Volume 15 Number 2 1987 Nucleic Acids Research

A high-frequency RFLP at the human liver/bone/kidney-type alkaline phosphatase locus

Mitchell J.Weiss, Richard S.Spielman and Harry Harris

University of Pennsylvania School of Medicine, Department of Human Genetics, 195 Med Labs, 37th & Hamilton Walk, Philadelphia, PA 19104-6072, USA

SOURCE/DESCRIPTION: A nearly full length cDNA that encodes human liver/bone/kidney-type alkaline phosphatase (L/B/K ALP) has been isolated from a Saos-2 human osteosarcoma cell cDNA library. This 2.5 kb cDNA is subcloned into pAT 153 (1).

POLYMORPHISM: BclI identifies a two-allele polymorphism with either a single band at 7.4 kb or two bands at 4.3 kb and 3.1 kb. A strong invariant band at 15.5 kb and a weak invariant band at 3.5 kb are also present in BclI digests.

FREQUENCY: Studied in 19 unrelated North American Caucasians.
7.4 kb allele: 0.74
4.3/3.1 kb allele: 0.26

NOT POLYMORPHIC FOR: PvuII, HindIII, BamHI (tested with a panel of 19 Caucasians).

CHROMOSOMAL LOCALIZATION: The human L/B/K ALP gene has been localized to chromosome 1 by use of a monoclonal antibody (2) and the cDNA hybridization probe (3) to identify the L/B/K ALP enzyme and DNA respectively in panels of human-rodent somatic cell hybrids.

MENDELIAN INHERITANCE: Co-dominant autosomal segregation of the polymorphic alleles has been observed in 3 informative families (20 individuals).

PROBE AVAILABILITY: Requests for probe to H.H. at the above address.

OTHER COMMENTS: Less common variants have been seen with PstI and SstI but are not fully characterized. The frequent BclI RFLP may be useful in linkage studies involving hypophosphatasia, a rare inherited disease characterized by deficient bone mineralization and low levels of L/B/K-type ALP in serum and tissue.

REFERENCE: 1. Weiss, M.J., et al., (1986) Proc. Natl. Acad. Sci. USA 83, 7182-7186. 2. Swallow, D.M. et al., (1986) Ann. Hum. Genet. 50, 229-235. 3. Moyra Smith personal communication.

ACKNOWLEDGEMENTS: We thank Joanne Borthwell for secretarial work and Daniel Sylvester for technical assistance. This work is supported by National Institutes for Health Grants GM 27018, GM 32592 and AM 35047 and March of Dimes Grant 858.