the pathogenesis of calcium pyrophosphate arthropathy and osteoarthritis.

Objectives

Methods A combination of physical cloning and candidate gene approach were employed to define CCAL2. Novel expressed sequence tags (ESTs) with expression in cartilage and which mapped to the critical region were identified from EST databases of GenBank. PCR generated DNA fragments from ESTs were radiolabelled using radioactive phosphorus and used as probes in Southern blot hybridization of high density plasmid artificial chromosome (PAC) filters. PACs were identified following autoradiography of the hybridisation membranes and the selected PACs were supplied by the UK HGMP resource centre in Cambridge. The Online Mendelian Inheritance in Man OMIM cytogenetic map was used to identify possible candidate genes within or near the critical region.

Results Six novel ESTs with high cartilage expression, identified 55 PACs following Southern blot hybridization. End sequencing of the PACs allowed the construction of a contig containing 25 PACs across the critical region. Two candidate genes were identified from OMIM. The first gene TRIO codes for a transmembrane multidomain protein which promotes the exchange of GDP for GTP in the extracellular matrix. An abnormality in this pathway is likely to produce an increase in extracellular triphosphate, which has a key role in inorganic pyrophosphate metabolism. The second gene ANK has only recently been mapped to the same location and it is responsible for articular calcification with associated arthritis in mice.

Conclusion The CCAL2 region has been physically mapped and two strong candidate genes are being screened for possible disease causing mutations. This gene should provide a greater understanding of pyrophosphate metabolism and of osteoarthritis with which there is a common association.

REFERENCE

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OP0115 POLYMORPHISM AT THE TYPE I COLLAGEN (COLIA1) AND RELATIVE RISK OF OSTEOPOROSIS AND VERTEBRAL FRACTURES IN POSTMENOPAUSAL WOMEN

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Background Twin and family studies have demonstrated that an important degree of the population variance in bone mineral density (BMD) is attributable to genetic factors.

Objectives A polymorphism in the collagen type I alpha 1 (COLIA1) gene has recently been associated with low bone mass and fracture incidence.

Methods We analysed the relationship between COLIA1 gene polymorphism, lumbar spine and hip BMD, T-score and fracture incidence in a population of 319 postmenopausal women classified by WHO standards: 98 non-osteoporotic women (NOPW) (57.4 ± 6.2 yrs), 146 osteoporotic women without fracture (OPW without fracture: OPWnF)(60.0 ± 5.2) and 75 osteoporotic women with fracture (OPW with fracture: OPWwF) (61.2 ± 6.3 yrs). The COLIA1 genotype was assessed by polymerase chain reaction and Bal I endonuclease digestion. Genotype

frequencies for the total group were 49.2% "SS" homozygotes, 39.5% "Ss" heterozygotes and 11.3% "ss" homozygotes.

Results We found significant differences in the percentage of homozygous "ss" between NOPW and OPW (6.1% and 13.6% respectively). However, the incidence of genotype "ss" in OPWnF was 6.2% and 28% in OPWwF. We observed no associations between the COLIA1 genotype and lumbar and hip BMD. However, the lumbar spine T-scores were lower in the "ss" group than in the "Ss" and "ss" group. The incidence of fractures (64 vertebral and 11 colles) varied significantly by genotype: "SS" 21.7%; "Ss" 15.9%; and "ss" 58.3% (chi-square = 15.43; p < 0.0001); this resulted in a fracture odds ratio of 5.96 (95% confidence interval 2.26-15.69). Logistic regression analysis of fracture prevalence showed that for prevalent fractures, the women with "ss" group had 4.17 times risk of the woman "SS" + "Ss" groups. When prevalence was adjusted for BMD and T-scores, the respective fracture risk was 2.6 and 2.94 for the "ss" group versus the other genotypes (SS+Ss).

Conclusion A slight association was found between lumbar T-score and gene COLIA1 polymorphism. Expression of the "ss" allele seems to be related with a higher incidence of fracture in postmenopausal women and was independent of bone mineral density.

SAT0099 SOFT TISSUE RHEUMATISM IN IRAQI DIABETIC PATIENTS

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Background MB ChB, DMR(RCP) London.

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Objectives To study the prevalence of soft tissue rheumatism in Iraqi diabetic patients (both IDDM and NIDDM) and to evaluate association between these sequelae and the duration of the disease.

Methods Limited joint mobility (LJM), Dupuytren's Contracture (DC), flexor tenosynovitis (FTS), frozen shoulder (FS) and carpal tunnel syndrome (CTS) were assessed in 100 Iraqi diabetics (50 insulin dependent, 50 non insulin dependent DM) and (50) non-diabetic control matched for age and sex, according to clinical examination (signs and symptoms) and electrophysiological study.

Results Prevalence of LJM, in IDDM vs. NIDDM was (56% vs. 36%), FTS (20% vs. 38%), DC(20% vs 16%), FS(22% vs 40%) and CTS(26% vs 16%).

There was significant statistical difference (p < 0.05) between IDDM and NIDDM, regarding LJM, FS, and FTS, the first was higher in IDDM and the last two were higher in NIDDM, while there was no significant and statistical difference regarding CTS and DC.

Conclusion Soft tissue Rheumatism occurs more frequently in both IDDM and NIDDM than in control (p < 0.05). Their occurrence appeared to be directly related to disease duration regarding LJM, DC and CTS. The most common sequelae in IDDM was LJM while FS was the most frequent abnormality detected in NIDDM.

Patients with IDDM had been found to be more susceptible to develop multiple rheumatic sequelae than patients with NIDDM(p < 0.05).