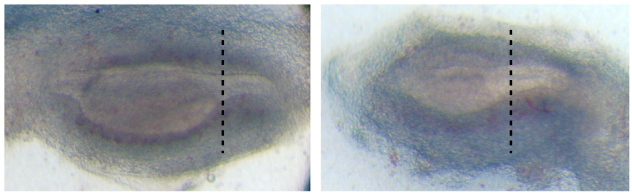
SUPPLEMENTARY INFORMATION

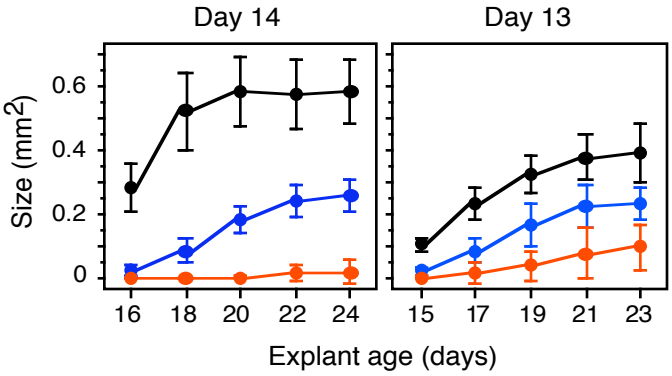
Supplementary information and data for Kavanagh *et al.* (2007) *Nature*, Predicting evolutionary patterns of mammalian teeth from development.

Supplementary Figures

Supplementary Figure 1. Bright field images of the day 14 (left) and day 13 (right) tooth explants showing site of dissection.



Supplementary Figure 2. Mean growth curves (with s.d.) of day 14 (n=12) day 13 (n=9) cut explant M1s (black) M2s (blue) and M3s (red).



Supplementary Tables

Supplementary Table 1. Results of Mann-Whitney *U* tests (with 2-tailed exact significance levels) for comparisons between ages of cut and intact explant molars at day 12 of culture (initiation at 12 = 1 day old).

Tooth	*P*	*n*=cut/intact
Day 14		
M2	0.000***	25/28
M3	0.001***	25/28
Day 13		
M2	0.000***	10/15
M3	0.000***	10/15
Day 14 bead experiments		
Activin A	0.014*	19/10
Bmp4	0.122	16/10

Supplementary Table 2. Measurements of cultured explants after 12 days in culture and the initiation day of M2 and M3. Asterisk marks the day 13 explant with M4 and dash marks missing data.

Experiment	tooth ID	M2 init	M3 init	M1 mm^2	M2 mm^2	M3 mm^2	M2/M1	M3/M1
DAY 14								
Apr 26, 2006	m10cut	-	-	0.45	0.27	0.11	0.600	0.244
Apr 26, 2006	m11cut	1	9	0.56	0.25	0.05	0.446	0.089
Apr 26, 2006	m12cut	2		0.47	0.26	0	0.553	0
Apr 26, 2006	m13cut	3	7	0.53	0.36	0.04	0.679	0.075
Jan 5, 2006	m01cut	2	9	0.50	0.31	0.04	0.620	0.080
Jan 5, 2006	m03cut	1		-	-			
Jan 5, 2006	m05cut	1	8	0.51	0.24	0.04	0.471	0.078
Jan 5, 2006	m07cut	2		0.55	0.29	0	0.527	0
Jan 5, 2006	m09cut	2		0.51	0.22	0	0.431	0
Jan 6, 2006	m01cut	5		0.65	0.36	0	0.554	0
Jan 6, 2006	m03cut	-	-	-	-	-	-	-
Jan 6, 2006	m05cut	1	7	0.43	0.31	0.11	0.721	0.256
Jan 6, 2006	m07cut	1	5	-	-	-	-	-
Jan 6, 2006	m09cut	1	4	-	-	-	-	-
Jan 6, 2006	m11cut	3		0.78	0.14	0	0.179	0
Dec 20, 2005	m01cut	2		-	-	-	-	-
Dec 20, 2005	m02cut	2		0.52	0.26	0	0.500	0
Dec 20, 2005	m03cut	2		0.41	0.20	0	0.488	0
Dec 20, 2005	m04cut	-	-	-	-	-	-	-
Dec 20, 2005	m05cut	2	8	0.56	0.28	0.06	0.500	0.107
Dec 20, 2005	m06cut	2		0.62	0.25	0	0.403	0
Dec 30, 2005	m01cut	2		0.75	0.39	0	0.520	0
Dec 30, 2005	m03cut	3		-	-		-	
Dec 30, 2005	m05cut	2	10	-	-	-	-	-
Dec 30, 2005	m07cut	3		0.68	0.21	0	0.309	0
Dec 30, 2005	m09cut	3		0.67	0.23	0	0.343	0
Dec 30, 2005	m11cut	4	8	0.71	0.23	0.11	0.324	0.155
Jan 5, 2006	m02cont			0.70				
Jan 5, 2006	m04cont	8		0.53	0.04	0	0.075	0
Jan 5, 2006	m06cont			-				
Jan 5, 2006	m08cont			0.63				
Jan 5, 2006	m10cont			0.66				
Jan 6, 2006	m02cont			-				
Jan 6, 2006	m04cont			0.65				
Jan 6, 2006	m06cont			-				
Jan 6, 2006	m08cont			0.76				
Jan 6, 2006	m10cont			-				

