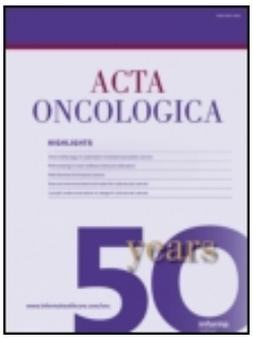

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LETTER TO THE EDITOR

Absence of *DKC1* exon 3 mutation in common human cancers

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To the Editor

Dyskeratosis congenita is a genetic disease caused by point muations in the *DKC1* gene [1]. Patients with dyskeratosis congenita show bone marrow failure syndrome characterized by abnormal skin pigmentation and mucosal leukoplakia [2]. Of note, a subset of patients with dyskeratosis congenita developed malignant tumors of various histologic origins [2]. Also, *DKC1* mutant mice were highly susceptible to tumor development, and the most common tumors were lung and breast tumors [3]. These observations suggested that *DKC1* may be a tumor suppressor gene. *DKC1* protein normally binds with small nucleolar RNAs and the RNA components of telomerase, and these functions are impaired in the cells of the *DKC1* mutant mice [3].

In the individuals with dyskeratosis congenita, *DKC1* gene mutation is detected usually in the exon 3, strongly suggesting that these mutations may related with the disease phenotypes [1,4,5]. It could be hypothesized that increased incidence of malignant tumors in the dyskeratosis congenita patients might be related to the *DKC1* mutations. It is of interest to see whether the *DKC1* gene is somatically mutated in human cancers. However, to date, the data on the somatic mutations of *DKC1* in human sporadic cancers is lacking.

The aim of this study was to see whether common human sporadic cancers harbor *DKC1* mutation. We have analyzed methacarn-fixed tissues of 140 gastric carcinomas, 104 colorectal carcinomas, 94 breast ductal carcinomas, 100 non-small cell caners and 69 hepatocellular carcinomas. All of the patients of the cancers were Asians (Koreans). The gastric carcinomas consisted of 60 diffuse-type, 49 intestinal-type and 31 mixed-type gastric adenocarcinomas by Lauren's classification, and 25 early and 115 advanced gastric carcinomas according to the depth of invasion. The colorectal carcinomas originated from cecum (n = 2), ascending colon (n = 19), transverse colon (n = 6), descending colon (n = 4), sigmoid colon (n = 28) and rectum (n = 45). The breast carcinomas consisted of 15 intraductal and 79 invasive ductal carcinomas. The non-small cell lung cancer samples consisted of 50 adenocarcinomas, 47 squamous cell carcinomas, 1 adenosquamous carcinomas and 2 large cell carcinomas. The hepatocellular carcinomas consisted of Edmondson grade I (n = 8), grade II (n = 30) and grade III (n = 31) according to Edmondson and Steiner's criteria [6].

Malignant cells and normal cells from the same patients were selectively procured from hematoxylin and eosin-stained slides using a 30G1/2 hypodermic needle (Becton Dickinson, Franklin Lakes, NJ) affixed to a micromanipulator, as described previously [7].

DNA extraction was performed by a modified single-step DNA extraction method [7]. Because the most common site of the germline mutations of *DKC1* was reported to be the exon 3 [1,4,5], we analyzed the exon 3 in this study. Genomic DNA each from tumor cells and corresponding normal cells were amplified with a primer pair covering the DNA sequences in the exon 3. For the detection of *DKC1* mutations, we analyzed the exon by

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polymerase chain reaction (PCR)-single strand conformation polymorphism (SSCP). Radioisotope ([^{32}P]dCTP) was incorporated into the PCR products for detection by SSCP autoradiogram. Other procedures of PCR and SSCP analysis were performed as described previously [8]. However, the SSCP from the tumors did not reveal any aberrantly migrating band compared to the wild-type bands from the normal tissues. To confirm the SSCP results, we also analyzed the PCR products by direct DNA sequencing, but we could not detect any evidence of DNA sequence alteration both in the normal tissues and in the tumor samples. We repeated the experiments twice, including tissue microdissection, PCR, SSCP and direct DNA sequencing analysis to ensure the specificity of the results, and found that the data were consistent.

Because the previous studies strongly suggested the association of germline *DKC1* mutations with tumor development both in human and mice [1,3–5], we expected to detect some *DKC1* mutations in the sporadic tumor samples. However, we detected no *DKC1* exon 3 mutation in the 507 samples. Our data could be interpreted by several ways. One possibility is that *DKC1* gene may not be mutated in human cancers, which is a contrast to the association of germline *DKC1* mutation with tumor development. The other possibility is that the *DKC1* mutation might be present in the other areas besides the exon 3. To confirm this, studies are needed that attempt to find *DKC1* mutation in other exons of *DKC1* gene. In conclusion, our data demonstrated that in disagreement with the germline mutation data of *DKC1* gene, somatic mutations in the *DKC1* exon 3 is uncommon in common human cancers. Also, the data suggested that somatic mutations in the *DKC1* exon 3 may not contribute the development of human cancers.

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References

[1] Heiss NS, Knight SW, Vulliamy TJ, Klauck SM, Wiemann S, Mason PJ, et al. X-linked dyskeratosis congenita is caused by mutations in a highly conserved gene with putative nucleolar functions. Nat Genet 1998;19:32–8.

[2] Dokal I. Dyskeratosis congenita in all its forms. Br J Haematol 2000;110:768–79.

[3] Ruggero D, Grisendi S, Piazza F, Rego E, Mari F, Rao PH, et al. Dyskeratosis congenita and cancer in mice deficient in ribosomal RNA modification. Science 2003;299:259–62.

[4] Knight SW, Heiss NS, Vulliamy TJ, Greschner S, Stavrides G, Pai GS, et al. X-linked dyskeratosis congenita is predominantly caused by missense mutations in the DKC1 gene. Am J Hum Genet 1999;65:50–8.

[5] Kanegane H, Kasahara Y, Okamura J, Hongo T, Tanaka R, Nomura K, et al. Identification of DKC1 gene mutations in Japanese patients with X-linked dyskeratosis congenita. Br J Haematol 2005;129:432–4.

[6] Edmondson HA, Steiner PE. Primary carcinoma of the liver: a study of 100 cases among 48,900 necropsies. Cancer 1954; 7:462–503.

[7] Lee JY, Dong SM, Kim SY, Yoo NJ, Lee SH, Park WS. A simple, precise and economical microdissection technique for analysis of genomic DNA from archival tissue sections. Virchows Arch 1998;433:305–9.

[8] Kim HS, Lee JW, Soung YH, Park WS, Kim SY, Lee JH, et al. Inactivating mutations of caspase-8 gene in colorectal carcinomas. Gastroenterology 2003;125:708–15.