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Guest editorial:

HIGHLIGHT REPORT: OCCUPATIONAL URINARY BLADDER CANCER

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Recently, Cordula Lukas and colleagues from TU Dortmund have revisited the relationship between the occurrence of urinary bladder cancer and polymorphisms of xenobiotic metabolizing enzymes (Lukas et al., 2017). Currently, the fraction of occupationally related bladder cancer is estimated as 7.1 % in men and 1.9 % in women (Rushton et al., 2012).

The majority of these occupational bladder carcinomas are associated with exposure to aromatic amines and azo dyes. Lukas et al. (2017) analyzed polymorphisms of N-acetyltransferase 2 (NAT2), glutathione S-transferase M1 (GSTM1), glutathione S-transferase T1, UDP-glucuronosyltransferase 1A (UGT1A), a polymorphism close to the oncogene c-myc (rs9642880) and a polymorphism close the p53 family member TP63 (Lukas et al., 2017). The strongest association with occupational urinary bladder cancer was obtained for GSTM1 and UGT1A, especially when both are co-occurring. The GSTM1 deletion was observed more frequently in varnishers and painters (Lukas et al., 2017). This was associated with exposure to aromatic amines and carbolineum. Interestingly, the polymorphisms were not only associated with increased bladder cancer risk but also with shorter relapse-free times (Lukas et al., 2017). It remains to be analyzed why GSTM1 and UGT1A influence bladder cancer prognosis.

Associations with polymorphisms have been studied in more than 1800 diseases and thousands of SNP associations have been found but typically SNPs only explain a minor share of the variance (Liaqat et al., 2015; Hashemi et al., 2015; Saadat, 2016; Malik et al., 2015). The first genome-wide association study in urinary bladder cancer has been studied approximately ten years ago (Kiemeney et al., 2008). Meanwhile, further studies have identified and validated fifteen genomic regions that are associated with increased risk of bladder cancer and studied the relevance of exposure to carcinogens (Figueroa et al., 2016; Rothman et al., 2010; Selinski et al., 2017a, b, 2016, 2015); Höhne et al., 2017; Ebbinghaus et al., 2017; Krech et al., 2017, 2016; Gundert-Remy et al., 2015). It is of particular relevance that several polymorphisms may statistically interact to cause a higher risk than each of the individual variants (Selinski, 2017). While variants of GSTM1 and UGT1A were most relevant in occupational bladder cancer this is not observed for NAT2. In future, studies are required that help to understand the discrepancy why NAT2 was relevant in cohorts enrolled in the past but not or much less in more recently collected case-control series.

REFERENCES

Ebbinghaus D, Bánfi G, Selinski S, Blaszkewicz M, Bürger H, Hengstler JG, et al. Polymorphisms of xenobiotic metabolizing enzymes in bladder cancer patients of the Semmelweis University Budapest, Hungary. J Toxicol Environ Health A. 2017;80:423-9.

Figueroa JD, Middlebrooks CD, Banday AR, Ye Y, Garcia-Closas M, Chatterjee N, et al. Identification of a novel susceptibility locus at 13q34 and refinement of the 20p12.2 region as a multi-signal locus associated with bladder can-cer risk in individuals of European ancestry. Hum Mol Genet. 2016;25:1203–14.

Gundert-Remy U, Damm G, Foth H, Freyberger A, Gebel T, Golka K, et al. High exposure to inorganic arsenic by food: the need for risk reduction. Arch Toxicol. 2015;89:2219-27.

Hashemi M, Sharifi-Mood B, Rasouli A, Aminiania S, Naderi M, Taheri M. Macrophage migration inhibitory factor -173 G/C polymorphism is associated with an increased risk of pulmonary tuberculosis in Zahedan, Southeast Iran. EXCLI J. 2015;14:117-22.

Höhne S, Gerullis H, Blaszkewicz M, Selinski S, Hengstler JG, Otto T, et al. N-acetyltransferase 1*10 genotype in bladder cancer patients. J Toxicol Environ Health A. 2017;80:417-22.

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.

Krech S, Selinski S, Bürger H, Hengstler JG, Jedrusik P, Hodzic J, et al. Occupational risk factors for prostate cancer in an area of former coal, iron and steel industries in Germany. Part 2: Results from a study performed in the 1990s. J Toxicol Environ Health A. 2016;79:1130-5.

Krech E, Selinski S, Blaszkewicz M, Bürger H, Kadhum T, Hengstler JG, et al. Urinary bladder cancer risk factors in an area of former coal, iron, and steel industries in Germany. J Toxicol Environ Health A. 2017;80:430-8.

Liaqat S, Hasnain S, Muzammil S, Hayat S: Polymorphism analysis in estrogen receptors alpha and beta genes and their association with infertile population in Pakistan. EXCLI J. 2015;14:1085-94.

Lukas C, Selinski S, Prager H-M, Blaszkewicz M, Hengstler JG, Golka K: Occupational bladder cancer: polymorphisms of xenobiotic metabolizing enzymes, exposures, and prognosis. J Toxicol Environ Health A. 2017;80:439-52.

Malik SS, Masood N, Yasmin A. Prostate cancer and glutathione S-transferase deletions. EXCLI J. 2015;14: 1049-54.

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.

Rushton L, Hutchings SJ, Fortunato L, Young C, Evans GS, Brown T, et al. Occupational cancer burden in Great Britain. Br J Cancer. 2012;107(Suppl 1):S3-7.

Saadat M. Distributions of susceptibility loci to late onset Alzheimer's disease on human chromosomes. EXCLI J. 2016;15:403-5.

Selinski S. Discovering urinary bladder cancer risk variants: status quo after almost ten years of genome-wide association studies. (Guest editorial). EXCLI J. 2017;16:1288-96.

Selinski S, Getzmann S, Gajewski PD, Blaszkewicz M, Hengstler JG, Falkenstein M., et al. The ultra-slow NAT2*6A haplotype is associated with reduced higher cognitive functions in an elderly study group. Arch Toxicol. 2015;89:2291-303.

Selinski S, Bürger H, Blaszkewicz M, Otto T, Volkert F, Moormann O, et al. Occupational risk factors for relapse-free survival in bladder cancer patients. J Toxicol Environ Health A. 2016;79:1136-43.

Selinski S, Blaszkewicz M, Ickstadt K, Gerullis H, Otto T, Roth E, et al. Identification and replication of the interplay of four genetic high-risk variants for urinary bladder cancer. Carcinogenesis. 2017a;38:1167-79.

Selinski S, Gerullis H, Otto T, Roth E, Volkert F, Ovsiannikov D, et al. Ultra-slow N-acetyltransferase 2 is associated with recurrence-free time in bladder cancer patients. Eur Urol. 2017b;71:994-5.