Thus, we were not able to replicate the findings of Grice et al. (1996).

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Exclusion of Atypical Vitelliform Macular Dystrophy from 8q24.3 and from Other Known Macular Degenerative Loci

To the Editor:

Atypical vitelliform macular dystrophy (VMD1; OMIM 153840) is an autosomal dominant disorder that can lead to blindness. VMD1 is characterized by complete penetrance but extremely variable expressivity, including with regard to age of onset and rate of progression. The findings for VMD1 include (1) macular and/or peripheral retinal lesions that may be small and yellow, intermediate and white, or large and depigmented, and (2) peripapillary abnormalities that are initially in the temporal nerve bundle but that progress circumferentially. The phenotype of VMD1 is similar to that of Best disease (VMD2; OMIM 153700); however, the macular lesions of VMD1 and VMD2 are clinically distinguishable (Mintz-Hittner et al. 1984).

An early linkage study in one large family reported linkage between the VMD1 locus and the soluble glutamate-pyruvate transaminase (GPT) locus, with a maximum two-point LOD score of 4.3 at 5% recombination (Ferrell et al. 1983). At that time, the GPT locus had been mapped tentatively to chromosome 16 (Wijnen and Meera Khan 1982). Recently, however, we have mapped the GPT locus to the long arm of chromosome 8 and have developed a PCR-RFLP assay for GPT typing (Sohocki et al. 1997). All previous GPT typing was by determination of the serologic phenotype only, and, because there are dramatic quantitative differences between the three common GPT serologic phenotypes (Welch 1972), GPT serotyping was difficult. Furthermore, within the last 4 years, several other loci associated with autosomal dominant macular degeneration (adMD) have been mapped to chromosomal sites (table 1). Given the refined localization of the GPT locus and given the additional mapped loci for adMD, it was important to reexamine the localization of the VMD1 locus in the previously studied family.

To further characterize the VMD1 locus, we recently

Table 1

Two-Point LOD Scores between the VMD1 Locus and Candidate Loci

Candidate Disease/Gene[a]	Chromosomal Localization	Marker	LOD Score at Recombination Fraction .00	.01	.05	.10	.20	.30	.40	Reference
VMD1	8q24.3[b]	D8S315	−38.2	−15.5	−8.29	−4.91	−1.9	−.63	−.11	Leach et al. 1996
VMD1	8q24.3[b]	GPT	−3.04	−1.19	−.50	−.23	−.04	.00	−.01	Ferrell et al. 1983
VMD1	8q24.3[b]	D8S1925	−8.90	−5.60	−3.00	−1.50	−.12	.24	.21	Leach et al. 1996
STGD1, FFM	1p21-p13	D1S188	−9.75	−5.74	−2.76	−1.47	−.42	−.03	.07	Gerber et al. 1995
RDS	6p21.1-cen	D6S271	−10.5	−6.72	−3.46	−2.05	−.92	−.48	−.25	Dib et al. 1996
STGD3	6q11-q15	D6S280	−3.35	−2.64	−1.33	−.75	−.27	−.08	−.00	Stone et al. 1994
MCDR1	6q14-q16.2	D6S1717	−3.58	−2.35	−.92	−.32	.07	.11	.31	Small et al. 1992
CYMD, DCMD	7p21-p15	D7S435	−11.5	−6.30	−3.22	−1.90	−.70	−.16	.04	Kremer et al. 1994
VMD2	11q13	D11S480	−10.0	−7.09	−4.04	−2.52	−1.14	−.51	−.18	Graff et al. 1994
STGD2	13q34	D13S158	−17.1	−9.12	−4.92	−2.83	−1.07	−.34	−.05	Zhang et al. 1994
RCD2	17p13	D17S796	−10.8	−7.04	−3.29	−1.77	−.56	−.14	−.01	Small et al. 1996
CORD2	19q13.3-q13.4	D19S49	−9.71	−6.28	−3.24	−1.95	−.86	−.38	−.13	Evans et al. 1994
SFD, TIMP3	22q12.1-q13.2	D22S304	−11.7	−8.12	−4.37	−2.75	−1.28	−.56	−.17	Wijesuriya et al. 1996; Weber et al. 1994

