235 AN ALTERED HPRT PROTEIN, CREATED BY AN IN VITRO MUTAGENESIS OF THE GENE, CAN BE RECOGNIZED SPECIFICALLY BY AN ANTIPEPTIDE ANTIBODY. Jiing-Kuan Yee, Douglas J. Jolly and Theodore Friedmann. University of California, San Diego, School of Medicine, Department of Pediatrics, La Jolla, CA.

Lesions in hypoxanthine guanine phosphoribosyl transferase (HPRT) gene are associated with the devastating Lesch-Nyhan syndrome and forms of gouty arthritis in human patients. We are interested in developing a retroviral vector by which the human HPRT gene can be introduced into mice, and its expression can be detected by immunocytochemical methods. Due to the nearly identical amino acid sequences of mouse and human HPRT, antibodies against human HPRT cross react with mouse HPRT. To overcome this problem, we constructed a retroviral vector which codes for a mutated HPRT protein by site-directed in vitro mutagenesis. The termination codon of human HPRT gene was mutated so that six extra amino acids (glu-asp-glu-ser-ser-ser) are added to the C-terminus of normal HPRT protein during translation. In DNA transfection, the mutated protein worked as well as the normal protein in rescuing HPRT$^-$ cells during HAT selection. The isoelectrofocusing point of this mutated protein is also altered on gels due to the addition of three acidic amino acids. A polyclonal antibody, directed against the last eight amino acids of C-terminus of the mutated protein, was raised. In immunoprecipitation this antibody can bring down the mutated human HPRT protein, but not normal human HPRT protein or mouse HPRT protein.

236 INDUCTION OF COMPLETE REMISSION IN T-ALL BY DEOXYCOFORMYCIN (dcf) AND ARA-A. Alice L. Yu, John Mendelsohn, Steve Matsumoto. University of California, San Diego, Department of Pediatrics and Medicine, San Diego, CA., USA.

The combination of dcf and Ara-A was used in a terminally-ill patient with refractory T-ALL who suffered from persistent and recurrent malignant pleural and pericardial effusion and severe lower leg edema secondary to abdominal lymphadenopathy. After 1st course of dcf at 5 mg/m plus continuous infusion of Ara-A at 8 mg/kg/d X 5d, he went into complete hematological remission at 3 weeks, along with resolution of lower leg edema, pericardial effusion, and decreased rate of reaccumulation of pleural effusion. He received a 2nd course with 2 daily injections of dcf plus 3 daily infusions of Ara-A and remained in marrow remission. However, a bone marrow relapse occurred at week 7. He was given two more courses of 3 daily injections of dcf plus 5 daily infusions of Ara-A. Although there was total ablation of ADA activity in the mononuclear cells of both peripheral blood and bone marrow, remission was not achieved. The above treatment was well tolerated with the exception of transient episodes of drowsiness and hallucination which occurred in 3 of the 4 courses. Myelosuppression was mild and transient in all but the 1st course. The serum Ara-A peaked at 12 to 28μM at the end of infusion. Ara-ATP in blood peaked at 47 and 44 nmol/ml in 1st and 2nd course, respectively, and dATP at 190 and 110 nmol/ml, respectively. These findings suggest that the combination of dcf and Ara-A at the given dose is effective and safe for the treatment of T-ALL.

237 IMPACT OF ASSOCIATED MEDICAL CONDITIONS ON CLINICAL FEATURES OF GOUT, Ts'ai-fan Yu, Mount Sinai Medical College, New York, NY 10029

Computer-assisted analyses show 47% of the 2152 patients of gout have associated medical conditions. Hypertension occurs in 25% of the patients; ischemic coronary heart disease, cerebral or peripheral circulatory insufficiency in more than 10%. Proteinuria is present in 20%, with renal insufficiency in <10% Maturity onset type of diabetes is in about 6%. Obesity or hyperlipidemia is found in >30%.

About 1/3 of the patients have one associated medical condition only, 12% with 2, 6% with 3 or more. Mean plasma urate in patients with 0 complication is 9.2±1.5 mg/dl. It steadily increases to 10.2±1.7 mg/dl as complications increase to 3 or more. Tophaceous deposits increase from 25% with 0 complication to 37%, 45% and 51% with increased number of complications; renal calculi increase from 20 to 34%. Increased number of acute gouty arthritis at times becomes protracted. Drugs for gout and for complications sometimes create undesirable side reactions.

Survival rate with long term follow-up shows steady decrease with increasing number of complications. Only 20% of the patients at death had no known complications. When present, they died at earlier ages.

The management of gout nowadays may seem to be simplified. In fact, it is not necessarily so, when one considers the management of the various complications, clinical as well as choice of drugs, etc.

238 PURINE NUCLEOTIDE METABOLISM IN CULTURED RAT SKELETAL AND HEART MUSCLE: A COMPERATIVE STUDY OF THE MECHANISMS OF ATP CONSERVATION. Esther Zoref-Shani, Asher Shainberg, Gania Kesler-Icekson, Lina Wasserman and Oded Sperling, Tel-Aviv Univ School of Medicine, Dept of Chemical Pathology, Beilinson Med Center, Rogoff-Wellcome Med Res Inst and Dept of Clin Biochemistry, Petah-Tikva and Bar-Ilan Univ, Dept of Life Sciences, Ramat-Gan, Israel.

Primary rat skeletal and cardiomyocyte cultures exhibited de novo and salvage synthesis of purine nucleotides. In the myotube cultures, the rate of de novo synthesis was faster but the rate of salvage synthesis from adenosine was slower. The rate of salvage nucleotide synthesis from adenine and hypoxanthine was similar in the two tissues, but was markedly slower than that in cultured fibroblasts. In comparison to the latter cells ,both muscle tissues exhibited low AMP and IMP nucleotidase activity. AMP deaminase activity in the skeletal myotubes was 7-fold greater than that in the cardiomyocytes. The flow of labeling between the nucleotides, gauged during incubation with labeled precursors, was compatible with the above differences in that in the myotube cultures the flow from AMP to IMP dominated whereas in the cardiomyocytes that from IMP to AMP dominated. The results suggest that in the myotubes the activity of the purine nucleotide cycle is intensive but AMP phosphorylation is slow, whereas in the cardiomyocytes, the activity of the nucleotide cycle is relatively slow but the phosphorylation of AMP is prompt.

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