Dinucleotide repeat polymorphism at the IGF2R locus

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Source/Description: The cDNA sequence of the human Mannose 6-Phosphate/Insulin-like Growth Factor 2 Receptor was described by Oshima *et al.*, (1988) (1). The 3'-untranslated region contains dinucleotide repeat sequences (1).

Primer Sequences: GCCGGCTGGTGAATTCAA (GT strand); GTATCATGAGAACCTGAAGAG (CA strand).

Frequency: Estimated from 90 chromosomes of 45 unrelated Caucasians. PIC = 0.412.

	Allele (bp)	Frequency	Allele (bp)	Frequency	
A1	166	0.067	A4	160	0.022
A2	164	0.189	A5	158	0.011
A3	162	0.711			

Chromosomal Localization: Mapped to chromosome 6q25-q27 by Southern blot hybridization to a panel of human/Chinese hamster somatic cell hybrids and in situ hybridization(2).

Mendelian Inheritance: Codominant segregation was demonstrated in six two generation families.

Other Comments: Conditions for the amplification reactions were as follows. Samples were processed through 35 temperature cycles consisting of 1 min at 94°C, 1 min at 55°C and 45 sec at 72°C. Sizes of the alleles were determined by comparison to the size of the amplified products of human Man-6-P/IGF2 Receptor cDNA clone (1) and M13mp18 DNA sequencing ladders.

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A CA-dinucleotide polymorphism at the D17S113 locus, which is closely linked to D17S74

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Source/Description: The clone VAW140 (1) was tested for CA repeats by Southern blot hybridization (2). One CA-hybridizing HindIII fragment was subcloned into mp8 in both orientations and sequenced at each end. A (CA)₁₅ repeat was identified and PCR primers designed to amplify this region.

Primer Sequences:

H2f4–1 (TG strand) CTT GTC CCT TTA CAA TGA GG
H2f4–2 (CA strand) TGC GGA TCC CAA ATA CAG G

Polymorphism/Frequencies:

B1	(+6)	160 bp	2/162	0.01
B2	(+2)	156 bp	6/162	0.04
B3	(0)	154 bp	129/162	0.80
B4	(–2)	152 bp	20/162	0.12
B5	(–4)	150 bp	1/162	0.01
B6	(–8)	146 bp	4/162	0.02

The observed heterozygosity was 27/81 (33%) for unrelated Caucasians. In a subset of 61 individuals typed for both this CA polymorphism and the TaqI RFLP described previously (1), the observed heterozygosities were 22/61 (36%) and 25/61 (41%) respectively. The observed combined heterozygosity was 39/61 (64%). This reflects apparent linkage equilibrium for these two variants, as the expected combined heterozygosity, assuming completely random association, is 62%.

Mendelian Inheritance: Proper inheritance patterns were observed in informative CEPH families 1341 and 1375. The TaqI RFLP is co-informative in these families and linkage was demonstrated with a maximum LOD score of 4.82 at $\theta=0$.

Chromosomal Location: 17q12-q24 is the provisional localization of D17S113 (1). The TaqI RFLP at this locus is linked to D17S74 with a maximum LOD score of 13.15 at $\theta=0.06$ (unpublished CEPH data), indicating that this marker may be useful for genetic analysis of an early onset breast cancer locus which has been linked to D17S74 (3).

PCR Conditions: Amplifications in 10 μ l volumes were initiated with 25 ng of genomic DNA in reactions containing 0.5 μ M each primer, 1 unit of Taq polymerase, 10 mM Tris pH 8.3, 50 mM KCl, 1.5 mM MgCl₂, 200 μ M dNTPs except 5 μ M dCTP plus 2.5 μ Ci alpha-³²P-dCTP at 3000 Ci/mmol. The thermal profile was 3 minutes at 94°C, followed by 15 cycles of 90 seconds at 94°C, 120 seconds at 55°C, 120 seconds at 72°C; then 15 more similar cycles with extension of the 72°C portion by 3 seconds per cycle.

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