[a] STGD1 = Stargardt disease; FFM = fundus flavimaculatus; RDS = retinal degeneration slow; STGD3 = Stargardt disease 3; MCDR1 = dominant North Carolina macular dystrophy; CYMD = cystoid macular dystrophy; DCMD = dominant cystoid macular dystrophy; STGD2 = Stargardt disease 2, macular dystrophy with flecks, type 2; RCD2 = retinal cone dystrophy 2; CORD2 = cone-rod retinal dystrophy; SFD = fundus dystrophy, pseudoinflammatory, of Sorsby; and TIMP3 = tissue inhibitor of metalloproteinases-3.

[b] As reported prior to this study.

updated the clinical information for the original family and collected new blood samples. The family was typed for the GPT locus by use of the RFLP assay (Sohocki et al. 1997). The family samples were tested also, in accordance with standard laboratory protocols, with the microsatellite marker D8S1925, which has been mapped to within 170 kb distal to the GPT locus, and with D8S315, which has been mapped to 9 cM proximal to the GPT locus (Leach et al. 1996). To determine whether the VMD1 locus might map to other adMD sites, the samples were tested further with microsatellite markers tightly linked to other adMD loci. Two-point LOD scores were calculated by the MLINK program of LINKAGE (Lathrop et al. 1984) (table 1). An autosomal dominant form of inheritance, with a penetrance of .99, was assumed for both males and females.

The new GPT assay corrected the GPT types of three individuals from the original study. With these corrected GPT types and with the additional blood samples taken from the VMD1 family for this study, linkage between the VMD1 locus and the GPT locus is no longer apparent (table 1). Additionally, linkage testing between the VMD1 locus and D8S1925 *excludes* linkage of the VMD1 locus to the most distal region of 8q24.3, over a genetic distance of ~15 cM proximal to the telomere. Linkage of the VMD1 locus to the known adMD loci tested also was excluded. Therefore, it is unlikely that the VMD1 locus in this family maps to 8q24.3 as originally reported, and it also is highly unlikely that the VMD1 locus maps to the known adMD loci.

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Diagnostic Testing for Prader-Willi and Angelman Syndromes: Response

To the Editor:

The letter by Monaghan et al. (1997) in the January 1997 issue of the *Journal,* discussing testing for Prader-Willi (PWS) and Angelman (AS) syndromes, raised several interesting points. Essentially the issues related to the sequence of diagnostic testing for PWS/AS (cytogenetics, methylation testing, and FISH), considering the pick-up rate of abnormal results and the costs involved. Several others have addressed this topic (Chu et al. 1994; Smith et al. 1995; Young 1995; American Society of Human Genetics/American College of Medical Genetics Test and Technology Transfer Committee 1996; Erdel et al. 1996; Kubota et al. 1996), but Monaghan et al. (1997) are the first to include discussion of the costs of testing. We would like to (*a*) relate our 12-mo experience of performing diagnostic tests for a referred group of patients suspected to have PWS or AS and (*b*) review the logistics and costs of multiple testing.

Our department of cytogenetics is well established, with a specimen receptionist, an excellent blood laboratory, and staff dedicated to FISH. Our newly instituted molecular laboratory has one staff scientist who performs DNA extractions and the methylation test. A staff cytogeneticist (A.S.) consults with patients/referring clinicians, obtains clinical information, and coordinates the whole process. Within the one department, the whole is well accommodated, with adjacent laboratories and offices. All concerned work closely together.

Cytogenetic analysis on high-resolution chromosomes (HRC) had been performed for many years in our laboratory. FISH for PWS/AS was piloted in 1991 and replaced HRC in 1993. We began methylation analysis in 1995. Our aim was to obtain a result on the index case from a single blood collection, using a coordinated approach. Routine cytogenetics and DNA extraction would be performed simultaneously. The suspension from the cytogenetic harvest would be forwarded to the FISH laboratory. Methylation analysis would be performed on an aliquot of the extracted DNA. Finally,