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Courtney, A. E., Patterson, C., & Maxwell, A. (2008). Heme Oxygenase-1 gene promoter polymorphisms and outcomes of clinical renal transplantation. *American Journal of Transplantation*, 8(5), 1079-1079.
<https://doi.org/10.1111/j.1600-6143.2008.02218.x>

Published in:
American Journal of Transplantation

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Letter to the Editor

Heme Oxygenase-1 Gene Promoter Polymorphisms and Outcomes of Clinical Renal Transplantation

To the Editor:

Hribova and colleagues (1) correctly point out the limitations of association studies in identifying effects of genetic variants on renal transplantation outcomes. They report no evidence for association between heme oxygenase-1 (HO-1 or HOX1) -413 A/T promoter polymorphism (rs2071746) and graft failure in 343 Caucasian donor/recipient pairs, in whom 147 grafts failed within 5 years.

From their sample size calculations, which are based on the odds ratios (OR) rather than the more appropriate hazard ratio (HR), they suggest that 382 cases (graft failures) and 382 controls (functioning grafts) at 5 years are necessary to detect an OR of 1.6, so unfortunately their own data were also underpowered.

Table 1 summarizes the four studies now published in regard to HO-1 gene polymorphisms and outcomes in clinical renal transplantation. Our study remains the largest cohort examined to date (2).

We would like to highlight that the lower 95% confidence limits for the HRs reported in our study (2) are not consistent with the S-allele providing even modest protective effects in renal transplantation. Carriage of an S-allele by the donor gave a HR of 0.89 (95% CI 0.71–1.11) for graft survival and a HR of 0.89 (95% CI 0.67–1.18) for recipient survival indicating that our results are not consistent with a HR for carriage of the S allele of less than 0.67 (or equivalently a HR for noncarriage of greater 1.5). For the recipient genotype the corresponding values were 1.19 (95% CI 0.95–1.48) and 1.22 (95% CI 0.93–1.62) so our results

are not consistent with an HR for carriage of the S allele of less than 0.9 (or equivalently a HR for noncarriage of greater than 1.1).

We did not 'reject the effect of the polymorphism' as suggested by Dr. Hribova and colleagues (1) but rather we concluded that our results provide no evidence for a protective effect for the S-allele, of the HO-1 gene promoter polymorphism, on graft or recipient survival following renal transplantation.

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Table 1: Studies considering the association between HO-1 gene promoter polymorphisms and outcomes in clinical renal transplantation

Study	Date	Polymorphism	Number	Follow-up	Outcome measure	Result
Exner (3)	2004	(GT) _n	101*	2 yr	1-yr creatinine	donor S-allele advantageous
Baan (4)	2004	(GT) _n	387 [†]	4.1 yr [‡]	5-yr graft survival	donor S-allele advantageous
Courtney (2)	2007	(GT) _n	707 [†]	8.2 yr [‡]	graft + recipient survival	no significant effect
Hribova (1)	2008	-413 A/T	343 [†]	unknown	5-yr graft survival	no significant effect

*Donor genotype only; [†]each of donors and recipients; [‡]median.