Project Title:

Idiopathic Infantile Hypercalcemia--European-Canadian Consortium

Project Description:

Idiopathic Infantile Hypercalcemia (IIH) is a constellation of diseases which cause episodes of hypercalcemia starting early in life and which can recur for decades. The long-term consequences of the disease are persistent hypercalciuria, nephrolithiasis & nephrocalcinosis. One of the frequent causes of IIH is a loss-of-function in CYP24A1, the enzyme responsible for inactivating the hormonal form of vitamin D, 1,25-(OH)₂D or its immediate precursor, 25-OH-D. Many mutations have now been recognized throughout the structure of the cytochrome P450 protein and many of these have been shown to result in loss of enzyme activity. Approximately 100 IIH patients have been identified with CYP24A1 mutations across Europe, USA, Canada and Australia. A sensitive LC-MS/MS-based assay for 24,25-(OH)₂D₃, one of the principal breakdown products of vitamin D, provides a useful indicator that mutations of CYP24A1 exist in the patient. IIH-ECC is a German, Swiss & Canadian consortium of pediatricians, biochemists and systems biologists studying the IIH disease and its murine model counterpart, the CYP24A1-null mouse. We are investigating better diagnostic methods, the sensitivity of patients/mice to vitamin D intake and triggering mechanisms for the hypercalcemic episodes.