700 CYSTIC FIBROSIS (CF) FACTOR - AN ABNORMAL SERUM GLYCOPEPTIDE. Miriam G. Blitzer and Emmanuel Shapira. Tulane University School of Medicine. The Hayward Genetics Center.Departments of Pediatrics and Pathology.New Orleans.

A CF-specific peptide affecting the rhythmic beat of cilia from rabbit tracheal explants and oyster gills has previously been partially purified and characterized. In the present study, a glycopeptide (molecular weight about 6000) was purified to homogeneity from sera of controls and CF patients. Both the CF and control glycopeptides were characterized by the absence of aromatic amino acids and were rich in lysine. The carbohydrate moiety of both was deficient in sialic acid and contained mannose and glucosamine. The purified glycopeptides were diluted in phosphate buffered saline, and the ciliary dyskinetic activities were compared in a double-blind fashion. Two preparations of the CF glycopeptide (1 µg/ml) revealed ciliary dyskinetic activity, whereas four control preparations did not alter ciliary rhythm, even at 50 µg/ml. The CF purified glycopeptide (10 µg/ml) caused dyskinesia within 30 seconds with swelling and accumulation of mucus-like droplets. A volcano-like appearance (see insert) was observed at a mucus gland. The glycopeptide from controls revealed no mucociliary activity and was indistinguishable from controls in medium. Abnormalities of glycoprotein metabolism have been suggested as an underlying defect in CF; the mucociliary activity of the CF glycopeptide might be part of such a generalized phenomenon. (Supported by the Cystic Fibrosis Foundation.)

701 CHROMOSOMAL VARIANTS IN HABITUAL ABORTION. Bruce D. Blumberg, Jeffery D. Shulkin, Jerome I. Rotter, T. K. Mohandas, Michael M. Kaback. Harbor-UCLA Medical Center, Division of Medical Genetics, Torrance, CA.

Parental balanced translocations are one etiologic factor in habitual abortion, and it also has been suggested that heterochromatic chromosomal variants, such as the "long Y," may be associated with recurrent fetal wastage. Such possible relationships were investigated by examining Q-banded lymphocyte karyotypes in 99 women (and 81 of their mates) with a history of 2 or more spontaneous pregnancy losses; couples with a previous malformed abortus or child were not included. Amniocyte karyotypes were used as controls; these were randomly selected from an amniocentesis series coinciding with the study period of 1976-1980. Control parental histories were negative for pregnancy loss. All karyotypes were evaluated without knowledge of subject's reproductive histories.

In 7 of the 180 parents of abortuses, a gross chromosomal anomaly was found (6 translocations, 1 mosaic). When quantitative polymorphisms were examined, there was a significant (t test) difference between cases and controls in the length of the centromeric heterochromatic region of chromosome 16 ($p<.05$ for females; $p<.01$ for males). Cases did not differ from controls in Y chromosomal length, in the lengths of the heterochromatic regions of chromosomes 1 or 9, or in the frequencies of the qualitative polymorphisms studied (3c,4c,13p,13s,14p,14s,15p,15s,21p,21s,22p,22s).

These results suggest an association between recurrent fetal loss and the heterochromatic polymorphism of chromosome 16. These data do not support the previously reported relationship of Y chromosomal length to habitual abortion.

703 DE NOVO 9:11 TRANSLOCATION IN A SPORADIC CASE OF TRICHO-RHINO PHALANGEAL (I) SYNDROME Carol W. Booth and William F. Maurer (Spon. by Celia Kaye, Lutheran General Hospital, Dept. of Pediatrics, Park Ridge, IL)

Tricho-rhino phalangeal syndrome (TRPS) is a multisystem malformation complex characterized by dysmorphic features, unusual hair, mild mental retardation and specific skeletal anomalies. Both autosomal dominant and autosomal recessive forms have been described. We have recently seen a 14-year-old white female with classic findings of this condition. Height was 134.3 cm (<<3%). The nose was pear shaped. Hair was sparse and grew slowly. The fingers were deviated at the proximal interphalangeal joints; x-rays showed cone-shaped epiphyses at the bases of the middle phalanges. She complained of right hip pain; x-rays showed findings compatible with avascular necrosis of the femoral head (Legg Perthes disease), a common finding in TRPS. There were no exostoses or nevi. The girl has learning difficulties and attends special education classes, but has normal intelligence. The parents and two brothers are unaffected. Chromosome study revealed a 46,XXt(9;11)(p22:q21) karyotype. Both parents have normal karyotypes. The concurrence of a sporadic case of a genetic condition and a de novo chromosomal translocation in a single patient suggests a possibly causal relationship. Chromosome markers have been described in Prader Willi syndrome and in hereditary bilateral retinoblastoma, two conditions which sometimes demonstrate Mendelian patterns of inheritance. Further patients need be studied to determine the usefulness of chromosome markers in TRPS.

