December 1, 1972.

Human Chromosome Mapping Newsletter

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Here is a new edition of the linkage list. I am including with it references which are relevant and which have appeared since the third edition of Mendelian Inheritance in Man went to press (June 1, 1971). Indeed I have included all write-ups concerning linkage added since that time.

The assignment of retinoblastoma to chromosome 13 and of IgA to chromosome 18 is very shaky by reason of the nature of the evidence.

Several apparent gene-to-chromosome assignments by cell hybridization as well as by the family study method have not stood up. Even with the new banding techniques it is not always possible to identify with certainty which chromosome one is dealing with or where the parts of a rearranged chromosome have come from. Thus it is necessary to have confirmation from several laboratories. The purpose of this list is to keep workers informed of possible linkages, but please realize that even assignment to the "established" group in this informally circulated list may not be proved.

It will be obvious that the maps of chromosome 1 and X are highly provisional. Information is accumulating relatively rapidly, however.

W. N. Kelley of Durham, N.C., tells me the adenine phosphoribosyltransferase temperature polymorphism (10260) is not clean cut. He questions, therefore, whether at this stage it can be used for estimating the map interval between APRT and haptoglobin on chromosome 16. Electrophoretic polymorphism of APRT is rare, according to the recent report of Mowbray, Watson and Harris (Annals of Human Genetics 36:153-162, 1972).

On the urging of Dr. A. Adam of Tel Aviv, I have removed Dubin-Johnson syndrome (23750) and Factor VII deficiency (22750) from the list of autosomal linkages in limbo. Adam writes me that he thinks linkage phase disequilibrium is an unlikely explanation for the association because it has been observed in so many groups in addition to Iranian Jews and because several apparent recombinants were observed in a family (No. 55) reported by Shani, Seligsohn et al. (Quart. J. Med. 39: 569, 1970).

Victor A. McKusick

Additions to Mendelian Inheritance in Man, relevant to linkage and assignment, made since the last published edition (1971).

Add to 10260 Adenine phosphoribosyltransferase variants

By study of man-mouse hybrid clones Ruddle's group (1972) could demonstrate that the APRT locus is on chromosome No. 16. Mapping in relation to the haptoglobin locus (14010) should be studied in families. Kelly et al. (1968) found apparent heterozygosity in four persons in three generations of a family. The level of enzyme activity ranged from 21 to 37 percent, requiring some special explanation. That the enzyme is a dimer is one possibility. Mowbray et al. (1972) found a continuous and unimodal distribution for residual red cell APRT activity after heating. The results were obtained from studies of freshly obtained blood. They suggested that the earlier results pointing to a common polymorphism in APRT manifested by thermostability differences may have been produced by study of old samples with variable amounts of freezing and thawing. Mowbray et al. (1972) found rare examples of electrophoretic polymorphism of APRT. APRT appears to be a dimer with identical subunits.

Mowbray, S., Watson, B. and Harris, H.: A search for electrophoretic variants of human adenine phosphoribosyl transferase. Ann. Hum. Genet. 36:153-162, 1972.

Ruddle, F.H.: New Haven, Conn., personal communication, 1972.

Add to 10265 Adenine B auxotroph, human complement for hamster

Studying hybrids between hamster cells carrying induced auxotrophic mutation and normal human cells, Kao and Puck (1972) defined a linkage between an adenine B auxotroph *complementing gene and a gene necessary for expression* of three esterase bands (13335). The syntenic group appears to be on chromosome No. 4 or No. 5. The human gene seems to be a regulatory one for esterase because the bands produced are of hamster type.

Kao, F.T. and Puck, T.T.: Genetics of somatic mammalian cells: demonstration of a human esterase activator gene linked to the Ade B gene. Proc. Nat. Acad. Sci. 69: 3273-3277, 1972.

Add to 10270 Adenosine deaminase

The ADA locus is linked to HL-A, the probable order being HL-A, PGM (3), ADA, P (Edwards et al., 1972). Evidence for the linkage of P and ADA had been presented by Weitkamp (1971).

Edwards, J.E., Allen, F.H., Glenn, K.P., Lamm, L.U., and Robson, E.B. : Personal communication, 1972. (To be published in Histocompatibility Testing 1972.)

Weitkamp, L.R.: Further data on the genetic linkage relations of the adenosine deaminase locus. Hum. Hered. 21:351-356, 1971.

