

p-ISSN 2355-8393

e-ISSN 2599-056X

# FOLIA MEDICA INDONESIANA

Vol. 55 No. 4 December 2019

**EFFECT OF IN-VITRO ALPHA LIPIC ACID ADDITION ON SPERMATOZOA MOTILITY IN SPERM PREPARATION PROCESS**

(Gede Wiro Bunesuda, Hamdan Lusardi, Indra Galih Marsur)

**THE CORRELATION BETWEEN *icaA* AND *icaD* GENES WITH BIOFILM FORMATION *Staphylococcus epidermidis* IN VITRO**

(Dian Rachmaedi, Kuslitan, Lindsati Nimsardjono)

**CORRELATION OF POPULATION AND ENVIRONMENTAL BEHAVIOR WITH RAT DENSITY RATE IN PLAGUE DISEASE-FOCUS, THREATENED AND SAFE AREAS IN TUTUR DISTRICT, PASURUAN REGENCY, 2016**

(Eti Noerista Lestari, Sutolowati Ardjani, Usman Had)

**ANALYSIS OF IFN- $\gamma$  AND IL-18 LEVELS AS MARKERS OF INFLAMMATION AND RESPONSE THERAPY OF ANTI-TUBERCULOSIS IN MDR LUNG TB PATIENTS**

(Herri Setyewati, Soedarsono, Yulistari, Umi Fatmawati)

**EFFECT OF GLUTAMINE SUPPLEMENT ADMINISTRATION ON THE REDUCTION OF MUSCULAR FATIGUE POST-ECCENTRIC EXERCISE**

(NIR Rudawan, Taufikurnichan)

**COMPARISON OF ANTHROPOMETRY AND PHYSICAL ABILITIES BETWEEN TRAINED AND UNTRAINED INDIVIDUALS IN SECOND GROWTH PHASE**

(Idam Khalid Akbar, Bambang Purwanto Hari Seljono)

**THE EFFECT OF *Cinnamomum burmanni* WATER EXTRACTION AGAINST *Staphylococcus aureus*, *Enterobacter* spp., *Pseudomonas aeruginosa*, AND *Candida albicans*: IN VITRO STUDY**

(Bernadette Dian Novia, Silvia Subandho)

**THE EFFECT OF SUBCONJUNCTIVAL BEVACIZUMAB ON ANGIOGENESIS IN RABBIT MODEL**

(Nuraida, Diana Yuliasri, Evelyn Komaradh, Heriyawati)

**THE EXPRESSION OF E6, HPV, p53 AND p16INK4A AT WELL, MODERATELY, AND POORLY DIFFERENTIATED CERVICAL ADENOCARCINOMA**

(Ganda Mestika, Nihenna Rahmawati, Nita Kurniasari, Anny Setia Rahaju, Rahmi Nila, Setyenny Mustadewati)

**CORRELATION OF MOTHERS WITH HISTORY OF DIABETES MELLITUS AND INFANTS WITH ANTI-GAD65**

(Nanda Fadhilah Wibia Salsanty, Gede Meinar Sari, Bambang Purwanto, Solislawati)

**EFFECTIVITY OF ERYTHROPOIETIN-ALPHA BETWEEN FIXED- AND ADJUSTED-DOSE IN CHRONIC KIDNEY DISEASE PATIENTS WITH ANEMIA ON HEMODIALYSIS**

(Midi Purwantiqias, Yulistari, Budi Suprati, Bayu Dhama Sani)

**Case Report:**

**THE ROLE OF INTRAVASCULAR ULTRASONOGRAPHY IN PATIENTS UNDERWENT PERCUTANEOUS CORONARY INTERVENTION**

(Yud Her Okwono, Nisla Yusra Putri)

**Case Report:**

**VENTRICULOPERITONEAL SHUNT CATHETER MIGRATION AND TRANSANAL EXTRUSION IN PERMANENT VEGETATIVE STATE ADULT PATIENT**

(Ara Al Fauz, Muhammad Arif Perineng, Joni Wahyuad, Edo Agus Subagio, Agus Turahan)

International Online Distribution by ProQuest™

[www.proquest.com](http://www.proquest.com)

Folia Medica  
Indonesiana

Vol. 55

No. 4

Page 246-325

Surabaya  
December 2019

p-ISSN: 2355-8393  
e-ISSN: 2599-056X

## Editorial Team



**Kuntaman Kuntaman**

**Editor in Chief**

Department of Medical Microbiology, Faculty of Medicine, Universitas Airlangga; Indonesian Society for Clinical Microbiology, Indonesia

0000-0003-4897-8879      [Google Scholar](#)      8700386400      6086035



**Viskasari Pintoko Kalanjati**

**Associate Editor**

Department of Anatomy Histology and Pharmacology, Faculty of Medicine, Universitas Airlangga, Indonesia; International Federation of Associations of Anatomists (IFAA), Indonesia

0000-0002-7005-0025      [Google Scholar](#)      54388384000      5975075



**Lucky Prasetiowati**

**Editorial Board**

PAAI, Indonesia

0000-0002-8929-9816      [Google Scholar](#)      57192906307      5995382



**Muhammad Miftahussurur**

**Editorial Board**

Universitas Airlangga, Indonesia; Baylor College Medicine, Houston, US

0000-0003-1415-6033      [Google Scholar](#)      56323903000      6031037



**Yoshio Yamaoka**

**Editorial Board**

Oita University, Japan

0000-0002-1222-5819      [Google Scholar](#)      55183784100      -



**Purwo Sri Rejeki**

**Editorial Board**

Department of Physiology and Biochemistry, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

0000-0003-2363-6362      [Google Scholar](#)      35088990700      6067303



**Delvac Oceandy**

**Editorial Board**

Division of Cardiovascular Sciences, Faculty of Biology, Medicine, and Health, The University of Manchester, Manchester, United Kingdom

0000-0002-6242-6491      -      6506557120      -



**Andrew Paul Smith**

**Editorial Board**

Centre for Occupational and Health Psychology, School of Psychology, Cardiff University, Cardiff, United Kingdom

0000-0001-8805-8028      -      35429650000



**Franco Servadei**  
**Editorial Board**

Department of Neurosurgery, Humanitas University, Italy

0000-0002-3595-3464

[Google Scholar](#)

7006077203



**Marten J Postma**  
**Editorial Board**

Faculty of Science, Swammerdam Institute for Life Sciences, University of Amsterdam, Netherlands

0000-0002-3167-3633

[Google Scholar](#)

-



**Aryati Aryati**  
**Editorial Board**

PDS PATKLIN, Indonesia

0000-0001-9055-0177

[Google Scholar](#)

