Sir,

We appreciate the data and comments provided by Abadie et al (2011) regarding our recent report ‘No association between germline allele-specific expression of TGFBR1 and colorectal cancer risk in Caucasian and Ashkenazi populations’ (Segui et al, 2011). They provide new compelling data corroborating our latest findings, which indicate that allele-specific expression (ASE) of TGFBR1 does not confer an increased risk of colorectal cancer (CRC).

In their letter, Abadie et al criticise the lack of a detailed description of the subjects studied by Segui et al (2011). In this study, we show the characteristics of the informative cases and controls with ASE results that could be evaluated from the Ashkenazi Jewish and Caucasian cohorts (Table 1).

Abadie et al point out that the significant discrepancies observed among studies, mostly between the first (Valle et al, 2008) and the following reports (Guda et al, 2009; Carvajal-Carmona et al, 2010; Tomsic et al, 2010; Segui et al, 2011), may be partially attributed to the differences in the populations analysed. The sets of patients and controls analysed by Segui et al (2011) were obtained from one population-based and one hospital-based case–control study, with different selection criteria than the cases and controls selected by Abadie et al. Despite the differences, their results are in concordance with ours.

Abadie et al carried out the same methodological approach as Valle et al (2008). Therefore, to approximate the patients’ selection criteria in both the series in this study, we selected among the informative CRC cases studied in the original report those with: (1) CRC diagnosed before 61 years of age with a first-degree relative affected with CRC and (2) CRC diagnosed before 51 years of age (Valle et al, 2008). In this subset of cases, the average ASE value was 1.31 (range 0.79–3.95; n = 69), very different from the average ASE value 1.07 (range 0.77–1.45; n = 92) obtained by Abadie et al in CRC cases, also using the SNaPshot technology (PE Applied Biosystems, Foster City, CA, USA). This observation suggests that the difference in the study population is not the cause of discrepancies between the original and subsequent reports.

The results shown by Abadie et al indirectly support that SNaPshot is especially sensitive to RNA quality. Tomsic et al (2010) already noticed that high-quality RNA is essential for reproducibility of ASE. Although poor RNA quality may be the cause of inconsistent results with SNaPshot or pyrosequencing, the latter has proved to be a much more robust technique (Tomsic et al, 2010; Segui et al, 2011). The procedure of blood collection and processing carried out by Abadie et al ensured very high RNA quality, probably explaining why SNaPshot provided consistent values among SNPs and low s.d.’s between independent replicates, even for rs7871490, a SNP located in a complex repetitive stretch.

The letter by Abadie et al clarifies the role of ASE of TGFBR1 in CRC susceptibility. Current evidence suggests that differences observed among studies are not directly attributable to study population or technique, provided high-quality RNA is used for allele expression experiments, and that allele-specific expression of TGFBR1 is not a strong risk factor for CRC.

Table 1 Characteristics of the informative cases and controls with ASE results studied by Segui et al (2011)

| Characteristic | MECC | BCCS |
|---------------|------|------|
| Age at CRC diagnosis (median ± s.d.) | 56 ± 9.7 | 66 ± 10.6 |
| Gender | M: 46/93 (49%) | M: 41/75 (55%) |
| | F: 47/93 (51%) | F: 34/75 (45%) |
| CRC family history (≥ 1FDR with CRC) | 10/92 (11%) | 10/60 (17%) |
| Ethnicity | Ashkenazi | Caucasian |
| Controls | n = 90 | n = 0 |
| Age at blood collection (median ± s.d.) | 59 ± 9.8 | 67 ± 10.6 |
| Gender | M: 45/89 (51%) | M: 44/89 (51%) |
| | F: 44/89 (49%) | F: 43/89 (49%) |
| CRC family history (≥ 1FDR with CRC) | 9/89 (10%) | 11/75 (15%) |
| Ethnicity | Ashkenazi | Caucasian |

Abbreviations: BCCS = Bellvitge Colorectal Cancer Study; CRC = colorectal cancer; F = female; FDR = first-degree relative; M = male; MECC = Molecular Epidemiology of Colorectal Cancer; s.d. = standard deviation.
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