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LETTER TO THE EDITOR

Absence of *PRKD1* Mutation, a Salivary Tumor-Specific Mutation, in Solid Tumors and Leukemias

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To the Editor:

A recent genomic study showed that somatic mutations of a serine/threonine kinase-encoding gene *PRKD1* were very common in polymorphous low-grade adenocarcinoma (PLGA) of salivary gland [1]. They found that *PRKD1* hotspot mutations encoding p.Glu710Asp were recurrent in 72.9 % of PLGAs but not in other salivary gland tumors. PRKD1 plays a role in cell adhesion, migration, vesicle transport and survival [2]. Functional studies demonstrated that this kinase-activating mutations altered glandular structures into larger, coalescent structures with filled lumens and irregular contours not uncommonly displaying infiltrating edges, a phenotype consistent with that induced by the forced expression of other oncogenes in this model system [3]. Because *PRKD1* p.Glu710Asp mutations are considered driver mutations and highly recurrent, it may be interesting to know whether the *PRKD1* p.Glu710Asp mutations occur in other human tumors besides PLGA.

For this, tumor tissues from 2444 Korean patients, including hematologic, epithelial and mesenchymal tumor from various origins, were used for this study (Table 1). The tumors did not include PLGAs where *PRKD1* p.Glu710Asp mutations are recurrent, because PLGA tissues were not available in this study. For solid tumors, malignant and normal cells were selectively procured from by microdissection [4]. Approval for this study was obtained from the institutional review board. We analyzed exon 10 of *PRKD1* gene that encompassed p.Glu710Asp mutation sites by polymerase chain reaction (PCR)-based single-strand conformation polymorphism (SSCP). Genomic DNA each from tumor and normal cells was amplified by PCR with a primer pair (5′-**AGGTTTTAGATGCCACAAAG**-3′ (forward) and 5′-**CCAGCTTACATTGCCATAG**-3′ (reverse); product size: 185 base pairs). Other procedures of the PCR-SSCP were described in our previous studies [5]. After SSCP, direct DNA sequencing reactions were performed in the cancers with mobility shifts.

On the SSCP, all of the PCR products for *PRKD1* exon 10 were clearly seen. However, none of the SSCP from the cancers displayed aberrantly migrating bands compared to wild-type bands from the normal tissues, indicating there was no evidence of *PRKD1* exon 10 mutations in the tumors. To confirm the SSCP data, we repeated the experiments twice, including tissue microdissection, PCR and SSCP to ensure specificity of the results, and found that the data were consistent.

One of the main concerns in cancer genetics is to identify whether any mutation found in a tumor is common in the other tumor types. Based on the earlier data that *PRKD1* mutation was recurrent in PLGAs [1], we attempted to determine whether somatic mutation of the recurrent site was present in other tumors in this study. The present study, however, detected no somatic mutations of *PRKD1* p.Glu710Asp in 2444 tumors from 24 types. Our data indicate that the *PRKD1* p.Glu710Asp may be specific to PLGA, but not to other tumor development. The discovery of the recurrent *PRKD1* mutations offered an opportunity for developing therapeutic and diagnostic tools targeting the mutations in tumors. Our data, however, suggest that such applications mutations should be limited to PLGA tumors.

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References

1. Weinreb I, Piscuoglio S, Martelotto LG, Waggott D, Ng CK, Perez-Ordonez B, Harding NJ, Alfaro J, Chu KC, Viale A, Fusco N, da Cruz PA, Marchio C, Sakr RA, Lim R, Thompson LD, Chiosea SI, Seethala RR, Skalova A, Stelow EB, Fonseca I, Assaad A, How C, Wang J, de Borja R, Chan-Seng-Yue M, Howlett CJ, Nichols AC, Wen YH, Katabi N, Buchner N, Mullen L, Kislinger T, Wouters BG, Liu FF, Norton L, McPherson JD, Rubin BP, Clarke BA, Weigelt B, Boutros PC, Reis-Filho JS (2014) Hotspot activating PRKD1 somatic mutations in polymorphous low-grade adenocarcinomas of the salivary glands. Nat Genet 46:1166–1169
2. Rozenrurt E (2011) Protein kinase D signaling: multiple biological functions in health and disease. Physiology (Bethesda) 26:23–33
3. Debnath J, Brugge JS (2005) Modelling glandular epithelial cancers in three-dimensional cultures. Nat Rev Cancer 5:675–688
4. Je EM, Kim MR, Min KO, Yoo NJ, Lee SH (2012) Mutational analysis of MED12 exon 2 in uterine leiomyoma and other common tumors. Int J Cancer 131:E1044–E1047
5. Yoo NJ, Kim HR, Kim YR, An CH, Lee SH (2012) Somatic mutations of the KEAP1 gene in common solid cancers. Histopathology 60:943–952