56054058600

6043865



**Dirk Jan Marie de Ridder**  
**Editorial Board**

Department of Development and Regeneration, Katholieke Universiteit Leuven, Belgium

-

[Google Scholar](#)

-



**Horie Shigeo**  
**Editorial Board**

Department of Urology, Faculty of Medicine, Juntendo University, Japan

0000-0002-8612-8368

-

57222920684



**Yusuke Suzuki**  
**Editorial Board**

Department of Nephrology, Faculty of Medicine, Juntendo University, Japan

-

-

8388474600



**Hiroaki Kimura**  
**Editorial Board**

Department of Physical Medicine and Rehabilitation, Hiroshima University Hospital, Japan

0000-0003-0005-5805

-

49763362000



**Bambang Purwanto**  
**Editorial Board**

Master Program of Sport Medicine, Dr. Soetomo General Academic Hospital, Indonesia

0000-0002-3786-7068

[Google Scholar](#)

57152859900

5987193



**Arend Frederik Bos**  
**Editorial Board**

Division Neonatology, Faculty of Medical Sciences, University of Groningen, Netherlands

-

-

36839156800



**Azimatul Karimah**  
**Editorial Board**

Dr. Soetomo General Academic Hospital, Surabaya, Indonesia

0000-0002-0261-7878

[Google Scholar](#)

55640202700

6058132





**Reny Itishom**  
**Editorial Board**

Department of Biomedical Sciences, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

0000-0002-9971-7786      [Google Scholar](#)      57209243610      5984521



**Christianto Lumenta**  
**Editorial Board**

Bogenhausen Academic Teaching Hospital, Technical University, Munich, Germany

0000-0002-4030-0708      -      55397690000      -



**Irwanto Irwanto**  
**Editorial Board**

Department of Child Health, Universitas Airlangga, Indonesia

0000-0002-7573-8793      [Google Scholar](#)      -      255759



**Jitti Hanprasertpong**  
**Editorial Board**

Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla, Thailand

0000-0002-0640-6824      [Google Scholar](#)      21740891300      -



**Surasak Sangkhathat**  
**Editorial Board**

Pediatric Surgery Unit, Department of Surgery, Prince of Songkla University, Songkhla, Thailand

0000-0003-3622-3233      -      6602156542      -



**Brahmaputra Marjadi**  
**Editorial Board**

Western Sydney University, Penrith, Australia

0000-0003-0898-3737      [Google Scholar](#)      28267975300      -



**Asra Al Fauzi**  
**Editorial Board**

PERSPEBSI (Perhimpunan Spesialis Bedah Saraf Indonesia- INS), Indonesia; Surabaya Neuroscience Institute (SNeI), Indonesia

0000-0002-5155-2476      [Google Scholar](#)      57215857858      5984620



**Wihasto Suryaningtyas**  
**Editorial Board**

PERSPEBSI, Indonesia; Dr. Soetomo General Academic Hospital, Indonesia

0000-0002-1187-3777      [Google Scholar](#)      57216140907      5987008



**Siti Khaerunnisa**  
**Editorial Board**

Department of Physiology and Medical Biochemistry, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

0000-0002-6358-8265      [Google Scholar](#)      57205438945      6072589



**Atika Wardah**  
**Assistant Editor**

Unit Konsorsium Jurnal dan Folia Medica Indonesiana, Indonesia

0000-0002-8065-4922      [Google Scholar](#)      -

# FOLIA MEDICA INDONESIANA

Vol. 55 No. 4 December 2019

**EFFECT OF IN-VITRO ALPHA LIPOIC ACID ADDITION ON SPERMATOZOA MOTILITY IN SPERM PREPARATION PROCESS**

(Gede Wira Buanayuda, Hamdani Lunardhi, Indra Gusti Mansur)

**THE CORRELATION BETWEEN *icaA* AND *icaD* GENES WITH BIOFILM FORMATION *Staphylococcus epidermidis* IN VITRO**

(Dian Rachmawati, Kuntaman, Lindawati Alimsardjono)

**CORRELATION OF POPULATION AND ENVIRONMENTAL BEHAVIOR WITH RAT DENSITY RATE IN PLAGUE DISEASE-FOCUS, THREATENED AND SAFE AREAS IN TUTUR DISTRICT, PASURUAN REGENCY, 2016**

(Evi Noerista Lestari, Susilowati Andajani, Usman Hadi)

**ANALYSIS OF IFN- $\gamma$  AND IL-10 LEVELS AS MARKERS OF INFLAMMATION AND RESPONSE THERAPY OF ANTI-TUBERCULOSIS IN MDR LUNG TB PATIENTS**

(Herni Setyawati, Soedarsono, Yulistiani, Umi Fatmawati)

**EFFECT OF GLUTAMINE SUPPLEMENT ADMINISTRATION ON THE REDUCTION OF MUSCULAR FATIGUE POST-ECCENTRIC EXERCISE**

(Afif Rusdiawan, Taufikkurrachman)

**COMPARISON OF ANTROPOMETRY AND PHYSICAL ABILITIES BETWEEN TRAINED AND UNTRAINED INDIVIDUALS IN SECOND GROWTH PHASE**

(Idzam Kholid Akbar, Bambang Purwanto, Hari Setijono)

**THE EFFECT OF *Cinnamomum burmannii* WATER EXTRACTION AGAINST *Staphylococcus aureus*, *Enterobacter spp.*, *Pseudomonas aeruginosa*, AND *Candida albicans*: IN VITRO STUDY**

(Bernadette Dian Novita, Silvia Sutandhio)

**THE EFFECT OF SUBCONJUNCTIVAL BEVACIZUMAB ON ANGIOGENESIS IN RABBIT MODEL**

(Nurwasis, Diana Yuliawati, Evelyn Komaratih, Heriyawati)

**THE EXPRESSION OF E6 HPV, p53 AND p16INK4A AT WELL, MODERATELY, AND POORLY DIFFERENTIATED CERVICAL ADENOCARCINOMA**

(Gondo Mastutik, Alphania Rahniayu, Nila Kurniasari, Anny Setijo Rahaju, Rahmi Alia, Sjahjenny Mustokoweni)

**CORRELATION OF MOTHERS WITH HISTORY OF DIABETES MELLITUS AND INFANTS WITH ANTI-GAD65**

(Nanda Fadhilah Witris Salmay, Gadis Meinar Sari, Bambang Purwanto, Sulistiawati)

**EFFECTIVITY OF ERYTHROPOIETIN-ALPHA BETWEEN FIXED- AND ADJUSTED-DOSE IN CHRONIC KIDNEY DISEASE PATIENTS WITH ANEMIA ON HEMODIALYSIS**

