PLOS ONE

CORRECTION

Correction: A Common Polymorphism within the IGF2 Imprinting Control Region Is Associated with Parent of Origin Specific Effects in Infantile Hemangiomas

The *PLOS ONE* Staff

The images for Figs 1 and 2 are incorrectly switched. The image that appears as Fig 1 should be Fig 2, and the image that appears as Fig 2 should be Fig 1. The Figure captions appear in the correct order. Please see the corrected Figs 1 and 2 here.

Citation: The *PLOS ONE* Staff (2015) Correction: A Common Polymorphism within the IGF2 Imprinting Control Region Is Associated with Parent of Origin Specific Effects in Infantile Hemangiomas. PLoS ONE 10(11): e0143806. doi:10.1371/journal.pone.0143806

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IH Number	Genotype: Pat/Mat	Clinical Study	Region	Age (days)	First Appeared	Phase	Sex	Oral Steroid	Inj Steroid	Chemo	Laser	Ulceration	Reason for Excision	Western	CTCF	BORIS	IGF2	H19	% H19 Meth Pyro	% H19 Meth Southern	% H19 Meth Blood Pyro
IGF2/H19/ CTCF/BORIS rtPCR																					
1	T/C	Y	L Lower Eyelid	95	1 Week	Prolif	F						Threatened Visual Axis		0.65	0.20	1.61	1.58	32.2		
2	T/C	Y	Upper lip	368	Near Birth	Prolif	F						Cosmesis	Y	8.00	5.20	1.20	N/A			
3	T/C	Y	L Paranasal	418	1 Week	Quiescent	F		+				Cosmesis	Y	3.65	13.34	4.35	4.59			
4	T/T	Y	R Malar	420	1 Week	Quiescent	F	+		+	+	+	Ulceration	Y	0.87	6.76	3.25	2.22	29.2	26	
5	T/T	Y	Lip and Nose	635	Near Birth	Quiescent	F	+		+	+	+	Ulceration	Y	2.21	9.89	4.75	2.65			
6	T/T	Y	Lip and Nose	2138	Near Birth	Invol	M	+	+		+	+	Ulceration	Y	11.55	2.91	0.38	3.65	14	14	
7	T/C	Y	L Preauricular	2304	Near Birth	Invol	M						Cosmesis	Y	0.60	0.40	0.60	0.20	29	35	
8	C/T	Y	L Upper Eyelid	95	3 Weeks	Prolif	F						Threatened Visual Axis	Y	0.89	0.55	1.99	2.28	26.5	25.8	
9	C/NA	N	Neck	165	near birth	prolif	F						Parental Preference		0.70	0.30	1.30	1.60			
10	C/NA	N	Nasal Tip	334	near birth	prolif	F						Cosmesis		1.10	1.40	1.40	2.60			
11	C/NA	N	Nasal Tip	365	near birth	prolif	M						Cosmesis	Y	1.00	1.30	2.20	2.00			
12	CC	Y	Nasal Tip	547	2 Weeks	Quiescent	F	+	+		+		Cosmesis	Y	2.14	2.39	2.54	2.60	27.5	35	
13	CC	Y	Scalp	760	2 Weeks	Quiescent	F						Parental Preference	Y	1.68	2.60	3.99	2.89			
