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The Correlation of *KRAS* Gene Expression and *P53* Immunoexpression in Colorectal Adenocarcinoma

Meike Rachmawati[1,2*], Herry Yulianti[1], Bethy S. Hernowo[1], Sri Suryanti[1], Indra Wijaya[3], Nur Rahadiani[4], Didik S. Heriyanto[5], Irianiwati Irianiwati[5]

[1]Department of Pathology Anatomy, Oncology and Stem Cells Research Centre, Padjadjaran University, Dr Hasan Sadikin Hospital, Bandung, Indonesia; [2]Department of Pathology Anatomy, Universitas Islam Bandung, Bandung, Indonesia; [3]Department of Interne Medicine, Padjadjaran University, Dr Hasan Sadikin, Hospital Bandung, Bandung, Indonesia; [4]Department of Pathology Anatomy, Indonesia University, Cipto Mangun Kusumo Hospital, Jakarta, Indonesia; [5]Department of Pathology Anatomy, Gajah Mada University, Sardjito Hospital, Jogjakarta, Indonesia

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***Correspondence:** Meike Rachmawati. Department of Pathology Anatomy/Oncology and Stem Cells Research Centre, Padjadjaran University/Dr. Hasan Sadikin Hospital, Bandung, Indonesia; Department of Pathology Anatomy, Universitas Islam Bandung, Bandung, Indonesia. E-mail: meikerachmawati@gmail.com

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Abstract

BACKGROUND: Colorectal Adenocarcinoma (ADCCR) is the third most cancer not only in the world but also in Indonesia. There were 623 cases of ADCCR at Dr Hasan Sadikin hospital within 2015-2017. Both KRAS and TP53 mutation are known as genes which involve in carcinogenesis through the same pathway, namely the chromosomal instability pathway. In West Java, researches focusing on mutation KRAS and p53 also a correlation between both biomarkers among ADCCR patients are still limited.

AIM: Therefore, this research aimed to perceive a correlation between KRAS gene expression with p53 immunoexpression in ADCCR.

METHODS: Cross section research design was performed to 62 cases of ADCCR as paraffin block taken from 4 hospitals in West Java, including Dr Hasan Sadikin hospital Bandung, Santosa hospital Bandung, Borromeus hospital Bandung and Syamsudin hospital Sukabumi from January 1st 2014 to 31s November 2018. KRAS mutation gene data taken from secondary data at molecular laboratory in Ciptomangunkusumo Hospital Jakarta and Dr Sardjito Hospital Jogjakarta, while the detection of p53 immunoexpression data using immunohistochemical staining was carried out in the Laboratorium of Anatomical Pathology of Padjadjaran University (Dr Hasan Sadikin Hospital). All data were analysed using Chi-Square test with p-value < 0,05 of significant level then proceeded with Stata ver.11 for windows.

RESULTS: The results of this study showed that KRAS gene expressions from 62 sample consist of 39 wild type KRAS (62.39%) and 23 mutant KRAS (37.1%). The p53 immunoexpression consists of 27 negative cases (non-mutant p53) and 35 mutant p53, which includes 10 cases as focal expression (16.33%) and 25 cases as diffuse expressions (40.33%). There is a significant association between KRAS gene expression and p53 immunoexpressions in ADCCR (p = 0.04), with mild positive correlation (Rho 0.28).

CONCLUSION: This study concluded that KRAS and p53 mutations are involved in carcinogenesis, and the p53 mutation is a more dominant risk factor than KRAS mutation among West Java people. P53 mutations with diffuse pattern tend to express mutant KRAS while p53 negative and having a focal pattern tend to express wt KRAS.

Introduction

Colorectal carcinoma (CRC) is a malignant epithelial tumour originating in the large bowel. Colorectal carcinoma ranks as the third most frequent cancer not only in the world but also in Indonesia [1], [2]. The worldwide mortality rate is about 608.000 deaths [2]. In Indonesia, the mortality rate is about 9.5% of all cancer deaths [3], [4]. According to data from the Department of Anatomy Pathology Dr Hasan Sadikin Hospital Bandung, the frequency of CRC is about 224 cases in 2015, 187 cases in 2016 and 212 cases in 2017.

Colorectal Adenocarcinoma (ADCCR) is the most frequent type 0f CRC in the world [1]. There are many mutation genes occur in ADCCR, such as Adenomatous Polyposis Coli (APC), TP53, Kirsten rat sarcoma virus (KRAS), PIK3CA, etc. [5]. These genes are involved in carcinogenesis through three major pathways such as chromosomal instability, mismatch repair and CpG island methylator phenotype (CIMP).