(Mida Purwiningtyas, Yulistiani, Budi Suprapti, Bayu Dharma Santi)

**Case Report:**

**THE ROLE OF INTRAVASCULAR ULTRASONOGRAPHY IN PATIENTS UNDERWENT PERCUTANEOUS CORONARY INTERVENTION**

(Yudi Her Oktaviono, Alisia Yuana Putri)

**Case Report:**

**VENTRICULOPERITONEAL SHUNT CATHETER MIGRATION AND TRANSANAL EXTRUSION IN PERSISTENT VEGETATIVE STATE ADULT PATIENT**

(Asra Al Fauzi, Muhammad Arifin Parenrengi, Joni Wahyuhadi, Eko Agus Subagio, Agus Turchan)

**International Online Distribution by ProQuest™**  
**www.proquest.com**

Folia Medica Indonesiana	Vol. 55	No. 4	Page 246-325	Surabaya December 2019	p-ISSN: 2355-8393 e-ISSN: 2599-056X
-----------------------------	---------	-------	--------------	---------------------------	--

# FOLIA MEDICA INDONESIA

p-ISSN 2355-8393, e-ISSN 2599-056X

Vol. 55 no. 4 December 2019

---

**Medical journal, published by Airlangga University School of Medicine, Surabaya, publishing original basic medical and clinical articles presented as research articles and review articles**

## EDITOR-IN CHIEF

**Ni Made Mertaniasih**, Department of Medical Microbiology, Faculty of Medicine,  
Universitas Airlangga, Surabaya, Indonesia

## DEPUTY EDITORS

**Muhammad Miftahussurur**, Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga, Indonesia

## EDITORIAL BOARD

**Arend Frederik Bos**, Division Neonatology, Faculty of Medical Sciences, University of Groningen, Netherlands

**Hiroaki Kimura**, Department of Physical Medicine and Rehabilitation, Hiroshima University Hospital, Japan

**Jitti Hanprasertpong**, Division of Gynecologic Oncology, Department of Obstetrics and Gynecology,  
Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla, Thailand

**Anucha Thatrimontrichai**, Prince of Songkla University, Thailand

**Surasak Sangkhathat**, Pediatric Surgery Unit, Department of Surgery, Prince of Songkla University,  
Songkhla, Thailand

**Aryati**, Department of Clinical Pathology, Faculty of Medicine, Universitas Airlangga, Indonesia

**Viskasari Pintoko Kalanjati**, Department of Anatomy and Histology, Faculty of Medicine,  
Universitas Airlangga, Surabaya, Indonesia

**Irwanto**, Department of Pediatrics, Faculty of Medicine, Universitas Airlangga, Indonesia

**Wihasto Suryaningtyas**, Department of Neurosurgery, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

**Asra Al Fauzi**, Department of Neurosurgery, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

**Azimatul Karimah**, Department of Psychiatry, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

**Lucky Prasetiowati**, Department of Anatomy & Histology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

**Bambang Purwanto**, Department of Medical Physiology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

## MANAGING EDITOR

**Ahmad Suryawan**, Department of Pediatrics, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

## PRODUCTION EDITORS

**Moch. Zuhdy**, Center for Medical Science Community, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

**Athfiyatul Fatati**, Center for Medical Science Community, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

**Alviana Nur Afifah**, Center for Medical Science Community, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

Published by : **GRAMIK (Graha Masyarakat Ilmiah Kedokteran)**  
(Center for Medical Science Community)  
Quarterly (March, June, September, and December)

Address : **Airlangga University School of Medicine**  
Jl. Prof dr Moestopo 47 Surabaya 60131  
Phone: 62-31-5013749, 5020251-3 ext. 135  
Fax : 62-31-5013749, 62-31-5022472  
E-mail: fmi@journal.unair.ac.id, foliamedica@gmail.com

Accredited no. 2/E/KPT/2015

# FOLIA MEDICA INDONESIA

p-ISSN 2355-8393, e-ISSN 2599-056X

Vol. 55 no. 4 December 2019

---

## CONTENTS

<b>EFFECT OF IN-VITRO ALPHA LIPOIC ACID ADDITION ON SPERMATOZOA MOTILITY IN SPERM PREPARATION PROCESS</b> (Gede Wira Buanayuda, Hamdani Lunardhi, Indra Gusti Mansur)	246 – 250
<b>THE CORRELATION BETWEEN <i>icaA</i> AND <i>icaD</i> GENES WITH BIOFILM FORMATION <i>Staphylococcus epidermidis</i> IN VITRO</b> (Dian Rachmawati, Kuntaman, Lindawati Alimsardjono)	251 – 259
<b>CORRELATION OF POPULATION AND ENVIRONMENTAL BEHAVIOR WITH RAT DENSITY RATE IN PLAGUE DISEASE-FOCUS, THREATENED AND SAFE AREAS IN TUTUR DISTRICT, PASURUAN REGENCY, 2016</b> (Evi Noerista Lestari, Susilowati Andajani, Usman Hadi)	260 – 267
<b>ANALYSIS OF IFN-<math>\gamma</math> AND IL-10 LEVELS AS MARKERS OF INFLAMMATION AND RESPONSE THERAPY OF ANTI-TUBERCULOSIS IN MDR LUNG TB PATIENTS</b> (Herni Setyawati, Soedarsono, Yulistiani, Umi Fatmawati)	268 – 274
<b>EFFECT OF GLUTAMINE SUPPLEMENT ADMINISTRATION ON THE REDUCTION OF MUSCULAR FATIGUE POST-ECCENTRIC EXERCISE</b> (Afif Rusdiawan, Taufikkurrachman)	275 – 279
<b>COMPARISON OF ANTROPOMETRY AND PHYSICAL ABILITIES BETWEEN TRAINED AND UNTRAINED INDIVIDUALS IN SECOND GROWTH PHASE</b> (Idzam Kholid Akbar, Bambang Purwanto, Hari Setijono)	280 – 284
<b>THE EFFECT OF <i>Cinnamomum burmannii</i> WATER EXTRACTION AGAINST <i>Staphylococcus aureus</i>, <i>Enterobacter spp.</i>, <i>Pseudomonas aeruginosa</i>, AND <i>Candida albicans</i>: IN VITRO STUDY</b> (Bernadette Dian Novita, Silvia Sutandhio)	285 – 289
<b>THE EFFECT OF SUBCONJUNCTIVAL BEVACIZUMAB ON ANGIOGENESIS IN RABBIT MODEL</b> (Nurwasis, Diana Yuliawati, Evelyn Komaratih, Heriyawati)	290 – 294
<b>THE EXPRESSION OF E6 HPV, p53 AND p16INK4A AT WELL, MODERATELY, AND POORLY DIFFERENTIATED CERVICAL ADENOCARCINOMA</b> (Gondo Mastutik, Alphania Rahniayu, Nila Kurniasari, Anny Setijo Rahaju, Rahmi Alia, Sjahjenny Mustokoweni)	295 – 300
<b>CORRELATION OF MOTHERS WITH HISTORY OF DIABETES MELLITUS AND INFANTS WITH ANTI-GAD65</b> (Nanda Fadhilah Witris Salmay, Gadis Meinari Sari, Bambang Purwanto, Sulistiawati)	301 – 305
<b>EFFECTIVITY OF ERYTHROPOIETIN-ALPHA BETWEEN FIXED- AND ADJUSTED-DOSE IN CHRONIC KIDNEY DISEASE PATIENTS WITH ANEMIA ON HEMODIALYSIS</b> (Mida Purwiningtyas, Yulistiani, Budi Suprapti, Bayu Dharma Santi)	306 – 310
<b>Case Report:</b> <b>THE ROLE OF INTRAVASCULAR ULTRASONOGRAPHY IN PATIENTS UNDERWENT PERCUTANEOUS CORONARY INTERVENTION</b> (Yudi Her Oktaviono, Alisia Yuana Putri)	311 – 321
<b>Case Report:</b> <b>VENTRICULOPERITONEAL SHUNT CATHETER MIGRATION AND TRANSANAL EXTRUSION IN PERSISTENT VEGETATIVE STATE ADULT PATIENT</b> (Asra Al Fauzi, Muhammad Arifin Parenrengi, Joni Wahyuhadi, Eko Agus Subagio, Agus Turchan)	322 – 325

