

IFN- γ , TGF- β AND IL-10 CYTOKINE POLYMORPHISMS IN CADAVERIC KIDNEY DONORS AND RECIPIENTS

WELSH BLOOD SERVICE

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Table 1. IFN- γ intron 1 microsatellite (CA repeats) phenotype and genotype frequencies

IFN- γ allele	Phenotype frequency (%)	Gene frequency
1	00.0	0.000
2	69.8	0.449
3	67.1	0.442
4	11.4	0.057
5	10.1	0.050
6	0.5	0.002

IL-10 allele frequencies were:

-3575	A = 0.41946	T = 0.58054
-1082	A = 0.50336	G = 0.49664
-592	A = 0.23937	C = 0.76063

Based on a significantly positive Δ value ($p_{\text{corr}} < 0.002$) three IL-10 3575/1082/592 haplotypes were identified (Table 2).

Table 2. 3-locus IL-10 -3575, -1082 -592 haplotypes with significant Δ values ($p < 0.01$)

-3575	-1082	-592	HF(x100)	Δ value
A	G	C	41.3	0.26
T	A	C	28.4	0.05
T	A	A	23.5	0.16

Frequencies of the TGF- β alleles were:

nt869	C = 0.33781	T = 0.66219
nt915	C = 0.07606	G = 0.92394

Only 3 of 4 TGF- β nt869/915 haplotypes were identified. The TC haplotype was not detected and TG was the most common with a HF of 84.8% (Table 3).

Table 3. TGF- β nt869/915 haplotypes

TGF- β haplotype	Phenotype frequency (%)	Gene frequency
CC	14.5	0.075
TG	84.8	0.667
CG	41.6	0.258

Comments

This large study generally confirms the findings of others and further validates our typing methodology. It also substantiates the quality of this data which now provides a platform to study the influence of these cytokine polymorphisms in renal transplantation.

Introduction

As part of a study of the influence of HLA and cytokines on the course and survival of renal allografts we typed a group of cadaveric kidney donors and recipients for IFN- γ intron 1, TGF- β nt869 and nt915, and IL-10 -3575, -1082 and -592 alleles.

Each of these cytokines plays a different role in the immune response. IL-10 is an anti-inflammatory cytokine and B cell proliferation factor, IFN- γ promotes the inflammatory response and upregulation of MHC expression whilst TGF- β plays a central role in the response to injury and repair.

Polymorphisms within these genes have been linked to differential production of the cytokine and/or increased rejection in solid organ transplants.

Methods

447 cadaveric donors and recipients were typed for the IFN- γ intron 1, TGF- β nt869 and nt915, and IL-10 -3575, -1082 and -592 alleles.

The microsatellite alleles (CA repeats) in intron 1 of IFN- γ were identified using PCR amplification and electrophoresis on a non-denaturing polyacrylamide gel.

TGF- β nt869 and nt915 and IL-10 -3575, -1082 and -592 single nucleotide polymorphisms were typed using PCR-induced heteroduplexes with TGF- β nt869 and nt915 polymorphisms identified in *cis*-linkage.

For IL-10 we calculated -3575, -1082, -592 gene and 3-locus haplotype frequencies (by maximum likelihood) and linkage disequilibrium (Δ) values and their significance. Phenotype and gene frequencies for IFN- γ and TGF- β were determined by direct counting.

Results

There was a good fit to Hardy-Weinberg equilibrium and the proportion of homozygotes was as expected (all p values > 0.2).

Five of the six known IFN- γ alleles were detected with the gene frequency ranging from 0.00224 to 0.44855 (Table 1). Alleles 2 and 3 were the most common with a phenotype frequency of 69.8% and 67.1%, respectively. Allele 1 was not detected.