Polymorphisms hit the headlines

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More than 300 associations between genetic polymorphisms and approximately 70 common diseases have been identified in genome-wide association studies (review: Hindorff et al. 2009, <http://www.genome.gov/gwastudies>). The design of most studies included a discovery group where candidate variants were identified, which were then validated using several sets of follow-up groups. The majority of all identified variants are of moderate risk or the so-called “wimp SNPs” with odds ratios lower than 1.5. However, because of their high number and relatively high frequency, these wimp SNPs may collectively have a relevant impact on whether an individual develops a disease.

In recent years, polymorphisms and their association with disease and xenobiotic metabolism have also been a cutting-edge topic in our journal (Hanioka et al. 2010; Fuciarelli et al. 2009). Further examples include:

- The effect of UDP glucuronosyltransferase variants on bisphenol A glucuronidation (Hanioka et al. 2011)
- The association between GSTM1 and T1 polymorphisms and chromosomal aberrations (Santovito et al. 2011)
- The modulation of PAH metabolites in individuals exposed to bitumen (Rihs et al. 2011)
- The variability of arsenic metabolism (Fujihara et al. 2011)

- The association of XPD/ERCC2 polymorphisms with skin lesion prevalence (Lin et al. 2010)
- The association of hOGG1 with oxidative DNA damage (Ke et al. 2009)
- The modulation of prostate cancer risk by GSTM3 (Kesarwani et al. 2009)

However, significant progress has also been achieved in the field of urinary bladder cancer. Genome-wide association studies have identified 11 polymorphisms since 2008 that are associated with urinary bladder cancer risk (Rafnar et al. 2011; Rothman et al. 2010; Kiemeny et al. 2010; Selinski et al. 2012a, b; Selinski et al. 2011; Lehmann et al. 2010; Golka et al. 2009). Therefore, the editors are pleased that Klaus Golka and colleagues from the IfADo Leibniz Research Centre in Dortmund, Germany, contributed a comprehensive state of the art review on genetic variants in urinary bladder cancer (Golka et al. 2011). The main take-home messages of the article are:

- All newly discovered SNPs have an odds ratios smaller than 1.5.
- Despite the low odds ratios, these “wimp SNPs” may nevertheless be relevant for the population-attributable risk, because of their relative frequent occurrence.
- The functions of the affected genes comprise xenobiotic metabolism, cell cycle and apoptosis control, and DNA repair.
- Several newly discovered SNPs are far away from the coding regions and possibly represent distant-acting enhancers.

In addition to providing a comprehensive overview of the recently discovered and validated SNPs, the review also summarizes the 163 “old SNPs” that have been reported in relation to bladder cancer, but not yet consistently

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validated. The article comes highly recommended to those working in the field of polymorphisms and cancer risk.

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