RESPONSE

Concerning the CYP17 MSPA1 polymorphism and breast cancer risk: a meta-analysis

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Feigelson and colleagues have raised some important points concerning the selection of the data sets and the application of meta-analysis to resolve some of the problems associated with determining the relationships between metabolic polymorphisms and susceptibility to various disease conditions. In recent years, many meta-analyses have been published with the aim of providing more objective and quantitative summaries of genetic association studies (Lau et al., 1998; Dunning et al., 1999; de Jong et al., 2001). However, there are always concerns that combining studies with different degrees of bias and studies of different quality may produce different conclusions (Lau et al., 1998).

Feigelson et al. argue in their letter that meta-analysis is not the best approach to resolve possible CYP17–breast cancer associations because of the different experimental designs and the mixtures of age and ethnicities in the data sets. In our paper table I (Ye and Parry, 2002) illustrates that many of the studies were related to associations because of the different experimental designs and studies that were performed based on these four studies, the results are strongly discussed in our paper. It is not surprising that the summary estimate of Feigelson et al. for the influence of the A2/A2 allele on advanced breast cancer is different from ours since they included their recent data (Feigelson et al., 2001) and that of three other studies. We fully admit that the ORs in some studies computed by comparing advanced to localized cases are not as precise as those obtained by comparing advanced to unaffected controls. However, when comparing table II in our paper with table I of Feigelson et al., we can see that the ORs computed by these two methods are not clearly different. Other differences in data usage can be seen in Table I of Feigelson et al., where they used the case–control data for post-menopausal breast cancer (112/277) from the study of Mitrunen et al. (2000) but did not include the case–control data for pre-menopausal breast cancer (67/203).

The nested case–control study of Feigelson et al. (2001) contains 235 cases of advanced breast cancer, which represents the largest number of advanced cases for any individual study thus far. The three other studies they included (Helzlsouer et al., 1998; Kristensen et al., 1999; Mitrunen et al., 2000) contain only 351 advanced cases. When a pooled analysis was performed based on these four studies, the results are strongly influenced by the data from the largest study (Feigelson et al., 2001), which greatly impacts on the final summary estimate. However, as we mentioned above, we have strong reservations concerning the combination of data from different ethnic groups, as performed by Feigelson et al. (2001). The different conclusions reached by us and Feigelson and colleagues concerning the association between the CYP17 MspA1 polymorphism and breast cancer risk clearly illustrates to the readers of Mutagenesis the unresolved problems of the selection of appropriate data sets in reaching definitive answers on cancer susceptibility.

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References