Author's response to reviews

Title: Short rare hTERT-VNTR 2-2nd alleles are associated with prostate cancer susceptibility and influence gene expression

Authors:

Se-Lyun Yoon (slyoon0116@hanmail.net)
Se-Il Jung (sijung@dau.ac.kr)
Eun-Ju Do (eunjuidida@hanmail.net)
Se-Ra Lee (ssera2018@hotmail.com)
Sang-Yeop Lee (blueddevil@naver.com)
In-Sun Chu (chu@kribb.re.kr)
Wun-Jae Kim (wjkim@chungbuk.ac.kr)
Jaeil Jung (prosdoc@hanmail.net)
Choung Soo Kim (cskim@amc.seoul.kr)
Sang-Hyeon Cheon (arlef@uuh.ulsan.kr)
Sun-Hee Leem (shleem@dau.ac.kr)

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Author's response to reviews: see over
Dear Editor,

We would like to submit our manuscript entitled “Short rare hTERT-VNTR 2-2nd alleles are associated with prostate cancer susceptibility and influence gene expression” by Se-Lyun Yoon, Se-Il Jung, Eun-Ju Do, Se-Ra Lee, Sang-Yeop Lee, In-Sun Chu, Wun-Jae Kim, Jaeil Jung, Choung Soo Kim, Sang-Hyeon Cheon and Sun-Hee Leem to BMC Cancer as a research article.

Tandem repeats belonging to the minisatellite class were found to be associated with many interesting features of human genome biology, diseases and evolution. In this study, we investigated the association between allelic variation in the hTERT-VNTR 2-2nd minisatellite region in intron 2 of the hTERT gene and susceptibility to prostate cancer. We performed a case-control study using DNA from 421 cancer-free male controls and 329 prostate cancer patients and detected three new rare alleles, two of which were observed only in cancer patients. We also found a statistically significant association between rare hTERT-VNTR2-2nd alleles and risk of prostate cancer [OR, 5.17; 95% confidence interval (CI), 1.09-24.43; \( P = 0.021 \)]. To determine whether the VNTR polymorphism is functional, we examined the transcriptional levels of a reporter gene with the TERT promoter in cancer cell lines. The results indicated that VNTRs inserted in the enhancer region regulate the expression of TERT. This is the first report that rare hTERT VNTRs contribute to prostate cancer predisposition, and VNTRs may be associated with enhanced levels of TERT expression in prostate cancer cell lines. Thus, the hTERT-VNTR2-2nd locus may function as a modifier of prostate cancer risk by regulation of gene expression.

The lengths of hTERT-VNTR 2-2nd alleles were ranged 2~3 kb that were quite difficult to amplify directly from human genomic DNA and to clone in E. coli for construction vectors; the cloning efficiency was dramatically decreased over 30-folds. We think this work is very unique in molecular cancer fields. The study should provide a helpful reference for understanding the function and complex genomic properties of TERT to aid scientists in the field of cancer genomics. This work is related our previous publications in Oncogene (2002, ...

We think that our results are compelling and that this manuscript is well suited to this journal.

This manuscript has been read and approved by all the listed authors. We hope that you will consider our manuscript positively.

Sincerely,

Sun-Hee Leem, Ph.D.

Department of Biological Science
Dong-A University,
Busan 604-714, Korea
Tel: +82-51-200-5639
Fax: +82-51-200-7269
E-mail: shleem@dau.ac.kr