Vol 3 | Issue 1 | Pages 64-65

Annals of Lung Cancer
ISSN: 2643-5713

Editorial

DOI: 10.36959/825/580

Nucleobindin-2 mRNA Level is Down Regulated in KRAS-mutation Lung Cancer Cell Lines Compared with EGFR/BRAF/KRAS Wild-type Lung Cancer Cell Lines

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Keywords

Lung cancer, Nucleobindin-2, Nesfatin-1, KRAS, qPCR

Abbreviations

EGF: Epidermal Growth Factor; MEK: Mitogen-Activated Protein Kinase; ERK: Extracellular Signal-Regulated Kinase; *GAPDH*: Glyceraldehyde 3-Phosphate Dehydrogenase

To the editor; Increased Nucleobindin-2 level has been determined as an independent prognostic factor for overall survival of patients [1,2]. However, pathophysiological significance of Nucleobindin-2 in lung cancers remains unclear. In the present study, we examined Nucleobindin-2 mRNA level in various types of human lung cancer cell lines.

Ten of lung cancer cell lines with *EGFR*/*BRAF*/*KRAS* wild-type (H1299, H1819, HCC95, H838, H1437, H661, HCC15, HCC78, H1648, HCC193) and eleven of lung cancer cell lines with *KRAS*-mutation [*KRAS*-G12C (H2122, HCC44, H1792, HCC4017, H358), *KRAS*-G12V (H441), *KRAS*-G12D (HCC515), *KRAS*-G12R (H1264, H157), *KRAS*-G12A (H2009), *KRAS*-Q61H (H460)] were used [3]. Nucleobindin-2 mRNA level was analyzed by RT-qPCR as previously rescribed [3]. Primers and probes for Nucleobindin-2 and glyceraldehyde 3-phosphate dehydrogenase (*GAPDH*) were obtained from Ori Gene Technologies (MK203097; Rockville, MD, USA;) and Applied Biosystems (Assay ID: Hs99999905_m1; Tokyo, Japan;), respectively. To normalize the amount of input cDNA, quantitative analysis was performed using the *GAPDH* as an internal reference. Relative expression values were computed using the comparative cycle threshold (Ct) method. All data in the figure are presented as mean ± standard deviation and were analyzed using one-way ANOVA to compare the means of all the groups. Turkey-Kramer multiple comparisons method was used to determine statistical differences between the means, with $p < 0.05$ deemed statistically significant using the InStat 2.00 program.

As shown in Figure 1, we discovered that lung cancer cell lines associated with *KRAS*-mutations had significantly decreased mRNA level of Nucleobindin-2 compared to lung cancer cells with *EGFR*/BRAF/*KRAS* wild-type ($p = 0.00105$).

KRAS-mutations are almost exclusively detected in lung adenocarcinomas [4]. In the case of non small cell lung cancer (NSCLC), KRAS mutations occur predominantly at codon 12 (> 80%) [4]. The most frequent codon variant is *KRAS*-G12C mutation (39%) [4]. Other common mutations include *KRAS*-G12V (18-21%) and *KRAS*-G12D (17-18%) variants [4]. *KRAS*-mutant lung cancers have generally been associated with poorer overall survival than *KRAS* wild-type tumors, particularly in the advanced-stage [5]. In the current study, *KRAS*-G12C was five of eleven, *KRAS*-G12V was one of eleven, and *KRAS*-G12D was one of eleven cell lines. Having those sets of *KRAS*-mutant lung cancer cell lines, we compared Nucleobindin-2 mRNA levels between *EGFR*/*BRAF*/*KRAS* wild-type and *KRAS*-mutant lung cancer cell lines. Based on our observation, it was speculated that Nucleobindin-2 was downregulated in *KRAS*-mutant lung cancer cell lines and

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Accepted: June 11, 2019

Published online: June 13, 2019

Citation: Sunaga N, Imai H, Okada J, et al. (2019) Nucleobindin-2 mRNA Level is Down Regulated in KRAS-mutation Lung Cancer Cell Lines Compared with EGFR/BRAF/KRAS Wild-type Lung Cancer Cell Lines. Ann Lung Cancer 3(1):64-65

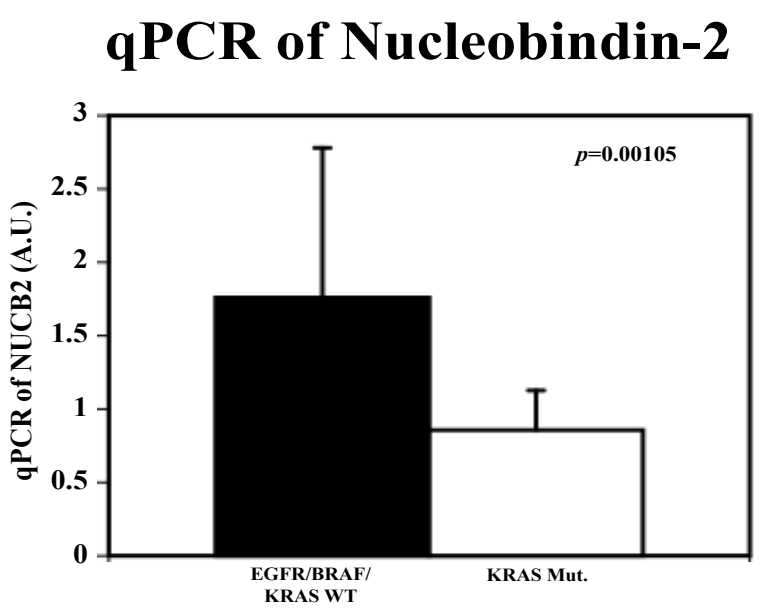

Figure 1: Comparison of Nucleobundin-2 mRNA levels between *EGFR/BRAF/KRAS* wild-type and *KRAS*-mutation lung cancer cell lines.

Nucleobindin-2 mRNA level was estimated using qPCR. The group of *EGFR/BRAF/KRAS* wild-type lung cancer cell lines were shown as closed column (N = 10) and *KRAS*-mutation lung cancer cell lines were shown as open column (N = 11). Statistical results are indicated as *p* value.

this downregulation was nothing to do with *KRAS* mutation types. Unlike other types of cancers, Nucleobindin-2 seems to play unique pathophysiological role on *KRAS*-mutant lung cancers because of unique downregulation instead of up regulation. When the relationship of Nucleobindin-2 levels and clinical significances are evaluated in lung cancer patients, reserachers need to pay attention about the presence or absence of *KRAS* mutation.

Acknowledgements

Lung cancer cell lines (H1299, H1819, HCC95, H838, H1437, H661, HCC15, HCC78, H1648, HCC193, H2122, HCC44, H1792, HCC4017, H441, H358, HCC515, H1264, H157, H2009, H460) used in this study were generously provided by Drs John D. Minna and Adi F. Gazdar of the University of Texas Southwestern Medical Center at Dallas.

Disclosure

None of the authors has any potential conflicts of interest associated with this case report.

Authors' Contributions

All authors had active participation in preparation of the manuscript. All authors read and approved the final manuscript.

Ethical Approval and Consent

The Ethics Committee of Gunma University Hospital approved this study.

Consent to Publish

All participants understand that the information will be published anonymously, but that full anonymity cannot be guaranteed. We understand that the text and any pictures or videos published in the article will be freely available on the internet and may be seen by the general public. Pictures, videos, and text may also appear on other websites or in print, may be translated into other languages or used for commercial purposes.

Competing Interests

We declare that we have no significant competing financial, professional, or personal interests that may have influenced the performance or presentation of the work described in this manuscript.

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