pressure palsy (HNPP) in one family were identified. The duplication
detection rate for D17S2218 is 15/36, D17S2220 - 28/36, D17S2223 - 17/36, D17S2226 - 11/36 and D17S2229 - 15/36. The high detection
rate of D17S2220 can be explained by the complex structure of the
polymeric marker, which have not only tetra but also dinucleotide
repeat inside. No individual marker was informative in every patient.
However, in all positive cases we were able to detect three different
alleles at least one STR. The described analysis is fast simple and
reliable for pre- and postnatal diagnosis of CMT1A and NHPP in
Belaussian families.

P0934. A coeliac disease genome-wide association study
identifies a novel susceptibility locus
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Coeliac disease is a common (1% prevalence) chronic inflammatory
disease of the small intestine, caused by an immune response to di-
etary wheat, rye and barley. HLA-DQ2 (present in 95% of coeliacics) is
necessary to present wheat epitopes to CD4 T cells, but not sufficient
for disease (present in 30% of the population). Previously, linkage
studies were the only cost-effective way to map and isolate non-HLA
genes contributing to coeliac disease. We have performed a genome-
wide association study and genotyped 310,605 SNPs with minor al-
lele frequency >1% in 778 coeliac cases and 1422 population controls
from the UK using the Illumina HumanHap300 BeadChip. Overall SNP
call rate was 99.87%. An extended region of highly significant associa-
tion was seen around the HLA locus (lg2p<7E-9, P<10-19, OR 7.04
[95% CI 6.08 - 8.15]). Excluding the HLA region, we observed one
other SNP that remained significant after permutation testing (P=2.0 x
10-7, empirical genome-wide significance P=0.045). This finding was
independently confirmed in Dutch and Irish collections (meta-analysis
P=3.8 x 10-11, OR 0.66 [95% CI 0.58 - 0.74]). This SNP maps around a
biologically plausible candidate gene and genetic variation in this
gene may predispose coeliac patients towards unwanted immune re-
sponses to cereal antigens. In addition to the replicated SNP, a greater
number of significant SNPs were observed than expected by chance:
P<10-6 (2 vs 0.3 expected) and P<10-5 (12 vs 3 expected). All SNPs
with P<0.005 are currently followed in multiple independent cohorts.

P0935. A genome-wide linkage scan in an extended Maltese
family with a high incidence of coeliac disease
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Gluten-sensitive enteropathy, or coeliac disease, is an autoimmune
disorder characterized by inflammation, villous atrophy and hyperplia-
sia of the small intestinal mucosa. Coeliac disease is caused by both
environmental and inherited factors. A small number of family based
linkage studies were performed so far, where the HLA locus and other
chromosomal regions were linked with the disease. In this study, link-
age analysis was performed in a Maltese family with a high incidence of
coeliac disease.

A whole genome linkage scan using 400 microsatellite markers was
performed in seventeen family members, four of whom where diag-
nosed as coeliac by biopsy and another two were symptomatic but
were following a gluten free diet. Multipoint parametric and non-par-
metric linkage analyses were performed by EasyLinkage v4.01 using
GENEHUNTER v2.1, assuming dominant and recessive modes of in-
heritance with variable penetrance. Disease allele frequency was
assumed to be 0.001.

Highest NPL (5.27; p=0.0039) and LOD (1.46) scores were observed
to marker D10S1731. NPL and LOD scores of 4.12 (p=0.0313) and 1.46,
respectively, were observed to another marker on chromosome 11p12.
These results were confirmed after fine mapping at these regions. No
evidence of linkage was observed to the HLA region on chromosome
6, where sequencing of HLA-DQA1, DQB1 genes confirmed that nei-
ther DQ2 nor DQ8 HLA heterodimers were found in this family.

These results suggest that non-HLA genes might be responsible for
the onset of coeliac disease in this Maltese family. Further investiga-
tions of the indicated loci are going to be performed by sequencing of
candidate genes.

P0936. COL4A3/COL4A4 mutations in Cypriot families explain
the recurrent hematuria-thin basement membrane nephropathy
phenotype and progress to focal segmental glomerulosclerosis and
occasionally to end stage renal failure. Extended founder effect
phenomena and mutation dating
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Focal Segmental Glomerular Sclerosis is a frequent histological finding
of heterogeneous aetiology caused by primary and secondary clinical
conditions. In 11 families with autosomal dominant inheritance of FSGS
and microscopic hematuria, 372 patients and healthy relatives were
investigated. Linkage analysis was performed with markers around four
chromosome regions and screening for mutations was accomplished by
the SURVEYOR plant endonuclease, followed by automated DNA
sequencing. For locus 2q36 the total LOD score was 7.75, clearly impli-
cating mutations in either the COL4A3 or COL4A4 gene. DNA sequenc-
ing revealed two COL4A3 and one COL4A4 mutations in 90 patients. In
one family there was compound heterozygosity and cosegregation of
two mutations in COL4A3 while two individuals had inherited both muta-
tions and developed the Alport syndrome. Mutation COL4A3 - G1334E
was found in eight families that share a common COL4A3 haplotype,
from three geographic locations of Cyprus. Five are from Kaimakli, a
city near Nicosa, thereby documenting a founder effect. This finding
may prove to explain a high frequency of patient referrals with chronic
renal failure from Kaimakli. Mutation dating suggested that this muta-
tion is about 300 years old. This is the first detailed investigation of
Cypriot families with COL4 pathology with Thin Basement Membrane
and FSGS as a prominent feature. Our data enhance the observation
that isolated microscopic hematuria is not always a benign condition.
Further epidemiological studies are needed in the Cypriot population
for investigating additional founder phenomena and providing proper
genetic counselling in concerned families and practicing physicians.

P0937. The association of a polymorphism within the COLS5A1
gene an Achilles tendon injury in a second Caucasian
population
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As many as 30-50% of sports injuries are tendon injuries of which a
large proportion are Achilles tendon injuries (ATI). The exact mecha-
nism underlying ATI are poorly understood, however it is widely ac-
ccepted that ATI is a result of the condition caused by the interaction
of both intrinsic, which includes a genetic component, and extrinsic
risk factors. Our group has reported an association between polymor-
phisms within the COLS5A1 gene with ATI in a physically active Cauca-
sian population. COLS5A1 codes for a polypeptide component of type V
collagen which is involved in the regulation of fibrillogenesis. The aim
of this study was therefore to repeat this previous association study
within a second Caucasian population.

The study comprised 152 Caucasian individuals from Australia, of
whom 91 were diagnosed with ATI and 61 asymptomatic control (CON)
individuals. The BstUI restriction fragment length polymorphism was
used to genotype all the individuals for the C>T transition at nucleotide
414 of exon 66 of COLS5A1 (rs12722).

There was a significant difference in the allele frequencies of the CO-
L5A1 BstUI RFLP between the ATI and CON subjects (p<0.001). The
frequency of the TC genotype was significantly higher in the ATI group