14	C/T	Y	Nasal Dorsum	1500	Near Birth	Invol	F		+				Cosmesis	Y	3.00	2.09	1.00	2.62	21		
Additional CTCF/BORIS rtPCR																					
15	N/A	N	scalp	81	Near Birth	Prolif	M	+			+		Ulceration		0.73	0.07					
16	N/A	N	Nasal Tip	299		Prolif	M				+	+	Ulceration		1.86	1.28					
17	N/A	N	Neck	380		Prolif	F						Parental Preference		0.70	0.88					
18	N/A	N	R Cheek	752		Quiescent	M						Cosmesis		0.85	0.91					
19	N/A	N	Scalp	1171		Invol	F						Cosmesis		2.13	0.91					
Western and DNA																					
20	T/C	Y	Forehead	104	1 Week	Prolif	F						Parental Preference	Y					32.4	34	63.9
21	T/T	Y	Neck	210	1 week	prolif	F	+				+	Ulceration	Y							
22	C/T	N	Back	244	"Near Birth"	Prolif	F						Cosmesis	Y					35.7	27.5	61.4
23	T/C	N	Chest Wall	294	"Near Birth"	Prolif	F						Cosmesis	Y							
24	T/T	Y	Forehead	308	2 Weeks	Prolif	F	+				+	Ulceration	Y					27.1	26	54.2
25	C/C	Y	Upper Lip	367	3 Weeks	Quiescent	F						Cosmesis	Y					34.8	21	57.4
26	T/T	Y	Forehead	435	2 weeks	Quiescent	F	+				+	Ulceration	Y						29.5	55.6
27	C/C	Y	Upper Lip	608	Near Birth	Quiescent	M						Cosmesis	Y					26.7	23	
28	T/T	Y	L Pre Auricular	751	2 Weeks	Quiescent	F						Cosmesis	Y							
29	C/C	N	Back	987	1 Week	Invol	F						Cosmesis	Y					25.8	23	61.4
30	C/C	Y	Neck	1600	Near Birth	Invol	F						Cosmesis	Y					23.2	19	
31	C/C	Y	R Upper Eyelid	1772	Near Birth	Quiescent	F						Cosmesis	Y					21.6	22	64.8
32	C/C	Y	Nasal Tip	2025	"Near Birth"	Quiescent	F						Cosmesis	Y					23.1	25	53.4
DNA Only																					
33	C/T	Y	Neck	21	2 Weeks	Prolif	F						Rapid Growth								
34	T/T	Y	L Upper Eyelid	95	3 Weeks	Prolif	F						Threatened Visual Axis								
35	T/C	Y	Forehead	285	1 Week	Prolif	F						Cosmesis						37.7	28	55.1
36	T/T	Y	Paranasal	333	2 Weeks	Prolif	F	+			+	+	Ulceration						28.8		
37	C/T	Y	Lower Lip	407	"Near Birth"	Quiescent	F						Cosmesis						17.8	27	56.2
38	C/C	Y	L Cheek	531	"Near Birth"	Quiescent	F						Cosmesis						33.9	30.5	52.9
39	T/C	Y	Lower Lip	1146	2 Weeks	Quiescent	F				+		Cosmesis						24.4		
40	C/C	Y	Forehead	1263	"Near Birth"	Prolif	F						Cosmesis								
Excluded																					
41	N/A	N	R Cheek	286									Not Glut 1 Positive								
42	N/A	N	Nasal	2240									Prior Resection of Same Lesion								