Add to 10470 Amylase, salivary (Amy 1)

The separate loci have been designated amylase 1 (salivary) and amylase 2 (pancreatic). Polymorphism of both the salivary and the pancreatic serum amylases has been demonstrated in man. Ward et al. (1971) studied amylase in salivary and identified electrophoretic variants. Merritt et al. (1972) found close linkage of the two amylase loci.

Merritt, A.D., Rivas, M.L. and Ward, J.C. : Evidence for close linkage of human amylase loci. Nature N.B. 239 : 243-244, 1972.

Ward, J.C., Merritt, A.D. and Bixler, D. : Human salivary amylase: Genetics of electrophoretic variant. Am. J. Hum. Genet. 23:403-409, 1971.

Add to 10471 Amylase, pancreatic (Amy 2)

Polymorphism is determined by agar gel electrophoresis. Kamaryt et al. (1971) assigned the locus to chromosome 1 by study of linkage with the "uncoiled" variant used by Donahue et al. in assigning the Duffy blood group locus to chromosome 1. Their conclusion, although apparently correct, was based on a single small family which gives a peak lod score at theta = 0 of less than 1.1. Hill et al. (1972) demonstrated probable linkage between the amylase 2 locus and the Duffy blood group locus, and this has been confirmed (Rivas et al., 1972). Pancreatic amylase is tested in urine.

Hill, C.J., Rowe, S.I. and Lovrien, E.W.: Probable genetic linkage between human serum amylase (amy-2) and Duffy blood group. Nature 235:162-163, 1972.

Kamaryt, J., Adamek, R. and Vrba, M.: Possible linkage between uncoiled chromosome un 1 and amylase polymorphism (Amy 2) loci. Humangenetik 11:213-220, 1971.

Rivas, M.L., Merritt, A.D., Lovrien, E.W. and Conneally, P.M.: The amylase (Amy_1, Amy_2) and Duffy linkage group. Am. J. Human Genet. 24:40a, 1972.

Jacobs, P.A., Brunton, M., Frackiewicz, A., Newton, M., Cook, P.J.L. and Robson, E.B.: Studies on a family with three cytogenetic markers. Ann. Hum. Genet. 33:325-336, 1970.

Lamm, L.U., Kissmeyer-Nielsen, F., and Henningsen, K.: Linkage and associated studies of two phosphoglucomutase loci (PGM1 and PGM3) to eighteen other markers. Analysis of the segregation at the marker loci. Hum. Hered. 20: 305-318, 1970.

Nguyen Van Cong, Billardon, C., Picard, J.Y., Feingold, J. and Frezal, J.: Fourth World Congress of Human Genetics, Paris, 1971.

Renwick, J.H.: The Rhesus syntenic group in man. Nature 234:475, 1971.

Weitkamp, L.R., Guttormsen, S.A., and Greendyke, R.M.: Genetic linkage between a locus for 6-PGD and the Rh locus: Evaluation of possible heterogeneity in the recombination fraction between sexes and among families. Am. J. Hum. Genet. 23:462-470, 1971.

Add to 11620 Cataract, nuclear

The kindred had been earlier described by Nettleship (1909). In 1963 Renwick and Lawler referred to it as congenital zonular cataract. In 1970, Renwick referred to it as total nuclear cataract. In the latter publication the the possibility that some other forms of dominant cataract might be linked with Duffy was discussed.

Renwick, J.H.: Eyes on chromosomes. J. Med. Genet. 7:239-243, 1970.

Add to 12730 Dyschondrosteosis

Lisker et al. (1972) found a family informative for Rhesus and haptoglobin. No indication of close linkage was provided, however.

Lisker, R., Gamboa, I. and Hernandez, J.: Dyschondrosteosis. A Mexican family with two affected males. Clin. Genet. 3: 154-157, 1972.

Add to 13335 Esterase regulator

Studying hybrids between chinese hamster cells carrying induced auxotrophic mutations and normal human cells, Kao and Puck (1972) defined a linkage between an adenine B auxotroph-complementing gene (10265) and a gene necessary for expression of three esterase electrophoretic bands . The pair of loci appeared to be on a B group chromosome. The human gene appeared to be a regulatory one for esterase because the bands produced were of the hamster type.

Kao, F.T., and Puck, T.T.: Genetics of somatic mammalian cells: demonstration of a human esterase activator gene linked to the Ade B gene. Proc. Nat. Acad. Sci. 69: 3273 - 3277, 1972.