FGFR3 gene, TCC(Ser) sense mutation at codon 249 of the receptor; when present in the germline, this mutation causes thanatophoric dysplasia, a lethal short-limb skeletal dysplasia (9). The findings that FGFR3 is commonly expressed in the cervical epithelium and that the S249C mutation is present in 25% of cervical carcinomas suggest that FGFR3 may play an important role in cervical tumorigenesis (4).

Because the number of cervical cancer specimens examined was relatively small (n = 12) in the study by Cappellen et al. (4), we sought to clarify the role of the FGFR3 S249C mutation in a larger sample of cervical carcinomas (n = 104). We analyzed tumors from a consecutive series of unselected patients who underwent primary cervical cancer surgery at this institution over a 10-year period (1990–1999). This study was approved by the Institutional Review Board of the Memorial Sloan-Kettering Cancer Center. Pathologic review was performed on each case to confirm a diagnosis of invasive cervical carcinoma. With regard to histologic subtype, 95 (91%) of the cervical cancers were squamous cell and nine (9%) were adenoarcinoma. With regard to surgical stage, eight were stage IA, 78 were stage IB, nine were stage IIA, five were stage IIB, two were stage IIIB, and one was stage IVC, according to criteria described previously (10). Stage was unavailable for one case. Histologic and stage distributions were typical for those generally seen in the cervical carcinoma population. After microdissection of tumor tissue from formalin-fixed, paraffin-embedded, or flash-frozen tissue specimens, genomic DNA was isolated with the use of standard procedures. A 161-base-pair polymerase chain reaction product containing codon 249 was generated with the use of the primers 5′-AGTGGCGGTGGTGGTGAGGGAG-3′ and 5′-TGTGCAGTACCTGACACCTTGACAG-3′, then subjected to direct sequence analysis. Of the 104 cervical carcinomas examined, all contained only the wild-type sequence (TCC) at codon 249 of FGFR3 (Fig. 1). These data suggest that the FGFR3 S249C mutation is likely to be very rare in this population of cervical carcinoma patients.

It is difficult to account for the discrepancy between the data of Cappellen et al. (4) and our data. Absence of the FGFR3 S249C mutation in a large sample of cervical carcinomas from our institution may reflect differences in the molecular genetics of cervical cancers from the population studied here (urban northeastern United States) and the French population studied by Cappellen et al., which could result from any number of ethnic, socioeconomic, lifestyle, or environmental influences that affect cervical tumorigenesis in the two patient populations. Such HPV strain differences have been hypothesized, but not proven, to underlie an observed discrepancy in the association between polymorphic p53 alleles and cervical cancer risk in different populations (11). Furthermore, our data pertain only to the S249C mutation in FGFR3. Even though this was the only mutation seen in cervical cancers following a mutation screen of the entire FGFR3 coding region by Cappellen et al., additional mutations affecting this gene in different patient populations could exist. Nevertheless, our data are consistent with the conclusion that FGFR3 S249C is unlikely to represent a common oncogenic mutation in cervical cancer generally.

References


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