Fig 1. Master Data Table. All samples are assigned arbitrary numbers for ease of reference. Samples are categorized according to which set of experiments were performed, then by paternal/maternal genotype regarding the IGF2 rtPCR experiment. All sub categories are then sorted by age at resection. All quantitative data is collated with clinical descriptors. Please see methods section under specimen collection for details regarding the selection of individual samples for each experiment.

doi:10.1371/journal.pone.0143806.g001

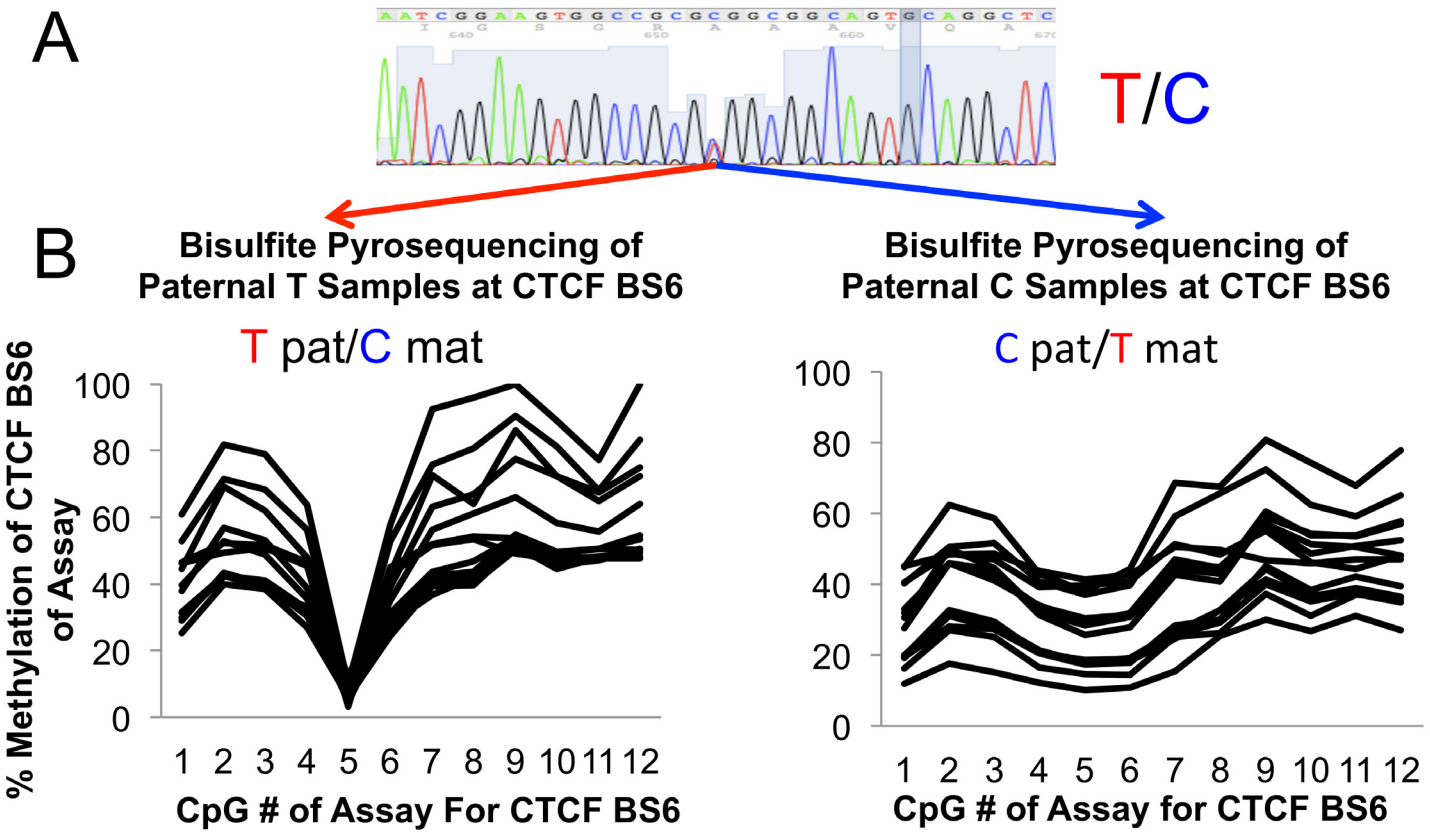
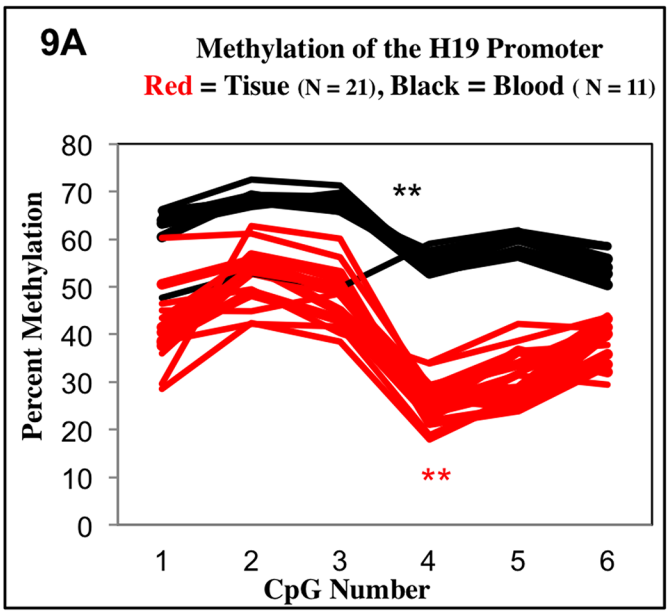


