**730** CHARACTERIZATION OF TWO GOLGI GALACTOSYLTRANSFERASE ISOZYMES WHICH CATALYZE THE BIOSYNTHESIS OF $Gm_1$ GANGLIOSIDE. Feige Kaplan and Peter Hechtman (Spon. by Charles R. Scriver) MRC Genetics Group, McGill University Montreal, Quebec, Canada.

Biosynthesis of gangliosides, a critical process in early development of neurological function, was studied in 3 week old rats. Analysis of the glycosylation steps in the biosynthetic pathway has been impeded due to the difficulty in solubilizing the membrane bound glycosyltransferase enzymes. We have solubilized UDP-gal $Gm_2$ ganglioside galactosyltransferase from rat liver Golgi by detergent extraction. Two isozymes which catalyzed the synthesis of $Gm_1$ ganglioside were separated by DEAE chromatography. Peak I, the more basic form, and Peak II, the more acidic form were highly unstable following chromatography but could be stored at -20°C in 50% glycerol. pH optima for Peaks I and II were 7 and 6. The Kms for UDP-gal for Peaks I and II were 7.9 x $10^{-4}$ M and 4.7 x $10^{-4}$ M; Kms for $Gm_2$ were 2.6 x $10^{-5}$ M and 1.5 x $10^{-5}$ M. Mn was essential for both activities. Peak I activity could be demonstrated in the presence of phospholipids or nonionic detergent. Peak II was active in the presence of nonionic detergent, but little or no activity could be demonstrated with phospholipid. Human liver Hex A activator protein could replace detergent for Peaks I and II. Only Peak II activity catalyzed the addition of gal to monosaccharide amino sugars. Both Peaks I and II catalyzed the addition of galactose to glycoprotein substrates. In summary, 2 distinct membrane bound $Gm_2$ ganglioside galactosyltransferase isozymes were resolved and characterized.

**731** PRENATAL DIAGNOSIS OF β-THALASSEMIA BY AMNIOCENTESIS. Haig H. Kazazian, Jr., Corinne D. Boehm, John A. Phillips, III, Pamela G. Snyder, Patricia J.V. Giardina, and Maurice J. Mahoney. Depts. of Peds., Johns Hopkins Univ. Sch. of Med., Baltimore; Cornell Med. Center, New York; and Yale Univ. Sch. of Med., New Haven.

We have conducted prenatal diagnosis for β-thalassemia (thal) by analysis of fetal DNA of amniotic fluid cells from 9 women at risk for affected children (4 Italian, 2 Greek, 2 Asiatic Indian, 1 Chinese). DNA of parents and their previous affected child was examined at 4 polymorphic restriction endonuclease sites near the thal mutation. Studies of an affected child allow us to determine which sites are "marking" the thal genes. One can then use linkage analysis to diagnose the thal status of the fetus. In 4 of the 9 fetuses studied, normal, thal trait, and affected genotypes could be differentiated. Diagnoses were: 1 normal, 1 affected, and 1 thal trait fetus; the latter 2 were confirmed by fetoscopy. Tests on the fourth fetus are pending. In the remaining 5 fetuses, thal major could be excluded in 3, but not in 2, both of which underwent fetoscopy. Screening of 20 additional couples at risk has shown that in 75% of their future pregnancies either exact fetal thal status can be determined or thal major can be ruled out. These results suggest that amniocentesis, with its low fetal risk and wide availability, can be the primary approach to prenatal diagnosis of β-thalassemia.

● **732** BURKITT LYMPHOMA (BL):CHROMOSOME FINDINGS IN SIBLINGS. Joseph Kochen and Nataline Kardon, Cornell Univ. Med. Col., North Shore Univ. Hosp., Dept. Peds., N.Y.

The chromosomal change found repeatedly in BL tumor cells is a marker chromosome (chr)14q+. This is often shown to result from a translocation of part of the long arm of chr 8. For this rearrangement to occur, this location must be especially vulnerable to breaks. The case of a 10 year old boy, with BL supports the hypothesis that a fragile site on chr 8 may predispose certain lymphoid cells to malignant transformation. He presented with ileocecal intussusception due to BL limited to terminal ileum and local mesenteric lymph nodes. The tumor was resected and he received radiotherapy and 6 months of chemotherapy. There is no evidence of disease 20 months after diagnosis. Tumor cell marker studies showed a predominance of B-cells with surface IgM kappa specificity. EBV studies were indicative of past infection. Blood and bone marrow morphology was normal. Chromosomal analysis of PHA stimulated peripheral blood lymphocytes showed a 46,XY karyotype with 40% breaks, gaps and endoreduplication in the 8q22 region (20/50 cells). Bone marrow and fibroblast analysis showed no breaks in chr 8. Repeat blood studies 6 months after treatment showed 8% breaks at 8q22. Examination of peripheral blood lymphocytes from the patient's healthy 13 year old sister, showed 12% breaks at 8q22. The karyotype of the parents was normal. The similar findings in both siblings suggest that the 8q22 region in lymphoid cells may be genetically vulnerable to breaks, i.e. by a viral agent, such as EBV. The affected cell line may then be at risk to transformation into malignant lymphoma.