Jan 6, 2006	m12cont			0.51				
Apr 26, 2006	m06cont	3		0.67	0.07	0	0.104	0
Apr 26, 2006	m07cont	3		0.51	0.12	0	0.235	0
Apr 26, 2006	m08cont			0.72				
Apr 26, 2006	m09cont	2						
Apr 26, 2006	m14cont	3		0.92	0.17	0	0.185	0
Apr 26, 2006	m15cont	3		0.50	0.16	0	0.320	0
Dec 20, 2005	m07cont	3		0.61	0.18	0	0.295	0
Dec 20, 2005	m08cont			-				
Dec 20, 2005	m09cont	6		0.84	0.16	0	0.190	0
Dec 20, 2005	m10cont	8		0.52	0.07	0	0.135	0
Dec 20, 2005	m11cont	3		-	-			
Dec 20, 2005	m12cont	3	6	0.74	0.16	0.08	0.216	0.108
Dec 30, 2005	m02cont	2		0.49	0.16	0	0.327	0
Dec 30, 2005	m04cont	6		0.83	0.10	0	0.120	0
Dec 30, 2005	m06cont	6		0.74	0.23	0	0.311	0
Dec 30, 2005	m08cont	2		0.76	0.07	0	0.092	0
Dec 30, 2005	m10cont			0.73				
DAY 13								
Mar 22, 2006	m01cut	2	9	0.50	0.31	0.06	0.620	0.120
Mar 22, 2006	m03cut	3	8	0.32	0.27	0.14	0.844	0.438
Mar 22, 2006	m05cut	2	4	0.52	0.29	0.14	0.558	0.269
Mar 22, 2006	m07cut*	2	4	0.34	0.22	0.23	0.647	0.676
Mar 22, 2006	m18cut	2	5	0.25	0.23	0.11	0.920	0.440
Dec 20, 2005	m02cut	2	9	-	-	-	-	-
Dec 20, 2005	m04cut	2	7	0.33	0.17	0.13	0.515	0.394
Dec 21, 2005	m06cut	2	9	0.38	0.17	0.06	0.447	0.158
Dec 21, 2005	m07cut	2	12	0.43	0.26	0.01	0.605	0.023
Dec 21, 2005	m08cut	2		0.44	0.19	0	0.432	0
Mar 22, 2006	m02cont			-				
Mar 22, 2006	m04cont			-				
Mar 22, 2006	m06cont	8		0.64	0.09	0	0.141	0
Mar 22, 2006	m09cont	5		0.44	0.14	0	0.318	0
Mar 22, 2006	m11cont			0.33				
Mar 22, 2006	m15cont	7		0.53	0.09	0	0.170	0
Mar 22, 2006	m17cont	10		0.50	0.03	0	0.060	0
Dec 21, 2005	m09cont			0.47				
Dec 21, 2005	m10cont	12		0.33	0.03	0	0.091	0
Dec 21, 2005	m11cont			0.43				
Dec 21, 2005	m12cont			0.50				
Dec 20, 2005	m05cont			0.40				
Dec 20, 2005	m06cont	5		-	-			
Dec 20, 2005	m07cont	5		0.42	0.20	0	0.476	0
Dec 20, 2005	m08cont	5		0.53	0.21	0	0.396	0

Supplementary Table 3. Results of Mann-Whitney *U* tests (with 2-tailed exact significance levels) for comparisons between sizes of cut and intact explant molars at day 12 of culture. Note that the Bonferroni corrected multiple comparison significance level for tests where data is used in both Supp Tables 3 and 5 is 0.025.

Tooth	*P*	*n* = cut/intact	*P* (exl. zeros)	*n* = cut/intact
Day 14				
M1	0.027	19/21	0.027	19/21
M2	0.000***	19/21	0.000***	19/13
M3	0.005*	19/21	0.889	8/1
M1+M2+M3	0.012*	19/21	0.012*	19/21
Day 13				
M1	0.123	9/12	0.123	9/12
M2	0.000***	9/12	0.004**	9/7
M3	0.000***	9/12	-	8/0
M1+M2+M3	0.005*	9/12	0.005*	9/12

Supplementary Table 4. Results of Mann-Whitney *U* tests (with 2-tailed exact significance levels) for comparisons between sizes of cut and intact M2s when each tooth is 8 days old.

Tooth	*P*	*n* = cut/intact	*P* (at day 12)	*n* = cut/intact
M2	0.019*	5/8	0.030*	5/8

Supplementary Table 5. Results of Mann-Whitney *U* tests (with 2-tailed exact significance levels) for comparisons between sizes of day 14 and day 13 cut explant molars at day 12 of culture. Day 13 M3s are greater, other are smaller than corresponding day 14 teeth. Note that the Bonferroni corrected multiple comparison significance level for tests where data is used in both Supp Tables 3 and 5 is 0.025.

