Author's response to reviews

Title: Urinary N1, N12-diacetylspermine predicts tumor invasiveness in patients with clinical Stage IA non-small cell lung cancer

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Dear Editor-in-Chief:

I would like to ask you to consider our manuscript entitled “Urinary N¹, N¹²-diacetylsperrnmine predicts tumor invasiveness in patients with clinical Stage IA non-small cell lung cancer” for publication in *BMC Cancer*. The manuscript consists of 29 pages of text, four tables, and three supplementary tables.

All authors have read and agreed to the content of the paper and their being listed as an author on the paper.

In order to select better candidates for limited resection, it is necessary to accurately differentiate histological non-invasive tumors from small-sized lung cancer. Urinary N¹, N¹²-diacetylsperrm (DiAcSpm) has been reported to be a useful tumor marker in various cancers. We investigated the correlation between the value of urinary DiAcSpm and pathological invasive factors in patients with resected clinical stage IA non-small cell lung cancer (NSCLC). The high urinary DiAcSpm group had significantly more frequent elevated serum CEA (p=0.023), lymph node metastasis (p=0.048), lymphatic permeation (p=0.046), and vascular invasion (p=0.010). Tumor size >2.0cm (p=0.001), serum CEA >5.0mg/dL (p<0.001), high urinary DiAcSpm (p=0.002), and TDR>0.75 (p<0.001) were more frequent in patients with invasive tumors than in those with non-invasive tumors. Multivariate analysis revealed that tumor size \( \leq \) 2.0cm (Risk ratio(RR)=2.901, 95% confidence interval(CI): 1.372-6.136, p=0.005), high urinary DiAcSpm (RR=3.374, 95%CI; 1.547-7.361, p=0.002), TDR<0.75 (HR=4.673, 95% CI; 2.178-10.027, p<0.001) were independent predictive factors for invasive tumors. Even in cases of stage IA NSCLC, case with increased urinary DiAcSpm was found and it was associated with tumor invasiveness. (Word count: 2418)

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We hope that our paper will appeal to readers of your journal. This manuscript has not been published previously and is not being considered concurrently by another publication. We appreciate your review of this work.
Sincerely yours,

Yusuke Takahashi