**733** AUTOSOMAL RECESSIVE TYPE OF WHISTLING FACE SYNDROME IN TWINS. Boris G. Kousseff. So. Il. Univ. Sch. of Med. Dept. of Peds. Springfield, IL (Spon. by Robert E. Merrill.

This syndrome was described by Freeman and Sheldon in 1938. Until now about 50 cases have been reported and the condition is considered to be an autosomal dominant trait. A couple of reports however, suggested the existence of an autosomal recessive type of the syndrome by reporting affected siblings, progeny of normal consanguineous parents.

The reported pregnancy resulted in concordant monochorionic diamnionic like sex twins who showed the clinical features of whistling face syndrome. Twin A weighed 3420 grams and was 50 cm. long. The facies appeared unusual with sloping forehead, prominent supraorbital ridge, sunken eyes and ocular telecanthus, short nose, colobomata of the nostrils, elongated philtrum, high arched palate, marked microstomia with puckered lips and an "H" shaped cutaneous dimpling of the chin. The hands had symmetrically clenched fingers with camptodactyly and ulnar deviation. Both feet showed mild talipes equinovarus.

Twin B was stillborn and had identical phenotype as Twin A. The birth weight was 3090 grams and the length-50 cm. Karyotype was normal.

HLA typing showed the twins to be dizygotic; twin A - A 11, 2; B 35, 12: C w 4; Twin B - A 3, 1; B 14, 37. Thus the first pair of twins with whistling face syndrome lend strong support to the existence of an autosomal recessive type of whistling face syndrome.

**734** COHEN SYNDROME: MODE OF INHERITANCE AND CLINICAL EXPRESSIVITY. Boris G. Kousseff. So. Ill. Sch. of Med. Dept. of Peds. Springfield, IL. (Spon. by Robert E. Merrill).

A diagnosis of Cohen syndrome was made in four mentally retarded siblings; two males and two females. Their I.Q.'s were between 35 and 45. The parents were nonconsanguineous and of normal intelligence. All four children had microcephaly (2-2½ S.D. below the mean), mild hypotonia and narrow, thin hands and feet with long fingers and toes. Three of them were of short stature (2-3 S.D. below the mean) with weight between the 10th and 50th percentile and evidence of mild truncal obesity. The eldest brother was not obese; his height was at the 15th percentile and his weight was at the 5th percentile. Most of the facial stigmata of the syndrome were present - exotropia, prominent ears, poorly formed philtrum and peculiar nose but the degree of expressivity of each stigma varied from one individual to the other. No prominent medial upper incisors were present in any of the siblings. Mild delay of puberty was documented by history in the older three siblings. No endocrine problems were documented in the sibship. All patients had normal karyotype.

The reported sibship lends strong support to the presumed autosomal recessive mode of inheritance of Cohen syndrome. It seems microcephaly and short stature should be added to the phenotype of the syndrome. The variable clinical expressivity even among siblings may be an important factor in the paucity of reports on Cohen syndrome.

**735** HLA ANTIGENS IN MUCOCUTANEOUS LYMPH NODE SYNDROME (MLNS). Alan M. Krensky, William Berenberg, Stafford Grady, Karen Shanley, Edmond J. Yunis. Harvard Medical School. Children's Hosp Med Ctr and Sidney Farber Cancer Inst Departments of Pediatrics and Pathology. Boston, Massachusetts.

Associations of specific histocompatibility antigens with certain human diseases may elucidate basic mechanisms of disease. Since there is evidence for a disordered immune response in MLNS, HLA antigens were evaluated by NIGH standard technique in 27 patients (3 Oriental, 1 black) fulfilling CDC criteria for MLNS. In contrast to previous Japanese studies, we found no incidence of HLA-Bw22. We did, however, find a significant increase in HLA-Bw51: CHANCES OF DISTRIBUTION OF HLA PHENOTYPES IN CAUCASIANS

| HLA phenotype | MLNS | | Controls | | Relative risk | p |
|---|---|---|---|---|---|---|
| | n | %positive | n | %positive | | |
| HLA-B5 | 23 | 30.4 | 244 | 4.9 | 8.5 | <0.002 |
| HLA-Bw51 | 23 | 30.4 | 244 | 2.8 | 14.8 | <0.002 |
| HLA-Bw22 | 23 | 0 | 244 | 4.0 | - | N.S. |

To our knowledge, this is only the second disease associated with HLA-B5 specificity. In preliminary studies, 10/17 Caucasian patients with MLNS were DR-2 (frequency in control population 23%, $p<0.01$). In other studies (Geha, et al), suppressor T-cells (OKT8) were found decreased in the acute phase of MLNS. Thus, MLNS, like systemic lupus erythmatosus and multiple sclerosis, is associated with both decreased suppressor cells and DR-2. Such findings may have genetic implications regarding inter-human variation in immune responsiveness. Infectious agents, toxins, or endogenous immune stimulation may trigger, in genetically susceptible persons, an inappropriate immune response.