Tooth	*P*	*n* = day14/day13	*P* (exl. zeros)	*n* = day14/day13
M1	0.000***	19/9	0.000***	19/9
M2	0.247	19/9	0.247	19/9
M3	0.003**	19/9	0.106	8/8
M1+M2+M3	0.014*	19/9	0.014*	19/9

Supplementary Table 6. Measurements of murine molar areas. Diets: f-faunivore, o-omnivore, h-herbivore. Lengths in mm.

Species	diet	M1 mm^2	M2 mm^2	M3 mm^2	M2/M1	M3/M1	M1-M3 length	Body length	Teeth/ Body
Aethomys hindei	o	4.26	3.19	2.23	0.749	0.524	5.9	155	0.038
Apodemus agrarius	o	1.31	0.93	0.53	0.713	0.403	3.6	116	0.031
Arvicanthis niloticus	o	4.11	3.67	2.76	0.892	0.671	5.9	145	0.041
Crateromys schadenbergi	o	21.24	20.05	16.96	0.944	0.798	-	-	-
Dasymys sp.	o	4.65	4.02	3.35	0.863	0.720	7.0	157	0.045
Grammomys rutilans	o	2.85	2.16	1.46	0.756	0.514	5.3	140	0.038
Hybomys univittatus	o	2.86	2.17	1.22	0.760	0.428	5.2	130	0.040
Hydromys chrysogaster	f	16.94	9.36	0	0.552	0	9.7	300	0.032
Hylomyscus stella	o	1.56	1.28	0.69	0.821	0.442	4.0	90	0.044
Hyomys goliath	h	22.85	20.17	19.93	0.883	0.872	-	-	-
Leptomys elegans	f	3.98	3.09	0.92	0.777	0.231	-	-	-
Lophuromys medicaudatus	f	2.29	1.44	0.63	0.629	0.277	4.2	122	0.034
Mallomys rothschildi	h	21.89	20.44	16.88	0.934	0.771	16.2	385	0.042
Mastomys natalensis	o	2.09	1.73	0.80	0.829	0.384	4.3	125	0.034
Micromys minutus	o	0.76	0.56	0.27	0.737	0.357	2.6	65	0.040
Mus musculus	o	0.99	0.71	0.29	0.722	0.297	3.0	80	0.038
Bandicota indica	o	11.64	9.48	6.48	0.815	0.557	9.6	178	0.054
Niviventer rapit	-	3.73	2.81	1.58	0.754	0.424	5.9	143	0.041
Notomys mitchelli	o	3.68	2.85	1.41	0.775	0.384	5.3	125	0.042
Oenomys hypoxanthus	o	4.01	3.24	2.17	0.808	0.541	6.4	155	0.041
Phloeomys sp.	o	29.93	26.30	19.84	0.879	0.663	-	-	-
Pogonomys sp.	o	2.97	2.31	1.46	0.779	0.492	5.3	122	0.043
Praomys jacksoni	o	2.01	1.55	0.80	0.770	0.397	4.5	120	0.038
Rattus leucopus	o	5.41	4.19	2.29	0.775	0.423	6.8	-	-
Rhabdomys pumilio	o	2.52	2.07	1.22	0.820	0.484	4.8	113	0.042
Stochomys longicaudatus	o	4.52	3.31	1.80	0.733	0.399	5.9	146	0.040
Sundamys muelleri	o	7.10	5.23	3.17	0.737	0.447	8.0	209	0.038
Thallomys paedulcus	-	1.92	1.57	1.05	0.820	0.548	4.5	155	0.029
Uromys caudimaculatus	o	12.15	10.73	5.85	0.883	0.481	11.3	300	0.038

Supplementary Table 7. Reduced Major Axis regression analysis. For developmental this was based on mean day 14 and day 13 molar proportions and (explants without M3s plotted separately; 11 for day 14 and one for day 13 explants). Ante-asymptotic M1 sizes are from day 6 and day 10 of culture for day 14 and day 13 explants, respectively. For diversity data we calculated the regression using 2D crown areas and commonly used maximum widths x lengths. Albeit less strongly, the latter measure of size retains the molar size relationship. For calculation of model predictions, see text and methods.

	Slope	95%CI	Intercept	95%CI	r^2
Developmental data					
All sizes at day 12	1.519	-	-0.673	-	0.999
Ante-asymptotic M1 size	2.024	-	-0.997	-	0.998
Diversity data					
Area	2.150	1.772–2.688	-1.219	-1.651–-0.925	0.740
Width x length	1.816	1.402–2.384	-0.871	-1.247–-0.584	0.485
Mathematical model predictions					
Inhibitory cascade	2	-	-1	-	1.000
Random relay*	1.404	1.141–1.673	-0.529	-0.742–-0.322	0.493

*For 1,000 randomizations, ranges for slope, intercept, and r^2 are: 0.917–1.786; -0.831–-0.145; 0.210–0.797