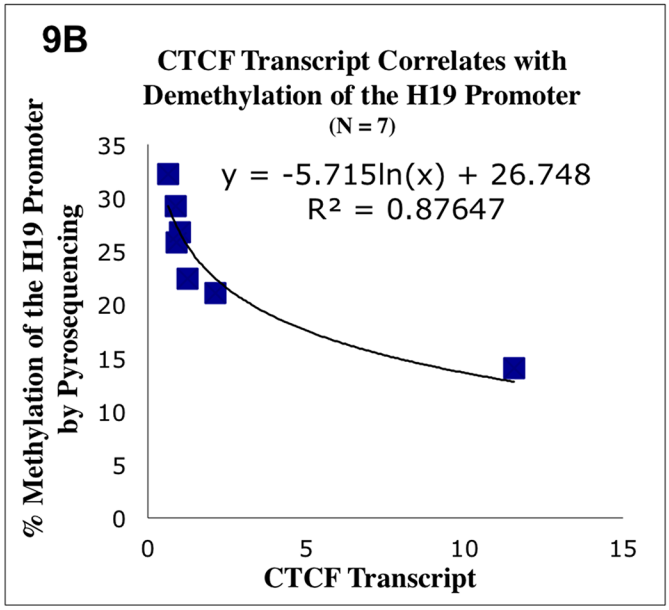
Fig 2. Deducing Parental Contributions From Direct Sequencing and Bisulfite Pyrosequencing. Fig 2A: 29 patients were genotyped via direct sequencing of blood samples for a known polymorphism within the core CTCF BS6 sequence (rs10732516.) All homozygous genotypes could be deduced from this information alone. **Fig 2B**: All samples (heterozygotes and homozygotes) were subjected to bisulfite conversion and quantitative methylation sensitive pyrosequencing. Methylation occurs only on the paternal chromosome for CTCF BS6. In normal tissue, such as patient matched control blood, this assay is capable of isolating the genotype of the paternal chromosome. As thymidine cannot be methylated, those individuals with a paternal T at rs10732516 were not methylated at CpG#5. Paternal C carrying individuals were methylated at CpG#5. Thus, the maternal and paternal contribution to CTCFBS6 can be deduced. This assay sidesteps the need for directly sequencing parents' DNA and eliminates the potential ambiguity ensuing from hetrozygous parents. Note: The methylation values of this assay are subject to primer bias, Tost et al (25.) This is evident by the 3 distinct groupings of methylation levels, which are artifactual.

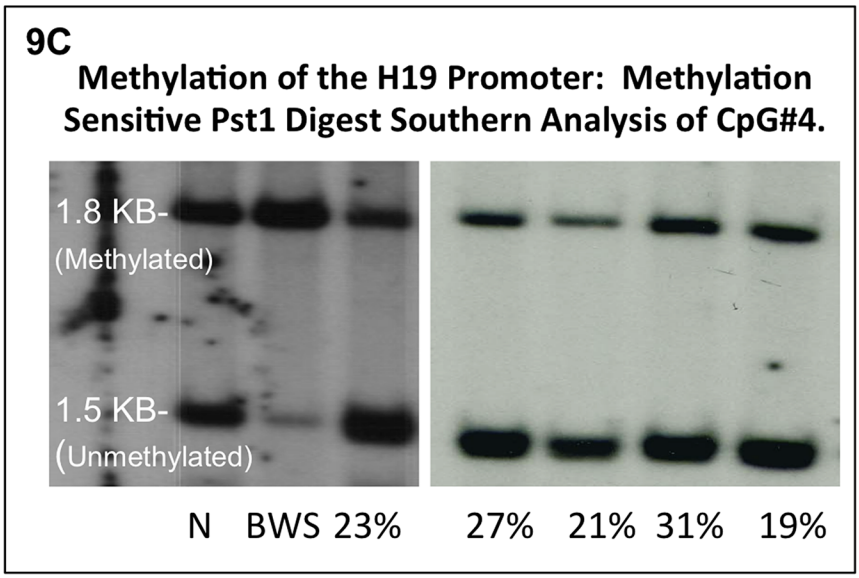
doi:10.1371/journal.pone.0143806.g002

There is an error in the last sentence of the Deducing Parental Contributions of Alleles at CTCF BS6 subsection under Materials and Methods. The correct sentence is: Comparing these results allows each parental contribution to be deduced, see Fig 2 for full details.

