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Hereditary hemochromatosis is a common autosomal recessive disorder of iron metabolism characterized by increased intestinal iron absorption which leads to progressive iron overload and organ dysfunction. The mechanism by which HFE, the product of the hemochromatosis gene, regulates intestinal iron absorption is unknown. Under the hypothesis that HFE should negatively regulate intestinal iron absorption, in this work we studied the effects of HFE expression on iron uptake and transepithelial iron transport in Caco-2 cells. We found that the primary effect of HFE overexpression was a marked reduction of apical iron uptake without modification of cell to basolateral iron transfer. This effect of HFE explains the increased absorption of iron observed in hereditary hemochromatosis.

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Properties of five rare human mutations causing medium chain acyl-CoA dehydrogenase deficiency

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Medium chain acyl-CoA dehydrogenase (MCAD) deficiency is an autosomal recessive disorder, which is known to cause sudden death in young children, and is therefore linked to Sudden Infant Death Syndrome (SIDS). A point mutation, causing lysine to be substituted for a glutamic residue (K304E), is the most prevalent mutation in affected patients, accounting for 90% of the affected alleles. This mutation is thought to be a folding mutation, resulting in incorrect subunit assembly. Other mutations are less common, often only affecting a single patient. Each mutation differs in the severity of the disease. We have cloned five of these rare mutations, Y42H, S220L, R256T, G285R and K304E and have expressed each in E.coli. We are currently investigating the effects of these mutations, to determine the severity of the mutation, and to discover whether as in the case of the K304E mutant, these mutations are also responsible for incorrect folding of the mature protein. Properties of the recombinant mutant enzymes over-expressed with and without chaperonin proteins will be presented.

Thyroid Hormones Function in Dialysis Patients candidates for Transplantation

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Chronic renal failure is one of the cases of moderate to severe euthyroidism which associated with some abnormalities in thyroid hormone metabolism. Dialysis does not significantly normalize the abnormalities, but transplantation leads to an improvement in the conditions. In this study to evaluate the relationship between serum levels of thyroid hormones and transplanted kidney function, first thyroid hormones were measured in 30 patients under dialysis selected for renal transplantation. The results were compared with those obtained from 40 control individuals. After renal transplantation the patients which have been treated with Cyclosporine, Prednisone and Azathioprine, divided into two subgroups according to their serum levels of urea nitrogen, creatinine and kidney function: patients with primary graft function (group I) and patients with delayed graft function (group II). The thyroid hormones were evaluated in two groups. In dialysis patients, the mean levels of measured thyroid hormones were at normal range but comparing with the control, mean levels of these hormones were lower except of T3Up which is increased, and no changes observed in the levels of TSH. Ten days ago graft, reduction in the serum levels of thyroid hormones were observed and elevation of the T3Up was found in both groups. The alterations in group II were more than group I. In the 30th day after graft, changes in group I reached normal levels and comparing with those of before operation marked improvement was noticed, but comparing with that of control the levels of T3, T3T4, T4, and FTI were still low. In the group I1 the levels of T3 and FTI were lower than that of normal and comparing with those of before operation. Reduction in the levels of T4, T3T4, FT4 and FTI was found. It was concluded that there is relationship between the levels of thyroid hormones and function of the transplanted kidney and it is more significant in the cases of T4 and T3.

Importance of Catalse Enzyme in Virulence of Isoniazid Resistant Strains of Mycobacterium Tuberculosis in Guinea-Pigs

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In this study, twenty five strains of Mycobacterium tuberculosis resistant to Isoniazid (INH) were isolated from patients with tuberculosis (TB). Nine strains (36%) were found to be virulent in Guinea-pigs (Root Index Virulence >1). The remaining sixteen strains (64%) were non-virulent (Root Index Virulence <1). Of the nine strains resistant to INH as well as virulent to Guinea-pigs, eight of them were found to be catalase positive and only one strain was catalase negative, whereas the remaining sixteen INH resistant strains were catalase negative. A strong association was observed between INH resistance and catalase positivity and virulence (p<0.0001, Chi Square test). This study support the hypothesis that catalase enzyme has an important role in virulence of INH-resistant strains of M. tuberculosis.