## THE EXPRESSION OF E6 HPV, p53 AND p16INK4A AT WELL, MODERATELY, AND POORLY DIFFERENTIATED CERVICAL ADENOCARCINOMA

**Gondo Mastutik<sup>1</sup>, Alphania Rahniayu<sup>1,2</sup>, Nila Kurniasari<sup>1,2</sup>, Anny Setijo Rahaju<sup>1,2</sup>, Rahmi Alia<sup>3</sup>, Sjahjenny Mustokoweni<sup>1,2</sup>**

<sup>1</sup>Department of Anatomic Pathology, Faculty of Medicine, Universitas Airlangga, Surabaya, <sup>2</sup>Dr. Soetomo General Academic Hospital, Surabaya, <sup>3</sup>Prof Dr Soekandar Hospital, Mojokerto, Indonesia

### ABSTRACT

*The objective of this study is to analyze the expression of E6 Humanpapilloma virus (HPV), p53, and p16INK4A in cervical adenocarcinoma grade well differentiated (WD), moderately differentiated (MD), and poorly differentiated (PD). A cross sectional study conducted at Department of Anatomic Pathology, Dr. Soetomo General Academic Hospital Surabaya Indonesia using formalin fix paraffin embedded (FFPE) from cervical normal and cervical adenocarcinoma grade WD, MD, and PD. The expression of E6 HPV, p53, and p16INK4A was performed by immunohistochemistry (IHC) staining. Data were analyzed with Kruskal-Wallis and continued with Mann-Whitney test. The expression of E6 HPV in the cervical adenocarcinoma showed 35.9% specimens represented negative and 64.1% specimens represented positive. There was no significant difference in the expression of E6 HPV and p53 in cervical adenocarcinoma between grade WD, MD, and PD. The p16INK4A was overexpressed, shown as diffuse appearance in 89.7% of the specimens. There was a significant difference in the expression of p16INK4A between grade WD and MD with PD. In conclusion, some of cervical adenocarcinoma were not caused by infection of HPV type 16 or 18 and the expression of p16INK4A might take a role in the developing of malignancy that caused by infection of HPV.*

**Keywords:** Grading of cervical adenocarcinoma; E6 HPV; p53; p16INK4A

### ABSTRAK

*Tujuan penelitian ini adalah menganalisa ekspresi E6 Humanpapilloma virus (HPV), p53, dan p16INK4A pada adenocarcinoma serviks grade well differentiated (WD), moderately differentiated (MD), dan poorly differentiated (PD). Penelitian cross sectional dilaksanakan di Departemen Patologi Anatomi, Rumah Sakit Umum Pendidikan Dr. Soetomo Surabaya Indonesia menggunakan blok paraffin (BP) dari jaringan serviks normal dan adenocarcinoma serviks grade WD, MD, dan PD. Evaluasi ekspresi E6 HPV, p53, dan p16INK4A dilakukan dengan pewarnaan immunohistochemistry (IHC). Data dianalisa dengan Kruskal-Wallis kemudian dilanjutkan dengan Mann-Whitney test. Ekspresi E6 HPV pada adenocarcinoma serviks menunjukkan 35.9% spesimen adalah negatif dan 64.1% spesimen adalah positif. Tidak terdapat perbedaan yang nyata ekspresi of E6 HPV dan p53 pada adenocarcinoma serviks antara grade WD, MD, dan PD. Terjadi overekspresi p16INK4A, yang menunjukkan sebaran merata pada 89.7% dari spesimen. Terdapat perbedaan yang nyata pada ekspresi p16INK4A antara grade WD dan MD dengan PD. Kesimpulan, beberapa spesimen adenocarcinoma serviks tidak disebabkan oleh infeksi HPV 16 atau HPV 18 dan ekspresi p16INK4A mungkin berperan dalam perkembangan keganasan serviks yang disebabkan oleh infeksi HPV.*

**Kata kunci:** Grade adenocarcinoma serviks; E6 HPV; p53; p16INK4A

**Correspondence:** Gondo Mastutik, Department of Anatomic Pathology, Faculty of Medicine, Universitas Airlangga, Jl. Prof Dr Moestopo 47, Surabaya 60132, Indonesia, E-mail: gondomastutik@fk.unair.ac.id, gondomastutik@gmail.com

pISSN:2355-8393 • eISSN: 2599-056x • doi: <http://dx.doi.org/10.20473/fmi.v55i4.17327>

• Fol Med Indones. 2019;55:295-300 • Received 24 May 2019 • Accepted 28 Nov 2019  
• Open access under CC-BY-NC-SA license • Available at <https://e-journal.unair.ac.id/FMI/>

### INTRODUCTION

Cervical cancer is the fourth most common cancer diagnosed in women worldwide. In Indonesia, it is the second most common cancer diagnosed in women after breast cancer, with an estimated 20,928 new cases and 4,097 deaths in 2012 (Ferlay et al 2013). Based on the histological classification of tumours, the most common

type of cervical cancer is squamous cell carcinoma (Wells et al 2003) and cervical adenocarcinoma comprises 15% of cervical cancer cases (Siriaunkgul et al 2013). The incidence rates of cervical adenocarcinoma tend to increase in Korean women (Oh et al 2013), in women in the United States (Adegoke et al 2012), and in the Netherlands where it is found predominantly in women of 25-39 years old (van der



Horst et al 2017). This trend is particularly evident among females aged <40 years and has occurred despite extensive cytology-based screening programs (Tornesello et al 2014). Adenocarcinoma originates from glandular precursor lesions of the endocervical mucosa that are difficult to reach by pap smear examination. Therefore, although screening programs have led to a substantial decrease in the incidence of squamous cell carcinoma (Andersson et al 2013), it is not protective for precursor cancer whose cells cannot be reached by screening programs, including cervical adenocarcinoma.

