Editorial:

RELEVANCE OF GENETIC DISPOSITION VERSUS ENVIRONMENTAL EXPOSURE FOR CANCER RISK: AN OLD CONTROVERSY REVISITED WITH NOVEL METHODS

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An old debate has been revisited using a novel technique (Schwender et al., 2012): is genetic predisposition or environmental exposure more relevant for cancer risk? In this context urinary bladder cancer represents a particularly well-studied example (Golka et al., 2012a, b; Roth et al., 2012; Ovsiannikov et al., 2012). The environmental influence on bladder cancer risk has been clearly documented for cigarette smoking and occupational exposure to aromatic amines and polycyclic aromatic hydrocarbons - both representing the most important factors (Golka et al., 2009; 2012a, b). Recently, several single nucleotide polymorphisms have also been identified that are associated with urinary bladder cancer risk, all of which have been confirmed in independent follow-up studies (Kiemeney et al., 2008, 2010; Rothman et al., 2010; Rafnar et al., 2011; Lehmann et al., 2010; Golka et al., 2011; Selinski et al., 2012a, b; Binder et al., 2012). In total 13 novel SNPs have been identified, as recently summarized (Selinski et al., 2012a, b).

Using a novel technique for interaction analysis Schwender et al. (2012) have now calculated an 'overall genetic risk' based on the interactions of the high risk alleles of recently identified genetic variants. The highest stable combination resulted in an odds ratio of 2.0, a ratio that is still lower

than the odds ratio of cigarette smoking which was 3.28 for the current smokers of the study population. However, both odds ratios are still low compared to some of the worst cases of occupational exposure, for example an odds ratio of 5-200 has been reported for workers exposed to betanaphtylamine, and 38-90 for 4-chloro-otoluidine-exposed individuals. The study of Schwender et al. (2012) is of interest to all who interested in the direct comparison of environmental and genetic influences on cancer risk.

REFERENCES

Binder H, Müller T, Schwender H, Golka K, Steffens M, Hengstler JG et al. Cluster-localized sparse logistic regression for SNP data. Stat Appl Gen Mol Biol 2012;11(4): article 13.

Golka K, Hermes M, Selinski S, Blasz-kewicz M, Bolt HM, Roth G et al. Susceptibility to urinary bladder cancer: relevance of rs9642880[T], GSTM1 0/0 and occupational exposure. Pharmacogen Genom 2009;19:903-6.

Golka K, Selinski S, Lehmann ML, Blasz-kewicz M, Marchan R, Ickstadt K et al. Genetic variants in urinary bladder cancer: collective power of the "wimp SNPs". Arch Toxicol 2011;85:539-54.

Golka K, Kopps S, Prager HM, Mende S v, Thiel R, Jungmann O et al. Bladder cancer in crack testers applying azo dye-based sprays to metal bodies. J Toxicol Environ Health 2012a;75A:566-71.

Golka K, Abreu-Villaca Y, Anbari Attar R, Angeli-Greaves M, Aslam M, Basaran N et al. Bladder cancer documentation of causes: multilingual questionnaire, 'bladder cancer doc'. Front Biosci (Elite Ed) 2012b;4:2809-22.

Kiemeney LA, Thorlacius S, Sulem P, Geller F, Aben KK, Stacey SN et al. Sequence variant on 8q24 confers susceptibility to urinary bladder cancer. Nat Genet 2008;40: 1307-12.

Kiemeney LA, Sulem P, Besenbacher S, Vermeulen SH, Sigurdsson A, Thorleifsson G et al. A sequence variant at 4p16.3 confers susceptibility to urinary bladder cancer. Nat Genet 2010;42:415-9.

Lehmann ML, Selinski S, Blaszkewicz M, Orlich M, Ovsiannikov D, Moormann O et al. Rs710521[A] on chromosome 3q28 close to TP63 is associated with increased urinary bladder cancer risk. Arch Toxicol 2010;84:967-78.

Ovsiannikov D, Selinski S, Lehmann ML, Blaszkewicz M, Moormann O, Haenel MW et al. Polymorphic enzymes, urinary bladder cancer risk, and structural change in the local industry. J Toxicol Environ Health 2012;75A:557-65.

Rafnar T, Vermeulen SH, Sulem P, Thorleifsson G, Aben KK, Witjes JA et al. European genome-wide association study identifies SLC14A1 as a new urinary bladder cancer susceptibility gene. Hum Mol Genet 2011;20:4268-81.

Roth E, Selinski S, Schikowsky C, Seidel T, Volkert F, Blaszkewicz M et al. Bladder cancer survival in a former industrial area in Saxony-Anhalt, Germany. J Toxicol Environ Health 2012;75A:1216-25.

Rothman N, Garcia-Closas M, Chatterjee N, Malats N, Wu X, Figueroa JD et al. A multi-stage genome-wide association study of bladder cancer identifies multiple susceptibility loci. Nat Genet 2010;42:978-84.

Schwender H, Selinski S, Blaszkewicz M, Marchan R, Ickstadt K, Golka K et al. Distinct SNP combinations confer susceptibility to urinary bladder cancer in smokers and non-smokers. PLoS One 2012; 7(12): 51880.

Selinski S, Lehmann ML, Blaszkewicz M, Ovsiannikov D, Moormann O, Guballa C et al. Rs11892031[A] on chromosome 2q37 in an intronic region of the UGT1A locus is associated with urinary bladder cancer risk. Arch Toxicol 2012a Sep;86:1369-78.

Selinski S, Lehmann ML, Blaszkewicz M, Ovsiannikov D, Moormann O, Guballa C et al. Urinary bladder cancer risk in relation to a single nucleotide polymorphism (rs2854744) in the insulin-like growth factor-binding protein-3 (IGFBP3) gene. Arch Toxicol 2012b;86:195-203.