125

STAGE-RELATED EXPRESSION OF HUMAN HOMEOBOXES GENES DURING DIFFERENTIATION OF CACO-2 CELL LINE.

G.Sebastio, M.D'Esposito*, M.Montanucci*, S.Auricchio and E.Boncinelli*. Dept. of Paediatrics,2nd School of Medicine,Naples,Italy; *International Institute of Genetics and Biophysics, C.N.R.,Naples,Italy.

Homeobox genes (Hox genes) control segmentation and segment specificity in Drosophila. Hox genes have been detected in several species from insects to vertebrates. Differential and stage-related expression has been observed in human embryonic tissues as well. We have investigated whether the cell line Caco-2 expresses Hox genes. Caco-2 is a cell line derived from a human colon carcinoma and exhibits a spontaneous enterocytic differentiation after cellular confluency in vitro. At 7, 14, 21 days after confluency we have found that Hox-2.3 and one Hox-3 hybridize to poly(A)$^+$ RNA with a stage-related fashion. Moreover, the 21 days pattern of hybridization resembles that one observed in normal adult human small intestine. We suggest that Caco-2 differentiation may be associated to specific activation of Hox genes. Finally, Caco-2 cell line represents a model to further investigate the role of Hox genes in intestinal development.

126

CLINICAL SPECTRUM AND MOLECULAR BASIS OF STEROID SULPHATASE DEFICIENCY.

Ballabio A, Carrozzo R, Parenti G, Sebastio G, Persico MG, Andria G.
Dpts of Pediatrics, Univ. of Naples and Reggio Calabria and Intern. Inst. of Genetics and Biophysics, Naples, Italy.

A deficiency of steroid sulphatase (STS) is the basic defect of X-linked ichthyosis (XLI) (1). We examined 21 Italian patients with STS deficiency belonging to 14 unrelated families. The patients studied were affected by: 1) XLI classical type (10 families), 2) XLI associated with Kallmann syndrome (2 families), 3) XLI with Becker muscular dystrophy (1 case), and 4) XLI with an X/Y translocation (1 case). We used a human STS cDNA probe, previously isolated by the immunoscreening of a λgt11 cDNA library (2), to investigate the molecular defect involved in our patients. The Southern blotting analysis of patients' DNA, using the STS cDNA sequence as probe, revealed in all cases a deletion of the STS gene, thus suggesting that a gene deletion is the most common molecular defect in STS deficiency, at least in Italy. REFERENCES: (1)Shapiro et al., Lancet 1978, ii, 456 (2) Ballabio et al., P.N.A.S. in press.

127

PLATELET CONTENT OF PHENYLALANINE (PHE) AND TYROSINE (TYR) SUCH AS PLATELET UPTAKE OF ^{3}H-PHE AND ^{3}H-TYR IN CHILDREN SUFFERING FROM PHENYLKETONURIA (PKU).

L.H.Rolf, K.Ullrich+, G.Kurlemann+, U.Nieder, P.Huynh
Departement of Neurology and Pediatrics+; University of Münster.

Phe was significantly increased ($p<0,025$) and Tyr decreased ($p<0,05$) in platelets (pl.) from patients with PKU as compared to that of controls (2 - 14 years; HPLC-method). No correlation was found to serum Phe/Tyr content. Amino acids calculated to pmol/10^8 platelets:

PKU	(n = 28	Phe: 6,0 ± 2,8	Tyr: 4,9 ± 1,2
contr.	(n = 25)	Phe: 4,9 ± 2,1	Tyr: 6,4 ± 2,9

The in vitro uptake of ^{3}H-Phe and ^{3}H-Tyr by platelets showed saturation kinetics. The uptake of ^{3}H-Tyr was not influenced by platelet Phe content. The relative release of ^{3}H-Tyr from preincubated platelets was the same in the PKU and control group. The values of maximal ^{3}H-Phe- and ^{3}H-Tyr-uptake in PKU patients and controls were as followed (calculated to pmol amino acid/10^8 platelets):

PKU	(n = 8)	Phe: 538 ± 207	Tyr: 731 ± 313
contr.	(n = 12)	Phe: 610 ± 198	Tyr: 953 ± 351

Our data indicate that the amino acid transport of Tyr into platelets o children with PKU is reduced. The reduced concentrations of dopa/dopamine in the CSF of these patients may be partially the result of an intracellular lack of the precursor tyrosine.