Human papilloma virus (HPV) has already been established as the cause of cervical cancer and it is related to other anogenital cancers (anus, vulva, vagina and penis) as well as head and neck cancers. HPV types 16 and 18 are responsible for about 70% of all cervical cancer cases worldwide (Bruni et al 2017). The E6 and E7 of the high risk HPV have associated with oncogenic transformation. E6 interacts with the product of tumour suppressor genes p53. It targets p53 for degradation via ubiquitin pathway, resulting in loss of G2/M checkpoint regulation. In addition, degradation of p53 by E6 HPV leads to irreversible DNA damage and the cells enter the cell cycle and cease to apoptose, resulting in the accumulation of genomic instability and genetic alteration. E7 interacts with retinoblastoma (RB) family member RB1, RBL1, and RBL2, then targets them for degradation, resulting in nuclear translocation of E2F and promotion of S-phase transition. The result of pRb downregulation of the loss of feedback inhibition and overexpression of p16INK4A (Scheffner et al 1990, Hietanen et al 2000, Crosbie et al 2013).

During the progression of cervical adenocarcinoma, cells differentiate into well-differentiated (WD), moderately-differentiated (MD), or poorly-differentiated (PD). However, the expression of p53 and p16INK4A in cervical adenocarcinoma grade WD, MD, PD is still not clear. The objective of this study was to analyze the expression of E6, p53, and p16INK4A in cervical adenocarcinoma grade WD, MD, and PD.

## MATERIALS AND METHODS

### Specimens

This was a cross sectional study conducted at the Department of Anatomic Pathology, Dr. Soetomo General Academic Hospital Surabaya Indonesia. The specimens were cervixes from the uterine prolapse cases and adenocarcinoma cases that had been diagnosed by pathologist. There were 10 formalin fix paraffin embedded (FFPE) of the uterine prolapse as control group and 39 FFPE of cervical adenocarcinoma that

consisted of 14 tissues were grade WD, 12 tissues were grade MD, and 13 tissues were grade PD.

### Immunohistochemistry staining

The expressions of E6 HPV, p53, and p16INK4A are detected by immunohistochemistry (IHC) staining using the HPV16 E6/18 E6 Antibody (C1P5): sc-460 (Santa Cruz Biotechnology), monoclonal antibody p53 clone Y5 (Biocare), and Anti-CDKN2A/ p16INK4A Antibody (clone 1E12E10) IHC-plus™ LS-B5261 (LS Bio).

The scoring of the positive interpretation for E6 HPV is performed when the nucleus and cytoplasm were stained clearly and scored using an arbitrary semiquantitative scale. Score 0 is given when there are no cells stained representing negative staining, score 1 when 5-25% of the cells stained representing mild positive staining, score 2 when 25-50% of the cells stained representing moderate positive staining, and score 3 when >50% of the cells stained representing extensive immunostaining (Chaudhary et al 2013).

Expression of p53 is evaluated when the nucleus is stained clearly and scored semiquantitatively. The score is 0 if up to 5% of the cells are positive, score 1 if 5-25% of the cells are positive, score 2 if 26-50% of the cells are positive, score 3 if 51-75%, and score 4 if more than 75% of the cells are positive (Baalbergen et al 2013).

Expression of p16INK4A is evaluated as positive when nuclear or cytoplasmic immunostaining is clearly demonstrated. Scoring of p16INK4A is performed using the criteria of Klaes et al. (2001). In this scoring, score 0 is given if there is no staining or <1% of the cells are positively representing negative, score 1 if 1-5% of the cells positively representing sporadic, score 2 if 5-25% of the cells are positively representing focal, and score 3 if >25% of the cells are positively representing diffuse (Kazlouskaya et al 2013).

### Statistical analysis

To evaluate different expression of E6 HPV, p53 and p16INK4A at normal cervix tissue and cervical adenocarcinoma tissue based on differentiated grading, the analysis was performed by using The Kruskal-Wallis ( $p < 0.005$ ) and continued with Mann Withney test ( $p < 0.005$ ).

## RESULTS

This study was performed to cervix specimen of 49 women with ages 30-81 years old and average  $51.78 \pm$

9.395 (mean + SD). There were 20.4% FFPE from cervical normal and 79.6% from cervical adenocarcinoma that consisted of 35.9%, 30.8%, and 33.3% FFPE from WD, MD, and PD tissues, respectively.

The expression of E6 HPV, p53, and p16INK4A in cervical adenocarcinoma grade WD, MD, and PD showed in IHC staining (Figure 1). The expression of E6 HPV in the cervical adenocarcinoma showed that those with score 0 were 14 (35.9%) specimens, score 1 were 11 (28.2%), score 2 were 11 (28.2%), and score 3 were 3 (7.7%). The expression of E6 HPV in cervical adenocarcinoma in grade WD, MD, and PD have the same "a" subscript (Table 1). It means that there was no significant difference in the expression of E6 HPV between cervical adenocarcinoma in grade WD, MD, and PD.

Expression of p53 in the cells of cervical adenocarcinoma WD, MD, and PD showed that those with score 0 were 12 (30.8%), score 1 were 15 (38.5%), score 2 were 3 (7.7%), score 3 were 4 (10.2%), and score 4 were 5 (12.8%). The result showed that there was no significant difference in the expression of p53 between cervical adenocarcinoma grade WD, MD, and PD ( $p > 0.05$ ) (Table 1). Expression of p16INK4A in cervical adenocarcinoma grade WD, MD, and PD showed that almost all of the specimens were positively diffuse (score 3) and there was no negative (Fig. 1). The result showed

that there was a significant difference in the expression of p16INK4A between cervical adenocarcinoma in grade WD and MD with PD (Table 1).

