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Letter to the Editor

SLCO Transport Genes in Prostate Cancer—Response

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We thank Figg and colleagues for their interest in our manuscript (1) and their comments about the potential role of organic anion–transporting polypeptide (OATP) transport proteins in prostate cancer outcomes. Consistent with findings reported by Hamada and colleagues (2), Sharifi and colleagues (3), and Yang and colleagues (4) in studies of men with advanced prostate cancer receiving androgen deprivation therapy (ADT), we show that a high-testosterone import allele of *SLCO1B3* SNP rs4149117 is also associated with an increased risk of prostate cancer–specific mortality (PCSM) in a population-based study of incident prostate cancer cases. Although the associated HRs in each study are small, the consistency of the observation is striking given the differences in the prostate cancer populations under evaluation.

As discussed by Figg and colleagues in their letter, our work and the work by Yang and colleagues (4) reported different findings for the *SLCO2B1* SNP rs12422149 [which encodes for a dehydroepiandrosterone (DHEA) sulfate (DHEAS) transporter]. Whereas Yang and colleagues observed a more rapid time to progression on ADT in men bearing a high-DHEAS import allele of *SLCO2B1* SNP rs12422149, we observed an increased risk of PCSM in men bearing the low-import allele. Certainly, differences could be due to chance alone, and a major challenge of this type of work has been the inconsistent confirmatory findings of SNP studies. As previously discussed, our study evaluated a different cohort of patients from those analyzed by Yang, Hamada, and Sharifi, and the role of OATP proteins over the entire life of the patients in our population may vary from that observed in patients with advanced disease on ADT. We agree with the statement of Figg and colleagues that DHEAS uptake by OATP2B1 is likely most important in men with reduced circulating androgens. Furthermore, while the men who died of prostate cancer in our study likely were on ADT at time of death, we also agree that DHEAS uptake is unlikely to be the mechanism by which this *SLCO2B1* SNP is associated with PCSM under these conditions.

Steroids represent a small subset of the wide range of endogenous and exogenous substrates transported by OATP proteins, including agents such as statins, cardiac glycosides, glitazones, metformin (and even taxanes; refs. 5, 6), all with known or postulated impacts on prostate carcinogenesis and/or progression (7–13). Given the lengthy natural history of prostate cancer in men with localized disease receiving definitive therapy (in our study, 59% of cases underwent prostatectomy and 27% radiation), genetic variation in uptake and exposure to agents, such as these, represent alternative hypotheses for the impact of OATP transporters on prostate cancer outcomes. We look forward to further studies delineating the mechanisms and contribution of *SLCO* genes to prostate cancer biology and outcomes.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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