr3, Ubr3, Ubr3, Ubr3, Ubr3, Ubr3, Pja2, Proteolysis 0.0500 Pja2, Pja3, Pja2, Pja3, Pja2, Pja3, Pj		Down		2		protein catabolic process	9	0.0200	
 Ranbp2, R						cellular macromolecule catabolic process	٩	0.0320	Ed36, Edem3, Ranbp2, Adam10,
2 1.33 cellular protein catabolic process 8 0.0460 Adam10, Cast, C3, C							5	0.0320	
B13A6-U-13 VS B13A6-U-3 39 0wn 104						proteolysis involved in cellular protein catabolic process	8	0.0440	
2 1.33 cellular protein catabolic process 8 0.0460 Mmp19, B19A6-U-13 VS B19A6-U-3 39 Down 104 ubiquitin-dependent protein catabolic process 4 0.0550 Pja2, Pja2									Cast, C3,
B13AG-U-13 VS B19AG-U-3 ubiquitin-dependent protein catabolic process 4 0.0550 Pja2, Pia52, Ubr2, Ubr2, Ubr2, Ubr2, Ubr2, Ubr2, Ubr2, Ubr32 39 Down 104 10000 10000 10000 10000 30 Down 104 modification-dependent macromolecule catabolic process 7 0.0900 1012, Ubr2, Ubr2, Ubr32 30 Down 11 0.0900 1000 10000 10000 100000 100000 100000 100000 100000 100000 100000 100000 100000 1000000 1000000 1000000 10000000 100000000 100000000000 1000000000000000000000000000000000000						cellular protein catabolic process	8	0.0460	Mmp19, Metap2, Pja2, Pias2,
VS B19A6-U- 39 Down 104 modification-dependent macromolecule catabolic process 7 0.0900 proteolysis 11 0.0980 glycosaminoglycan metabolic process 7 0.0900 glycosaminoglycan metabolic process 3 0.0250 3 1.32 aminoglycan metabolic process 3 0.0400 mRNA transport 3 0.0550 mRNA transport 3 0.0550 4 1.2 RNA transport 3 0.0620 RNA transport 3 0.0620 RNA transport 3 0.0620 MX7 RNA localization 3 0.0620 NX7 RNA localization 3 0.0630 mucleobase, nucleoside, nucleotide and nucleic acid transport 3 0.0750 Chest 12, Decn, Gns 0.0900 Decess 3 0.0100 Chest 12, Decn, Gns 0.0500 Chest 12, Decn, Gns 0.0500 MX7 RNA localization 3 0.0620 NX7 RNA localization 3 0.0630 Chest 2, Decess 3 0.1100 Chest 2, Decess 3 0.0100 Chest 2, Decess 3 0.1100 Chest 2, Decess 3 0.0100 Chest 2,	B19A6-U-13					ubiquitin-dependent protein catabolic process	nt protein catabolic process 4 C	0.0550	
39 Down 104 modification-dependent macromolecule catabolic process 7 0.0900 Ubr2, Ubr3, Usr3, U	VS B19A6-U-		104			ubiquitin-dependent protein catabolic process			
modification-dependent protein catabolic process 7 0.0900 proteolysis 11 0.0980 3 1.32 aminoglycan metabolic process 3 0.0250 polysaccharide metabolic process 3 0.1100 mRNA transport 3 0.0550 establishment of RNA localization 3 0.0620 4 1.2 RNA transport 3 0.0620 G3bp2, RNA transport 3 0.0620 Nxf7 RNA localization 3 0.0630	39					modification-dependent macromolecule catabolic process		0.0900	Ubr2,
modification-dependent protein catabolic process 7 0.0900 proteolysis 11 0.0980 3 1.32 aminoglycan metabolic process 3 0.0250 polysaccharide metabolic process 3 0.1100 Chst12, polysaccharide metabolic process 3 0.1100 MRNA transport 3 0.0550 establishment of RNA localization 3 0.0620 A 1.2 RNA transport 3 0.0620 MRTA RNA transport 3 0.0620 Nxf7 RNA localization 3 0.0620 Nxf7						······	-		Ubr3,
proteolysis 11 0.0980 glycosaminoglycan metabolic process 3 0.0250 3 1.32 aminoglycan metabolic process 3 0.0400 Chst12, Dcn, Gns polysaccharide metabolic process 3 0.100 0.0550 3 0.0550 mRNA transport 3 0.0620 G3bp2, Ranbp2, Nathonary 3 0.0620 G3bp2, Ranbp2, RNA transport 3 0.0620 Nxf7 4 1.2 nucleic acid transport 3 0.0620 Nxf7 RNA localization 3 0.0620 Nxf7 RNA localization 3 0.0620 Nxf7 RNA localization 3 0.0620 Nxf7						modification-dependent protein catabolic process	7	0.0900	Usp32
proteolysis 11 0.0980 glycosaminoglycan metabolic process 3 0.0250 3 1.32 aminoglycan metabolic process 3 0.0400 Chst12, polysaccharide metabolic process 3 0.1100 mRNA transport 3 0.0550 establishment of RNA localization 3 0.0620 4 1.2 RNA transport 3 0.0620 G3bp2, RNA transport 3 0.0620 Nxf7 RNA localization 3 0.0620 Nxf7									