● **704** ISOLATION OF DNA SEGMENTS FROM THE HUMAN X CHROMOSOME Gail A.P. Bruns, James F. Gusella, Cheryl Keys, David Housman, Park S. Gerald. Harvard Medical School, Children's Hospital Medical Center, Department of Pediatrics and Massachusetts Institute of Technology, Department of Biology, Boston and Cambridge.

We have utilized the methods of Gusella et al (PNAS 77, 2829, 1980) to isolate DNA segments from the human X chromosome. DNA was prepared from a human-Chinese hamster hybrid cell line containing the human X and essentially no other human chromosome. This DNA was ligated to phage DNA, the recombinant phage encapsulated and grown in E.coli. The plaques were exposed to labelled whole human and Chinese hamster DNA. Plaques which did not anneal with Chinese hamster DNA but did anneal with human DNA were isolated. The human DNA segments were recovered from these selected recombinant phage and tested for their ability to anneal with DNA from hybrid cells containing various human chromosomes. Six different recombinant phage have been studied sufficiently to demonstrate that they contain human DNA which is complementary to the human X and apparently to no other human chromosome. Further studies with hybrid cells containing known portions of the human X indicate that the recombinant DNA segments are derived from specific regions of the X. The methods utilized are efficient and demonstrate the feasibility of isolating a large number of DNA segments from the human X. These segments are suitable for detecting DNA polymorphisms and for study of X chromosome inactivation. (Presented in part to the Association for Research in Nervous and Mental Disease, December 5, 1980.)

● **702** CLONING OF cDNA FOR HUMAN ARGININOSUCCINATE SYNTHETASE (ASS) mRNA AND STUDIES OF ENZYME OVERPRODUCTION. Hans-Georg Bock, Tsung-Sheng Su, William E. O'Brien, and Arthur L. Beaudet, Baylor College of Medicine, Department of Pediatrics, Houston, TX.

In order to study mRNA and DNA alterations in citrullinemia and to explore the basis of metabolite regulation and enzyme overproduction in cultured cells, we have isolated cloned cDNA for ASS. The human cell line RPMI-2650 (wild type, wt) was used to isolate canavanine resistant (Can^r) variants which overproduce the enzyme. Activity of ASS in nmol/min/mg protein was as follows: wt cells grown in arginine medium, 0.14; wt cells grown in citrulline medium, 0.86; and Can^r cells grown in either medium, 25.0. Immunological studies indicated similar relative differences in amounts of enzyme antigen. A marked increase in translatable mRNA for ASS was demonstrated in Can^r cells. A sucrose gradient fraction of mRNA from Can^r cells was used to synthesize cDNA which was cloned in pBR322. A near full length cDNA clone for ASS was identified by differential filter hybridization and the identity confirmed by plasmid selected mRNA translation. Dot hybridizations and blot hybridizations after agarose gel electrophoresis demonstrated increased amounts of hybridizable mRNA proportional to the increase in enzyme activity in Can^r cells. The patterns of restriction digestion of genomic DNA from wt and Can^r cells were indistinguishable. The patterns were complex and suggestive of more than 1 or 2 gene copies. The data suggest that a regulatory difference between Can^r and wt type cells allows a major change in mRNA accumulation without gene amplification.

● **705** BIOCHEMICAL CHARACTERIZATION OF PERINATAL LETHAL OSTEOGENESIS IMPERFECTA (OI) AND ITS PRENATAL DETECTION. P.H. Byers, G.S. Barsh, K.E. Peterson, J.H. Phillips, J. Shapiro, K.A. Holbrook, L.S. Levin, D.W. Rowe. (Spon. by C.R. Scott). U. of Washington, Seattle; Johns Hopkins U., Baltimore; U. of Connecticut, Farmington.

Perinatal lethal OI is characterized by severe bone fragility with in utero fracture & death in the perinatal period. Fibroblasts from 4 affected infants that we studied failed to secrete type I procollagen normally. In one case a structural mutation in one of the proα1(I) chains of type I procollagen prevents secretion of molecules which contain that chain. The basis of abnormal secretion in the other strains is not yet clear. We have now studied collagen metabolism in cells derived from an affected fetus detected by prenatal ultrasound and x-ray examinations. Amniotic fluid cells & dermal fibroblasts from the affected infant failed to secrete a substantial proportion of the type I procollagen they synthesized during 6, 12 & 18 hour labeling periods while appropriate control cells secrete virtually all the procollagen synthesized in the same periods. Ultrastructural examination of skin from the infant indicated that epidermal structures were normal but that there was a paucity of collagen in the dermis. These studies indicate that the perinatal lethal form of OI is due to a variety of defects that lead to decreased secretion of type I procollagen. The disorder can be detected prenatally by ultrasound examination & the diagnosis confirmed by x-ray & by study of collagen metabolism in affected cells.