Supplementary Table 1: Length and percentage identity of ECRs 5' to or within human *IGF1*, identified by pairwise comparison with other vertebrates

		Sequence (%) identity (bp)				
ECR	Human chromosome12 position *IGF1* TSS located at 101398287 (bp conserved in 3 or more species)	Dog	Mouse	Rat	Chicken	Zebrafish
1	101341482-101341804 (322)	77 (322)	83 (287)	78 (322)	77 (123)	40 (109)
2	101343525-101343976 (451)	83 (451)	81 (451)	82 (451)	16 (284)	-
3	101373191-101373287 (97)	80 (96)	76 (96)	72 (96)	77 (96)	81 (16)
4	101380731-101381290 (559)	86 (559)	83 (530)	76 (545)	77 (317)	55 (33)
5	101386282-101386490 (208)	81 (208)	79 (208)	79 (208)	74 (208)	-
6	101396324-101396718 (394)	85 (744)	80 (490)	78 (443)	63 (146)	38 (272)
7	101397085-101397741 (656)	83 (656)	74 (569)	74 (537)	74 (100)	100 (9)
8	101397902-101398246 (344)	83 (344)	75 (344)	73 (344)	73 (246)	18 (97)
9	101398454-101399669 (1215)	86 (1095)	77 (1057)	80 (1037)	82 (550)	86 (101)
10	101460479-101461339 (860)	77 (860)	82 (860)	81 (860)	25 (409)	x
11	101469505-101469639 (134)	79 (134)	92 (134)	86 (134)	-	x
12	101474435-101475187 (752)	87 (752)	79 (752)	79 (752)	x	x

(x denotes no sequence available for alignment; - denotes no sequence identity)

Supplementary Table 2: Mean circulating IGF1 level (ng/ml) by IGF1 genotype in previously reported SNPs.

SNP	MAF	Genotype	Al-Zahrani			Canzian*			MOG and Guernsey (pooled)**			
			N	Mean (95% CI)	P_{trend}	N	Mean	P_D	N	Mean (95%CI)	P_D	P_{trend}
rs35767	0.18	CC				1565	243.2	0.02	720	146.3 (140.5-152.0)	0.05	0.07
		CT				633	252.0		247	151.9 (144.9-158.9)		
		TT				84	238.0		32	150.9 (136.4-165.4)		
rs5742678	0.26	CC	190	142.6 (135.9-149.4)	0.009				552	146.2 (140.3-152.2)	0.28	0.51
		CG	129	154.9 (145.8-163.9)					399	149.6 (143.5-155.7)		
		GG	27	163.8 (137.0-190.6)					47	143.5 (131.4- 155.5)		
rs1520220	0.19	CC	225	142.9 (136.5-149.2)	0.003				704	148.0 (142.2-153.7)	0.93	0.68
		CG	107	158.8 (148.1-169.4)					276	148.4 (141.8-155.1)		
		GG	13	167.2 (134.9-199.6)					22	138.6 (121.7-155.6)		
rs6220	0.28	AA	208	141.5 (135.0-148.0)	0.002	1218	247.6	0.03	542	147.7 (141.6-153.8)	0.95	0.96
		AG	162	153.0 (145.0-161.0)		917	255.2		441	147.9 (141.8-153.9)		
		GG	34	168.4 (142.3-194.5)		185	247.0		64	147.9 (136.7-159.0)		
rs2946834	0.33	CC	154	140.1 (132.9-147.4)	0.02				497	149.8 (143.7-155.9)	0.13	0.14
		CT	151	155.0 (145.9-164.1)					447	146.1 (139.9-152.4)		
		TT	38	154.8 (136.9-172.7)					96	145.1 (135.6-154.5)		

(*Adjusted for age and centre; **Adjusted for measurement batch, age and menopausal status, P_D= p-value under a dominant model; P_{trend} for MOG and Guernsey pooled is a likelihood ratio test for each SNP based on a co-dominant model)

Supplementary Table 3: Mean circulating IGF1 level (ng/ml) by IGF1 genotype for SNPs in ECRs

Region SNP MAF	Genotype	MOG*		
		N	Mean (95% CI)	P
12 rs35760 MAF=0.19	AA	329	147.5 (143.1, 151.8)	
	AG	158	150.3 (144.1, 156.6)	0.78
	GG	17	142.2 (123.3, 161.1)	
10 rs10778177 MAF=0.17	CC	350	147.0 (142.8, 151.3)	
	CT	137	152.0 (145.3, 158.7)	0.64
	TT	16	138.6 (119.2, 158.1)	
2 rs4764884 MAF=0.23	CC	290	146.7 (142.1, 151.4)	
	CT	177	150.7 (144.9, 156.6)	0.46
	TT	24	146.6 (130.8, 162.4)	