The panel labels for Figs 9 and 11 appear incorrectly in the published article. Please see the corrected Figs 9 and 11 here.







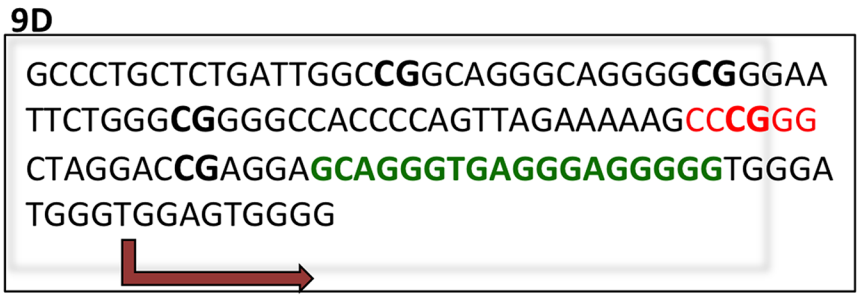


Fig 9. CTCF Expression and H19 Promoter Methylation. Fig 9A: Increased CTCF transcript level correlates with demethylation of the H19 Promoter. Those samples with the highest CTCF expression were the least methylated ranging from 34% to 14%. However, demethylation of the H19 promoter did not correlate strictly with H19 transcript expression (S6 Supplementary Information). **Fig 9B and 9C**—The H19 promoter (see **Fig 9D**) is hypomethylated, demonstrated by bisulfite converted pyrosequencing (9B) and methylation sensitive restriction digest with southern hybridization (9C.) 25 IH samples, and 13 matched blood controls were subjected to bisulfite converted pyrosequencing. 13 IH samples and 13 matched blood controls were subjected to southern

analysis with methylation sensitive Pst1 digestion. Two representative gels show, 5 IH samples, a Beckwith-Weidman positive control and a 50% methylated normal control. **Fig 9D**: sequence showing the H19 promoter—CpG#4 of the bisulfite sequencing test corresponds to the CCCGGG Pst1 digestion site of the Southern analysis. Other CpG's tested are in bold. This CpG is in close proximity to the transcription start site of H19 (blue arrow) and an overlapping putative CTCF binding site identified by positional weight matrix analysis.