## DISCUSSION

Chronic infection of HPV is correlated with the development of cervical cancer (Wells et al 2003). HPV 16, 18 are the most common genotypes of HPV that are presenting in cervical adenocarcinoma (An et al 2005, Tornesello et al 2011, Siriaunkgul et al 2013). In Korean women, the prevalence of HPV infection in cervical adenocarcinoma was 90%. The infection of HPV 16 and/or HPV 18 accounted for 78% of HPV-positive adenocarcinomas. Multiple HPV types were found in 13% of the cases. Mostly HPV 16 and HPV 18 are highly associated with most of cervical adenocarcinomas (An et al 2005). In Thailand, predominant genotype is HPV 18, being twice as common as HPV 16 (Siriaunkgul et al 2013). In Uppsala Sweden, 95% were HR HPV positive; HPV18/45 predominated (77%), followed by HPV16 (27%) (Andersson et al 2013). In the Netherlands, HPV18 is mainly the risk factor for the development of adenocarcinoma, while HPV16 is associated with both SCC and adenocarcinoma (Bulk et al 2006). Because of that in this study we used the E6 of HPV 16 and HPV 18.

Table 1. Different expression of E6 HPV, p53, and p16INK4A at cervical normal and well differentiated, moderately differentiated, and poorly differentiated adenocarcinoma

E6	AWD <sup>a</sup>	AMD <sup>a</sup>	APD <sup>a</sup>	CN <sup>b</sup>	Total	p= 0.001
0	4 (28.6%)	5 (41.7%)	5 (38.5%)	10 (100%)	24 (49%)	
1	6 (42.9%)	2 (16.7%)	3 (23.1%)	0 (0%)	11 (22.4%)	
2	2 (14.3%)	5 (41.7%)	4 (30.8%)	0 (0%)	11 (22.4%)	
3	2 (14.3%)	0 (0%)	1 (7.7%)	0 (0%)	3 (6.1%)	
p53	AWD	AMD	APD	CN		p= 0.179
0	4 (28.6%)	3 (25%)	5 (38.5%)	6 (60%)	18 (36.7%)	
1	6 (42.9%)	4 (33.3%)	5 (38.5%)	3 (30%)	18 (36.7%)	
2	1 (7.1%)	1 (8.3%)	1 (7.7%)	1 (10%)	4 (8.2%)	
3	1 (7.1%)	1 (8.3%)	2 (15.4%)	0 (0%)	4 (8.2%)	
4	2 (14.3%)	3 (25%)	0 (0%)	0 (0%)	5 (10.2%)	
p16 <sup>INK4A</sup>	AWD <sup>a</sup>	AMD <sup>a</sup>	APD <sup>b</sup>	CN <sup>c</sup>		p= <0.0001
0	0 (0%)	0 (0%)	0 (0%)	9 (90%)	9 (18.4%)	
1	0 (0%)	0 (0%)	1 (7.7%)	1 (10%)	2 (4.1%)	
2	0 (0%)	0 (0%)	3 (23.1%)	0 (0%)	3 (6.1%)	
3	14 (100%)	12 (100%)	9 (69.2%)	0 (0%)	35 (71.4%)	

Note: Different superscript shows significant differences. AWD=Well differentiated adenocarcinoma, AMD=moderately differentiated adenocarcinoma, APD= poorly differentiated adenocarcinoma, CN=cervical normal

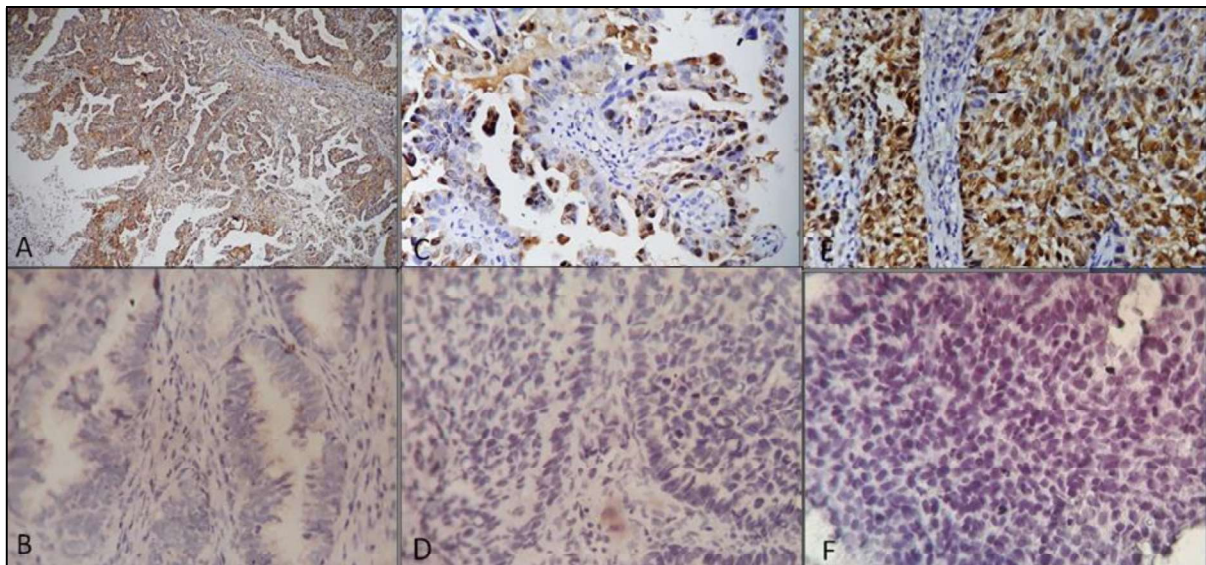


Fig. 1. Expression of E6 HPV, p53, and p16INK4A in cervical adenocarcinoma grade well differentiated (WD), moderately differentiated (MD), poorly differentiated (PD). A. Expression E6 HPV, positive in adenocarcinoma WD, 100X; B. Expression E6 HPV, negative in adenocarcinoma WD, 400X; C. Expression p53, positive in adenocarcinoma MD, 400X; D. Expression p53, negative in adenocarcinoma MD, 400X; E. Expression p16INK4A, positive in adenocarcinoma PD, 400X; F. Expression p16INK4A, negative in adenocarcinoma PD, 400X.

The histology of cervical adenocarcinoma exhibits a variety of architectural patterns and ranges from WD, MD, and PD. The WD of cervical adenocarcinoma may show exophytic papillary growth or infiltrative growth, or both. The invasive tumor may be composed of irregular cystic and tubular glands, glands with intraluminal papillary infoldings, or cribriform glands. In the MD tumors the growth is more confluent with sheets of small cribriform glands. The poorly differentiated adenocarcinomas show solid areas of undifferentiated cells that may be undistinguishable from poorly differentiated squamous cell carcinoma (Pirog, 2017). This grading change occurs along with the development of malignancy so that it will affect the expression of tumor suppressor gene, p53 and p16INK4A.