128

A DELETION IN ONE PRO-ALPHA1(III) COLLAGEN GENE IN EHLERS-DANLOS SYNDROME TYPE IV

A.Superti-Furga, R.Gitzelmann, and B.Steinmann
Dept. of Metabolism, University Children's Hospital, CH-8032 Zurich, Switzerland

We have previously reported a now 23-year-old patient with a long history of bleeding due to dominantly inherited Ehlers-Danlos syndrome type IV ("vascular" type) whose fibroblasts produced a structurally abnormal type III collagen with shortened triple-helical structure (Superti-Furga et al.,Pediat Res 20:1043,1986). Immunoblot analysis of proto-alpha1(III) chains in his fibroblasts identified a normal-sized species and an additional species of lower molecular weight. Similarly, Northern blots probed with cDNAs for type III collagen showed equal quantities of a normal and a mutant mRNA for type III collagen, the mutant mRNA being 600 bp shorter than the normal one. Southern blots probed with genomic clones for type III collagen showed an abnormal pattern, best explained by a multi-exon deletion of approx. 3 kb in the middle of the gene, within the triple-helical coding region. This is the first description of a mutation in the human alpha1(III) collagen gene.
(Genomic clones courtesy of Dr.F.Ramirez, SUNY Medical School, New York, USA)

129

Epidemiology of Down's syndrome in Southern Poland. J.J.Pietrzyk,B.Majerska, Ist Department of Pediatrics, Institute of Pediatrics, Kraków, Poland.

All live and still-born newborns were registered in five regions of Southern Poland. A population of 33120 newborns was ascertained. This group constitutes of 54 infants with Down's syndrome, giving the birth prevalence of 1.63/1000. The occurence risk depended neither on pregnancy order nor paternal age, both standardized for maternal age. The latter standardized for pregnancy order significantly influenced the risk of Down's syndrome($X^2_1=37.6$ $p<0.0005$). The distribution of incidence and relative risk of Down's syndrome depending on maternal age revealed the "J" shaped pattern, beign highest beyond the age 45 (53/1000 and RR=42.25). No association between the prevalence of Down's syndrome and parental occupation was found. Also the distribution of probands' birthdates revealed no significant seasonal trend. Highest standardized incidence of the disease /2.6/1000/ was observed for the Oświęcim region a typically industrial area. The relative risk of bearing a child with Down's syndrome in this region in comparison to the remaining population was RR=1.9 ($X^2_1=5.03$).

130

LINKAGE OF DNA MARKERS ON CHROMOSOME 13 WITH WILSON DISEASE

RHJ Houwen[1], H Scheffer[2], GJ te Meerman[2], D Penninga[2], J Fernandes[1] and CHCM Buys[2].
[1] Dept of Pediatrics, University Hospital Groningen
[2] Dept of Human Genetics, University of Groningen

Wilson disease (WD) is an autosomal recessive disorder, characterized by massive copper deposition in the liver, basal ganglia and other organs,due to an impairment of biliary copper excretion. The basic defect in WD is still unknown. Recently a linkage has been reported between the gene for WD and the esterase D locus in a large inbred Israeli-Arab kindred. This implies that the q14 band of chromosome 13 would be the location of the WD gene, at least in part of the Middle East population.
To examine this assignment we are now studying a number of unrelated WD families of Caucasian origin. Linkage studies are carried out using a cDNA probe of esterase D and random probes from a chromosome 13 library; among them one from the relevant chromosomal segment 13q14. Preliminary results are from a first seven Dutch WD families, with 35 children classified as affected or normal based on serum copper, ceruloplasmin and 24h urinary copper excretion.In these families one recombinant was found for the two probes localized in 13q14.A positive lodscore was obtained for both probes corroborating the assignment of the WD gene to band q14 of chromosome 13 and suggesting absence of heterogeneity.