glycosaminoglycan metabolic process 3 0.0250 3 1.32 aminoglycan metabolic process 3 0.0400 Chst12, polysaccharide metabolic process 3 0.1100 mRNA transport 3 0.0550 establishment of RNA localization 3 0.0620 G3bp2, RNA transport 3 0.0620 G3bp2, Ranbp2, nucleic acid transport 3 0.0620 Nxf7 RNA localization 3 0.0620 Nxf7						proteolysis	11	0.0980	
3 1.32 aminoglycan metabolic process 3 0.0250 3 1.32 aminoglycan metabolic process 3 0.0400 Chst12, Dcn, Gns polysaccharide metabolic process 3 0.1100 MRNA transport 3 0.0550 establishment of RNA localization 3 0.0620 G3bp2, RNA transport 3 0.0620 G3bp2, Ranbp2, nucleic acid transport 3 0.0620 Nxf7 RNA localization 3 0.0630							2	0.0250	
3 1.32 aminoglycan metabolic process 3 0.0400 Chst12, Dcn, Gns polysaccharide metabolic process 3 0.1100 MRNA transport 3 0.0550 establishment of RNA localization 3 0.0620 A 1.2 RNA transport 3 0.0620 G3bp2, Ranbp2, nucleic acid transport 3 0.0620 Nxf7 RNA localization 3 0.0620 Nxf7				3	1.32	giycosaminogiycan metabolic process	3	0.0250	
polysaccharide metabolic process 3 0.1100 mRNA transport 3 0.0550 establishment of RNA localization 3 0.0620 A 1.2 RNA transport 3 0.0620 G3bp2, RNA transport 3 0.0620 Nxf7 RNA localization 3 0.0620 Nxf7 RNA localization 3 0.0630						aminoglycan metabolic process	3	0.0400	Chst12,
polysaccharide metabolic process 3 0.1100 mRNA transport 3 0.0550 establishment of RNA localization 3 0.0620 G3bp2, RNA transport 3 0.0620 G3bp2, RNA transport 3 0.0620 Nxf7 nucleic acid transport 3 0.0620 Nxf7 RNA localization 3 0.0630									Dcn, Gns
MRNA transport 3 0.0550 establishment of RNA localization 3 0.0620 4 1.2 RNA transport 3 0.0620 G3bp2, RNA transport 3 0.0620 Mxf7 nucleic acid transport 3 0.0620 Nxf7 RNA localization 3 0.0630						polysaccharide metabolic process	3	0.1100	
establishment of RNA localization 3 0.0550 RNA transport 3 0.0620 A 1.2 RNA transport 3 0.0620 G3bp2, RNA transport 3 0.0620 Nxf7 RNA localization 3 0.0620 Nxf7 RNA localization 3 0.0630 Xxf7							2	0.0550	
establishment of RNA localization 3 0.0620 A 1.2 RNA transport 3 0.0620 G3bp2, Ranbp2, Nucleic acid transport 3 0.0620 Nxf7 RNA localization 3 0.0630				4	1.2	TIRNA transport	3	0.0550	G3bp2, Ranbp2, Nxf7
A1.2RNA transport30.0620G3bp2, Ranbp2, Nxf710.0620Nxf7RNA localization30.0630V10.06300.0750V						establishment of RNA localization	3	0.0620	
RNA transport 3 0.0620 G3bp2, Ranbp2, 4 1.2 nucleic acid transport 3 0.0620 Nxf7 RNA localization 3 0.0630 nucleobase, nucleoside, nucleotide and nucleic acid transport 3 0.0750									
4 1.2 Ranbp2, nucleic acid transport 3 0.0620 Nxf7 RNA localization 3 0.0630 nucleobase, nucleoside, nucleotide and nucleic acid transport 3 0.0750						RNA transport	3	0.0620	
RNA localization 3 0.0630 nucleobase, nucleoside, nucleotide and nucleic acid transport 3 0.0750						nucleic acid transport	2	0.0620	
RNA localization30.0630nucleobase, nucleoside, nucleotide and nucleic acid transport30.0750							з	0.0020	
nucleobase, nucleoside, nucleotide and nucleic acid transport 3 0.0750						RNA localization	3	0.0630	
nucleobase, nucleoside, nucleotide and nucleic acid transport 3 0.0750									
						nucleobase, nucleoside, nucleotide and nucleic acid transport	3	0.0750	

Comparison	Regulation	Number of regulated genes	KEGG pathway	Number of regulated genes in pathway	Enrichment P- value
B19A6-S-14 vs.	Up	2			
B19A0-3-41	Down	11			
	Up	12			
		104	Fatty acid metabolism	5	0.00034
			Steroid biosynthesis	3	0.0021
B19A6-U-13 vs. B19A6-U-39	Down		Drug metabolism - cytochrome P450	4	0.0026
			Fat digestion and absorption	3	0.0037
			Valine, leucine and isoleucine degradation	4	0.0050
			Tryptophan metabolism	3	0.0052

Figure S1



Fig. S1 Relative gene copy number of the unstable cell line (B19A6-U-13 and B19A6-U-39) and the stable cell line (B19A6-S-14 and B19A6-S-41). GAPDH was used for normalization (a). β -actin was used for normalization (b)

Figure S2



Fig. S2 Changes in of gene copy number of the CAG promoter, TACI, Fc and downstream flanking sequence of Fc in high generation cells relative to low generation cells. β - actin was used for normalization.