BglII RFLP for the human fumarylacetoacetate hydrolase (FAH) gene

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Source and Description of Clone: The probe pHAC is a 480 bp PstI/EcoRI fragment from the 3' end of pHHA2, a 1.5 kb human fumarylacetoacetate hydrolase cDNA clone containing all the FAH coding sequence (1).

Polymorphism: BglII detects a three-allele polymorphism with variant fragments of 16.4 kb (D1), 12.7 kb (D2) and 6.6 kb (D3). One constant band is present at 3.0 kb.

Frequency: Estimated from 35 unrelated (at least at the second degree) French-Canadian individuals.

D1: 0.25

D2: 0.38

D3: 0.37

Heterozygosity for BglII alleles is 0.66.

Not Polymorphic For: BamHI, EcoRV, HaeIII, HindIII, HpaII, and PstI studied in 15 unrelated individuals. The DNA source is blood lymphocytes.

Chromosomal Localization: The human FAH gene has been localized to 15q23-25 (1).

Mendelian Inheritance: Codominant segregation demonstrated in eighteen families (64 individuals).

Probe Availability: Available for collaboration. Contact Dr. R.M. Tanguay.

Clinical Relevance: Fumarylacetoacetate hydrolase is the enzyme deficient in type 1 hereditary tyrosinemia (2).

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References: 1) Phaneuf, D. et al. (1991) *Am. J. Hum. Genet.* **48**, 525-535. 2) Tanguay, R.M. et al. (1990) *Am. J. Hum. Genet.* **47**, 308-316.

KpnI and RsaI RFLPs for the human fumarylacetoacetate hydrolase (FAH) gene

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Source and Description of Clone: pHHA2 is a 1.5 kb human fumarylacetoacetate hydrolase cDNA clone isolated from a human liver λ gt11 cDNA library and subcloned at the EcoRI site of plasmid pGEM-7Zf. The cDNA insert (EMBL accession number M55150) contains all the FAH coding sequence (1).

Polymorphism: KpnI reveals 2 two-allele polymorphisms (Ba and Bb): 15.9 kb (B1), 5.5 kb (B2) and 3.7 kb (B1), 2.5 kb (B2). Two constant bands of 10.7 kb and 6.6 kb are also observed. A 10.4 kb allelic DNA fragment which is masked by the superposed 10.7 kb constant band can be visualized with a 414 bp EcoRI/SphI subfragment (pHHA) from the 5' end of pHHA2.

RsaI recognizes a two-allele polymorphism: 2.0 kb (C1) and 0.3 kb (C2). Six invariable bands of 2.3 kb, 1.8 kb, 1.6 kb, 1.3 kb, 1.0 kb and 0.7 kb are detected.

Frequency: Studied in 36 unrelated French-Canadians.

Set Ba	Allele	B1: 0.62	C1: 0.62
		B2: 0.38	C2: 0.38

Set Bb	Allele	B1: 0.97
		B2: 0.03

Heterozygosities for Ba and Ca allele sets are 0.47 and 0.06 for Bb allele set. Observed frequencies of heterozygotes and homozygotes fit Hardy-Weinberg equilibrium.

Not Polymorphic For: BamHI, EcoRV, HaeIII, HindIII, HpaII, and PstI in a panel of 15 unrelated individuals. The DNA source is blood lymphocytes.

Chromosomal Localization: The human FAH gene has been mapped to 15q23-25 (1).

Mendelian Inheritance: Confirmed in seventeen families (61 individuals) for the Ba1/Ba2 alleles, in two families (6 ind.) for Bb1/Bb2 and in six families (20 ind.) for the RsaI alleles.

Probe Availability: Available for collaboration. Contact Dr. R.M. Tanguay.

Clinical Relevance: Fumarylacetoacetate hydrolase is the enzyme deficient in type 1 hereditary tyrosinemia (2).

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References: 1) Phaneuf, D. et al. (1991) *Am. J. Hum. Genet.* **48**, 525-535. 2) Tanguay, R.M. et al. (1990) *Am. J. Hum. Genet.* **47**, 308-316.

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