doi:10.1371/journal.pone.0143806.g003

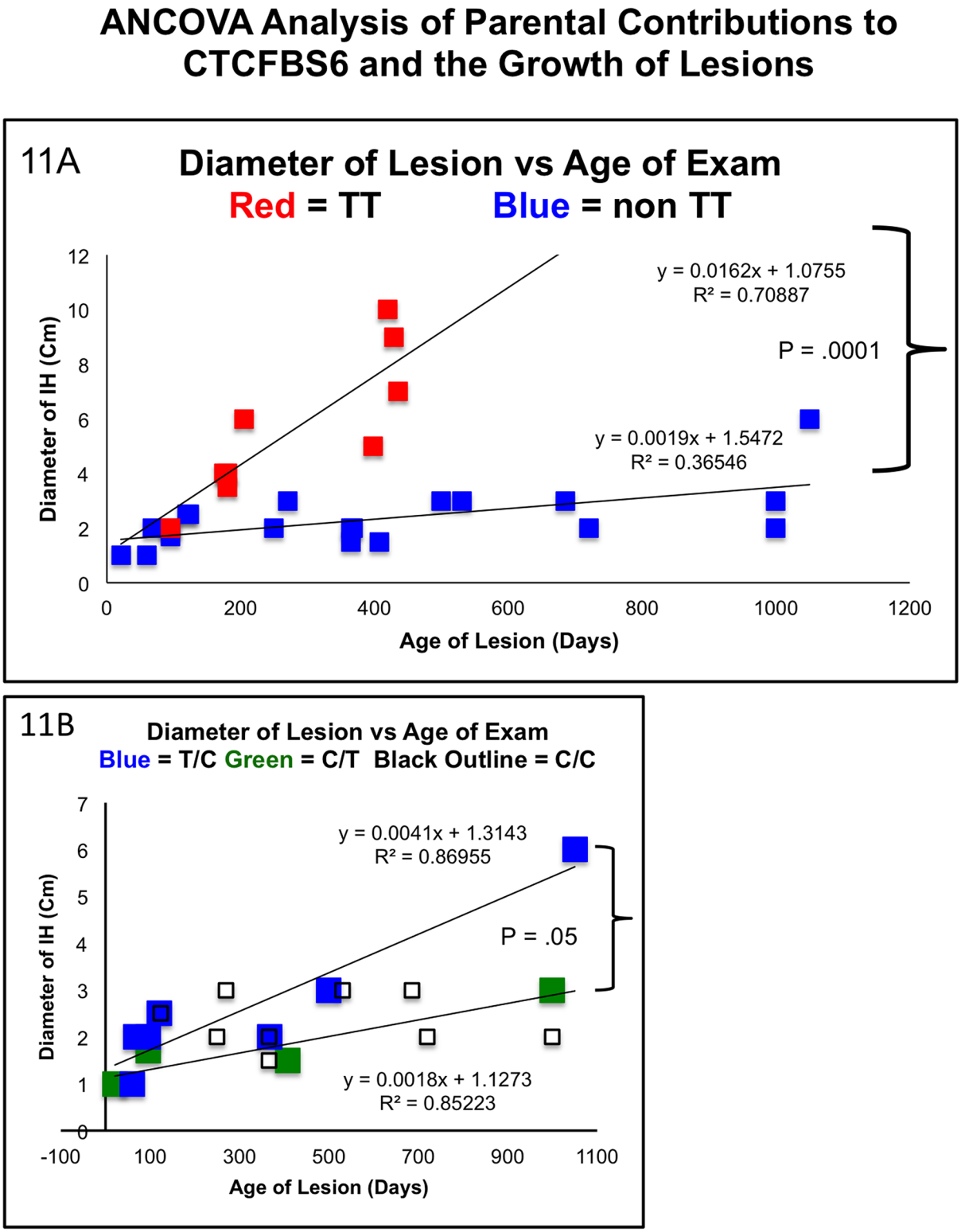


Fig 11. Clinical Correlation of Hemangioma Growth Rates with Parental Contributions to CTCF BS6. Fig 11A: This retrospective analysis of 29 samples, 9 TT, 20 non TT, demonstrates significantly distinct growth curves over a large age range. The ANCOVA model has identified age as a predictor of size p = .0007. The association between tumor size and age is significantly different among the genotypes of TT, C/T, T/C and CC p < .0001. Of Note the paternal contribution is presented first and the maternal is second. The interaction terms of parentally specific genotypes allowed us to test if the slopes of the curves between tumor size and age are different among the genotypes. This analysis indicted that an increase in 1 day of age is associated with .016cm of

growth in the TT group. This is significantly higher than the non TT group p = .0019. **Fig 11B**: Growth analysis focusing on the "non T/T" group. Each non TT growth curve varied independently and significantly from the TT samples (CC vs. TT: P<0.0001, CT vs. TT: P<0.0008, TC vs. TT: P = 0.0025). Furthermore, these data suggest parent of origin specific effects as those samples with identical genotypes but opposite parental contributions displayed statistically significant differences in growth curves. The paternal T/maternal C genotype grew at approximately twice the rate as their paternal C/ maternal T carrying counterparts (p = .05). The homozygous C group appeared to have a roughly flat growth rate between the heterozygotes and did not significantly vary with either heterozygote group (CC vs. C/T p = .99, CC vs. T/C p = .74)

doi:10.1371/journal.pone.0143806.g004

The publisher apologizes for the errors.

Reference

1. Schultz B, Yao X, Deng Y, Waner M, Spock C, Tom L, et al. (2015) A Common Polymorphism within the IGF2 Imprinting Control Region Is Associated with Parent of Origin Specific Effects in Infantile Hemangiomas. PLoS ONE 10(10): e0113168. doi: 10.1371/journal.pone.0113168 PMID: 26496499