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SLCO POLYMORPHISMS CONFER RISK OF DISEASE PROGRESSION AND DEATH FROM PROSTATE CANCER - LETTER

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A report by Wright and colleagues evaluated genetic variation in *SLCO1B3* and *SLCO2B1* versus outcomes in prostate cancer (1). Their major findings were: (i) *SLCO1B3* and *SLCO2B1* were highly expressed in castration-resistant prostate cancer (CRPC) metastases versus untreated controls; (ii) no SNPs in *SLCO2B1* or *SLCO1B3* were related to the risk of prostate cancer recurrence/progression; and (iii) that the *SLCO2B1* (rs12422149A>G; "A" allele) and *SLCO1B3* (rs4149117) were related to increased risk of prostate cancer specific mortality (PCSM).

In 2008, we showed that a *SLCO1B3* polymorphism (rs4149117; Ser112Ala) resulted in decreased testosterone import, and that OATP1B3 (encoded by *SLCO1B3*) was overexpressed in prostate tumors versus normal tissues; we recently validated the latter result (2, 3). Subjects with prostate cancer carrying 112Ala also had slower disease progression during androgen deprivation therapy (ADT) and improved overall survival after prostate cancer diagnosis (2, 4). Larger studies by Wright *et al.* and Yang *et al.* are consistent with our findings where OATP1B3 112Ala is again related to slower prostate tumor progression on ADT (5) and improved CRPC survival (1).

Data pertaining to *SLCO2B1* polymorphisms are not consistent. Yang *et al.* (5) demonstrated that DHEA uptake and growth rate was greater in cells expressing OATP2B1 312Glu (encoded by the rs12422149 "G" allele in *SLCO2B1*), than cells expressing the 312Arg isoform (encoded by the "A" allele). Men carrying the "G" allele also had shorter time to progression during ADT that was attributed to increased intratumoral DHEA. On the other hand, Wright *et al.* did not observe a difference in progression while they did observe an increased risk of PCSM with the "A" allele (instead of the "G" allele).

Wright *et al.* state that the difference between the studies arose because they were studying eugonadal men while Yang *et al.* studied castrated men. Since Wright *et al.* evaluated PCSM, it is likely that the vast majority of these men did actually receive castration therapy prior to death; still, there was a greater proportion of men with GA or AA alleles in the PCSM cohort. Moreover, Wright *et al.* included men progressing following prostatectomy or radiation therapy into the progression cohort with those receiving androgen deprivation therapy (ADT); Yang et al. only evaluated progression on ADT.

Therefore, the relationship between the *SLCO1B3* rs4149117 SNP and prostate cancer outcomes is consistent with previous data presented by us (2, 4, 5), and data pertaining to *SLCO2B1* polymorphisms are not consistent.

References

1. Wright JL, Kwon EM, Ostrander EA, Montgomery RB, Lin DW, Vessella R, et al. Expression of SLCO transport genes in castration-resistant prostate cancer and impact of genetic variation in SLCO1B3 and SLCO2B1 on prostate cancer outcomes. Cancer Epidemiol Biomarkers Prev. 20:619–27. [PubMed: 21266523]
2. Hamada A, Sissung T, Price DK, Danesi R, Chau CH, Sharifi N, et al. Effect of SLCO1B3 haplotype on testosterone transport and clinical outcome in caucasian patients with androgen-independent prostatic cancer. Clin Cancer Res. 2008; 14:3312–8. [PubMed: 18519758]
3. Pressler H, Sissung TM, Venzon D, Price DK, Figg WD. Expression of OATP Family Members in Hormone-Related Cancers: Potential Markers of Progression. PLoS One. 6:e20372. [PubMed: 21625523]
4. Sharifi N, Hamada A, Sissung T, Danesi R, Venzon D, Baum C, et al. A polymorphism in a transporter of testosterone is a determinant of androgen independence in prostate cancer. BJU Int. 2008; 102:617–21. [PubMed: 18537956]
5. Yang M, Xie W, Mostaghel E, Nakabayashi M, Werner L, Sun T, et al. SLCO2B1 and SLCO1B3 May Determine Time to Progression for Patients Receiving Androgen Deprivation Therapy for Prostate Cancer. J Clin Oncol.