E6 HPV in this study represented the infection of HPV 16 and or 18 (HPV 16/18), showed that 35.9% and 64.1% specimens of cervical adenocarcinoma represented negative and positive for E6 HPV 16/18, respectively. This suggested that some of cervical adenocarcinoma tissues were not infected by HPV type 16 or 18, so it might be related with other HPV types or any others causes. This study was in accordance with other study that the prevalence of HPV in cervical adenocarcinoma varied from 62 to 100%, depending on geographic region and tumor subtype (Baalbergen et al 2013). The expression of E6 HPV in cervical

adenocarcinoma between grade WD, MD, and PD, there are no significant different. This data suggested that the infection of HPV type 16 or 18 did not affect the grading differentiation of cervical adenocarcinoma.

This study showed that the score 0 for the expression of p53 in the cells of cervical adenocarcinoma grade WD, MD, and PD was 30.8%, and score 1, 2, 3, and 4 were 69.2%. It suggests that some specimens have not and have shown the expression of p53. The wild type p53 has half-life of about 5-20 minutes (Dowell et al 1994) and then degraded, whereas the E6 HPV 16 and 18 binds to p53 and also stimulate degradation (Crosbie et al 2013), so it would be negative for IHC staining. The ubiquitin form of p53 as result of degradation by E6 HPV and mutant type p53 should be positive by IHC staining. Other studies showed that the mutation of p53 gene in cervical adenocarcinoma is more frequent than that in squamous cell carcinoma or cervical intraepithelial neoplasia. There is a single nucleotide substitutions in p53 gene detected in 36% cervical adenocarcinoma cases and this mutation is independent from HPV infection status (Tornesello et al 2014). In cervical adenocarcinoma, the positivity of p53 is associated with poor survival. The survival rate in cervical adenocarcinoma is 67%, and it is not influenced by estrogen receptor, progesterone receptor, MIB-1, or bcl-2 with strongly positive staining, but significantly influenced by the expression of p53. The p53 staining is

strongly positive. The survival is significantly worse than that in tumors scored as negative or weak positive (Baalbergen et al 2013).

This study found that the expression of p16INK4A was overexpressed in cervical adenocarcinoma grade WD, MD, and PD. This was demonstrated by the diffuse appearance in 89.7% (35/39) of the specimens. It was also showed that a significant difference in the expression of p16INK4A in cervical adenocarcinoma between grade WD and MD with PD. The expression of p16INK4A in WD and MD was diffusely positive. This result was the same with the finding in other study that p16INK4A was expressed in diffusely or strongly expression in cervical intraepithelial neoplasia I, II, III, squamous cell carcinoma, endocervical glandular dysplasia, adenocarcinoma in situ, and invasive adenocarcinoma (Tringler B et al 2004); as well as in endocervical carcinoma (Liang et al 2016). The finding in this study was in accordance with the results of other studies. The overexpression of p16INK4A in uterine cervix adenocarcinoma is common and significantly associated with HPV infection (mainly high-risk HPV types). It suggests that p16INK4A is a putative molecular biomarker that consistently discriminates uterine cervix adenocarcinomas from benign lesions and from endometrioid adenocarcinomas of the uterine corpus (Missaoui et al 2006). The overexpression of the p16INK4A was typical for dysplastic and neoplastic epithelia of the uterine cervix. The expression of p16 increases from normal to invasive squamous carcinoma in the uterine cervix emphasizing that it might be a useful marker for predicting risk of developing cervical cancer in women (Izadi-Mood et al 2012).

## CONCLUSION

There was no significant difference in the expression of E6 HPV and p53 in cervical adenocarcinoma between grade WD, MD, and PD, but there was a significant difference in the expression of p16INK4A between grade WD and MD with PD. This finding suggest that the expression of p16INK4A might take a role in the developing of malignancy that caused by infection HPV.

## ACKNOWLEDGMENT

This study was supported by the Ministry of Research, Technology, and Higher Education of the Republic of Indonesia by the university operational funding fiscal years at 2017. Thank you for the Indonesian Government and the Faculty of Medicine Airlangga University.

## REFERENCES

- Adegoke O, Kulasingam S, Virnig B (2012). Cervical cancer trends in the United States: a 35-year population-based analysis. *J Womens Health (Larchmt)* 21, 1031-7
- An HJ, Kim KR, Kim IS, et al (2005). Prevalence of human papillomavirus DNA in various histological subtypes of cervical adenocarcinoma: a population-based study. *Mod Pathol* 18, 528-34
- Andersson S, Mints M, Wilander E (2013). Results of cytology and high-risk human papillomavirus testing in females with cervical adenocarcinoma in situ. *Oncol Lett* 6, 215-9
- Baalbergen A, Smedts F, Ewing P, et al (2013). HPV-type has no impact on survival of patients with adenocarcinoma of the uterine cervix. *Gynecol Oncol* 128, 530-4
- Bruni L, Barrionuevo-Rosas L, Albero G, et al 2017. Human Papillomavirus and Related Diseases in Indonesia. Summary Report 27 July 2017 [Online]. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre) 2017. Accessed April 12, 2018
- Bulk S, Berkhof J, Bulkman NW, et al (2006). Preferential risk of HPV16 for squamous cell carcinoma and of HPV18 for adenocarcinoma of the cervix compared to women with normal cytology in The Netherlands. *Br J Cancer* 94, 171-5
- Chaudhary A, Pandya S, Singh M, et al (2013). Identification of high-risk human papillomavirus-16 and -18 infections by multiplex PCR and their expression in oral submucous fibrosis and oral squamous cell carcinoma. *Head and Neck Oncology* 5, 1-10
- Crosbie EJ, Einstein MH, Franceschi S, et al (2013). Human papillomavirus and cervical cancer. *The Lancet* 382, 889-99
- Dowell SP, Wilson PO, Derias NW, et al (1994). Clinical utility of the immunocytochemical detection of p53 protein in cytological specimens. *Cancer Res* 54, 2914-8
- Hietanen S, Lain S, Krausz E, et al (2000). Activation of p53 in cervical carcinoma cells by small molecules. *Proc Natl Acad Sci U S A*, 97, 8501-6
- Izadi-Mood N, Asadi K, Shojaei H, et al (2012). Potential diagnostic value of P16 expression in premalignant and malignant cervical lesions. *J Res Med Sci* 17, 428-33
- Kazlouskaya V, Shustef E, Allam SH, et al (2013). Expression of p16 protein in lesional and perilesional condyloma acuminata and bowenoid papulosis: clinical significance and diagnostic implications. *J Am Acad Dermatol* 69, 444-9
- Klaes R, Friedrich T, Spitkovsky D, Ridder R, Rudy W, Petry U, et al. (2001). Overexpression of p16INK4A

