The BCL3 locus on chromosome 19 displays an informative microsatellite polymorphism

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Source/Description: The B-Cell Leukemia/Lymphoma 3 (*BCL3*) locus on chromosome 19 band q13 is sometimes affected in chronic lymphocytic leukemia (1), and shows genetic linkage with late-onset Familial Alzheimer Disease (2). An EMBL3 bacteriophage clone (αD) from a chr 14;19 translocation breakpoint junction library (3), was found to contain a $(CA)_{16}$ microsatellite array within intron 2 of the *BCL3* gene at nucleotides 698−792 (GenBank accession no. M31731).

Polymorphism: A 4 allele variable number tandem $(CA)_n$ microsatellite repeat polymorphism with an observed heterozygosity of 0.47 is detected using the primers:
BCL3−1: 5′ TGG-CAT-AAA-TGT-TGA-GTA-AG 3′
BCL3−2: 5′ TAA-GGG-CGA-GTA-TTG-TTT-CA 3′

Alleles

	Size (bp)	Number of (GT) dinucleotides	Observed Allele Frequency (N = 52 unrelated chromosomes)
A1	137	17	0.10
A2	135	16	0.76
A3	131	14	0.12
A4	127	12	0.02

Mendelian Inheritance: Co-dominant inheritance was observed in 40 meioses.

Other Comments: The polymerase chain reactions were carried out in 10 μl volume (50 mM KCl, 10 mM Tris (pH = 8.8), 1.5 mM $MgCl_2$, 250 μM dNTPs, 5.0 pM each primer, 0.3 Units of Taq polymerase, 0.1 μl Perfectmatch using forty cycles of 94°C, 58°C and 72°C for one minute each.

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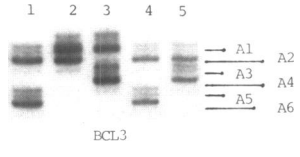

Detection of the XmnI RFLP at the human PAH locus by PCR

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Source/Description: Eight RFLPs have been used to haplotype the human phenylalanine hydroxylase (PAH) gene locus (1). We isolated, subcloned and sequenced a 1.7 kb HindIII-BamHI fragment from cPKU 13 (2) to determine the location of the XmnI polymorphic site. We subsequently designed oligonucleotide primers for PCR amplification of a 205 bp fragment containing the XmnI RFLP site.

Primer Sequences: 5′-CTGTACTTGTAAGATGCAGC-3′ and 5′-ACTGTCCCAAGCAATCAAAG-3′

Polymorphism: XmnI (GAANN/NNTTC) identifies a two allele polymorphism with 9.4 kb (−) (A1) or 6.5 kb (+) (A2) fragments.

Frequency: Frequencies of these alleles in 686 chromosomes of known haplotype: Southern blot: Non-PKU: A1 — 0.618, A2 — 0.382. PKU: A1 — 0.654, A2 — 0.346 (4).

Chromosomal Location: The human PAH gene has been localized to 12q22-q24 (5).

Mendelian Inheritence: Mendelian inheritance was demonstrated in all two-generation families examined.

Other Comments: PCR was performed using genomic DNA 0.5 μg of each primer, and 200 μM of each dNTP in 100 μl of a buffer containing 10 mM Tris−HCl (pH 8.3), 50 mM KCl, 1.5 mM $MgCl_2$ and 0.01% gelatin. Amplification proceeded for 35 cycles, each consisting of 40 seconds of denaturation at 92°C, 30 of annealing at 55°C, and 40 of extension at 72°C. The PRC product (205 bp) can potentially be cleaved by XmnI into 110 bp and 95 bp fragments (see figure).

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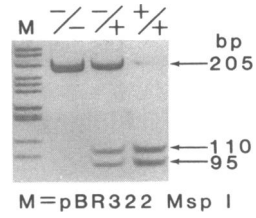

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