(*IGF1 Levels are adjusted for age; Variants have MAFs >10% and so were tested under a co-dominant genetic model and p=likelihood ratio test based under this genetic model)

Supplementary Table 4: Sequences of the primers used to amplify evolutionarily conserved regions of the human IGF1 locus, which were subsequently screened for genetic variants

Region (amplimer)	Position on chromosome 12	Left Primer sequence 5'-3'	Right Primer sequence 5'-3'
1 (1)	101369768-101369990	CAAGTTGGCCACCACCTATC	TCTGCCCAAAACCCTTGTAA
1 (2)	101369926-101370132	CATGGTCGGGGAGTAATTCA	GCCAGTGATGAACAACCAGA
2	101343552-101344035	TTCAGCTCACCTTGGTTTCC	TGTCACAGGCAGATCATACTCA
3	101401455-101401689	AAAGCTGTTTGGCTTCTCAA	GGTTTGGAAAGTCTGGGTTC
4 (1)	101409007-101409347	TGGAGAGCCAAAACCATCTC	TGGATGCTTTGTTATTCCTGA
4 (2)	101409347-101409647	TTCAGGAATAACAAAGCATCCA	TGTTGTCTGTCTTCACACATTCC
5	101414549-101414819	TTACCTTAGGACAAATGCAGAGG	AGCAAAGAGGTGTTATTTGACAAG
6	101424677-101425027	CCACAATGAAAATGCCCTGT	GGGCTGCTACAATAGGCATAC
7 (1)	101425571-101425884	GGCAGAGACGTCTTATGAATTG	AAGAGCTGCTTGCCCAACT
7 (2)	101425833-101426042	CTTTGCCCATGAAAGTCCTC	GTCCCGGAACTCTGCACTTA
8	101426261-101426618	GCCCTTAGCCATAGAGAGGA	CAGCAGTCTTCCAACCCAAT
9 (1)	101426734-101427041	TTTGAGGACTTTATTCCATTGC	TCTGCGAACCCTGTCACTAA
9 (2)	101426937-101427306	TTGGGCATGGTGACAAATAA	CCGAGTGCTGTCTTCCAATC
9 (3)	101427224-101427506	CGATAAGACCCTCTCCAGCA	CAGTGACAGGCAGCCTAGTAGA
9 (4)	101427428-101427713	GCAAAGACTATGCCGAGCTG	ATTGCTAGCCAGCTGGTGTT
9 (5)	101427646-101428012	GGAGTCTGTGTGCCAGAGTG	GGTCCAGGTTATTTCCACCA
10 (1)	101488772-101489118	AAGAAGATCCCAGCGTTTCA	TGATGGTGGTGTTTAGGAA
10 (2)	101489096-101489383	ATTCCTAAACACCACCATGC	GGAAGACCATTAGTGCACAGC
10 (3)	101489284-101489548	CCTTCCCCTAGGCAGCA	CTAGAAAGGCAAGGCTGGA
10 (4)	101489466-101489728	CCTCAGTAGGGTTTTCCGTTC	AATCATGCACTTGGGGACAG
11	101497788-101498034	TATTCAGGGCAAAGGGCTTG	GAGAAGTTCAAAATGCGTTCC
12 (1)	101502657-101502984	CTTCCTGAACTGCTTTTGGA	GCATTTAACTATCACATTGCAAGC
12 (2)	101502890-101503237	TTTTCATTTGATCTCTAGCCAAG	TTGATGCCAAACACAGATGAG
12 (3)	101503189-101503564	AAAGGCGATAATTGTGTAAACC	TTTCTCCCCACCGCAGAG

Supplementary Table 5: Primer and probe sequences for Custom designed Taqman SNP genotyping assays (Applied Biosystems) and primer sequences and restriction endonucleases (New England Biolabs) for Restriction fragment length polymorphism (RFLP) assays.

SNP	Sequence 5'-3'	FAM-probe	VIC-probe
rs35455143	F:CAGTGACTTAACTCTAGTTAATAACTTCCTTGT R:TGGCTAACAATTGAAGGACATCCAT	ATCTATTTGACAAAAGTC	TCTATTTGACGAAAGTC
rs35765817	F: TGCGTCAGCATTTGGAAGAGAA R:AAAGTTAGAATCATTAGCCTTTCTGTCTCC	CCCAAATCTACTAATTGTT	CCAAATCTACTGATTGTT
rs5742678	F: CCCAAGACTTCTGTACACGGT R:CCAGGATCCTATGTGGTTTGTGAAG	AGCATTGTCACTATTG	AAGCATTGTGACTATTG
rs11829707	F:CCGAGCTGTAAAACCCAACT R: CAATGGCAAAGGCAAGTGTA	n/a RFLP using MnI	
rs3839984	F:TAGCCAAATACCACAAGGGAAAG R:CCACAAACCAATGCCCTGAAGCTA	n/a RFLP using Bsm1	