- as a specific marker for dysplastic and neoplastic epithelial cells of the cervix uteri *Int J Cancer* 2001 92, 276-84
- Liang L, Zheng W, Liu J, et al (2016). Assessment of the Utility of PAX8 Immunohistochemical Stain in Diagnosing Endocervical Glandular Lesions. *Arch Pathol Lab Med*, 140, 148-52
- Missaoui N, Hmissa S, Frappart L, et al (2006). p16INK4A overexpression and HPV infection in uterine cervix adenocarcinoma. *Virchows Arch* 448, 597-603
- Oh CM, Jung KW, Won YJ, et al (2013). Trends in the incidence of in situ and invasive cervical cancer by age group and histological type in Korea from 1993 to 2009. *PLoS One* 8, e72012
- Pirog EC (2017). Cervical Adenocarcinoma: Diagnosis of Human Papillomavirus-Positive and Human Papillomavirus-Negative Tumors. *Arch Pathol Lab Med* 141, 1653-67
- Scheffner M, Werness BA, Huibregtse JM, et al (1990). The E6 oncoprotein encoded by human papillomavirus types 16 and 18 promotes the degradation of p53. *Cell* 63, 1129-36
- Siriaunkgul S, Utaipat U, Suthipintawong C, et al (2013). HPV genotyping in adenocarcinoma of the uterine cervix in Thailand. *Int J Gynaecol Obstet* 123, 226-30
- Tornesello ML, Annunziata C, Buonaguro L, et al (2014). TP53 and PIK3CA gene mutations in adenocarcinoma, squamous cell carcinoma and high-grade intraepithelial neoplasia of the cervix. *J Transl Med*, 12, 255
- Tornesello ML, Losito S, Benincasa G, et al (2011). Human papillomavirus (HPV) genotypes and HPV16 variants and risk of adenocarcinoma and squamous cell carcinoma of the cervix. *Gynecol Oncol*, 121, 32-42
- van der Horst J, Siebers AG, Bulten J, et al (2017). Increasing incidence of invasive and in situ cervical adenocarcinoma in the Netherlands during 2004-2013. *Cancer Med*, 6, 416-23
- Wells M, Östör AG, Crum CP, et al (2003). Tumours of the uterine cervix, epithelial tumours. In 'Pathology and Genetics of Tumours of the Breast and Female Genital Organs', Eds IARC Press, Lyon, 259-72





## FOLIA MEDICA INDONESIAANA

[UNIVERSITAS AIRLANGGA](#)

P-ISSN : 23558393 <> E-ISSN : 2599056X Subject Area : Education



0.525

Impact Factor



1020

Google Citations



Sinta 2

Current Accreditation

[Google Scholar](#) [Garuda](#) [Website](#) [Editor URL](#)

### History Accreditation

2018

2020

2021

2022

2023

2024

2025

### Garuda [Google Scholar](#)

#### [Longer Lag Time in Early-Stage Retinoblastoma](#)

Faculty of Medicine, Universitas Airlangga

[Folia Medica Indonesiana Vol. 58 No. 2 \(2022\): June 103-107](#)

2022

[DOI: 10.20473/fmi.v58i2.24975](#)

[Accred : Sinta 2](#)

#### [The AKT Pathway and Satellite Cell Activation in Skeletal Muscle Mass Regulation](#)

Faculty of Medicine, Universitas Airlangga

[Folia Medica Indonesiana Vol. 58 No. 1 \(2022\): March 68-73](#)

2022

[DOI: 10.20473/fmi.v58i1.13354](#)

[Accred : Sinta 2](#)

#### [Viral Load And Cd4+ among Hiv/Aids Patients Receiving Antiretroviral Therapy In Jayawijaya District, Papua Province, Indonesia](#)

Faculty of Medicine, Universitas Airlangga

[Folia Medica Indonesiana Vol. 58 No. 1 \(2022\): March 10-14](#)

2022

[DOI: 10.20473/fmi.v58i1.18247](#)

[Accred : Sinta 2](#)

#### [Back Matter Vol.58 No.1 March 2022](#)

Faculty of Medicine, Universitas Airlangga

[Folia Medica Indonesiana Vol. 58 No. 1 \(2022\): March](#)

2022

[DOI: 10.20473/fmi.v58i1.34145](#)

[Accred : Sinta 2](#)

#### [Acute Diarrhea Patients among Children Under Five Hospitalized in a Tertiary Hospital in East Java, Indonesia](#)

Faculty of Medicine, Universitas Airlangga

[Folia Medica Indonesiana Vol. 58 No. 1 \(2022\): March 33-38](#)



**KOMITE ETIK PENELITIAN KESEHATAN  
FAKULTAS KEDOKTERAN UNIVERSITAS AIRLANGGA  
SURABAYA**

**KETERANGAN KELAIKAN ETIK  
("ETHICAL CLEARANCE")**

**No. 298/EC/KEPK/FKUA/2015**

KOMITE ETIK PENELITIAN KESEHATAN FAKULTAS KEDOKTERAN UNIVERSITAS AIRLANGGA SURABAYA, TELAH MEMPELAJARI SECARA SEKSAMA RANCANGAN PENELITIAN YANG DIUSULKAN, MAKA DENGAN INI MENYATAKAN BAHWA PENELITIAN BERJUDUL :

**EKSPLORASI TIPE HUMAN PAPILOMA VIRUS YANG MENGINFEKSI  
PENDERITA SQUAMOUS CELL CARCINOMA SERVIKS, ADENOCARCINOMA  
SERVIKS, DAN KONDILOMA AKUMINATA**

PENELITI UTAMA :

**Dr. Gondo Mastutik, drh.,M.Kes.  
Prof. Dr. Suhartono Taat Putra, dr.,MS.  
Alphania Rahniayu, dr.,Sp.PA.**

UNIT / LEMBAGA / TEMPAT PENELITIAN :

- Dept. Patologi Anatomi Fakultas Kedokteran Universitas Airlangga
- Institute of Tropical Disease (ITD) Universitas Airlangga

**DINYATAKAN LAIK ETIK.**

Surabaya, 26 Oktober 2015



**dan KETUA KEPK  
Wakil Ketua KEPK**

*Prof. Moersintowarti B. Narendra, dr, MSc, Sp.A(K)*