

FOLIA MEDICA INDONESIANA

Vol. 54 No. 1 March 2018

THE ROLE OF HIF-1 α IN REGIONAL LYMPH NODES METASTASIS IN COLORECTAL ADENOCARCINOMA
Lulus R. Mulyati, Sulastri, Yanti Hikma, Herminah Palitawati

ANALYSIS OF MASPIN EXPRESSION IN INVASIVE DUCTAL CARCINOMA OF THE BREAST
ON STAGES IIA AND IIIB
Siti Nurul Huda, Dwi Lantika

COMPARATION OF PHENOTYPIC AND GENOTYPIC PROFILE OF CARBAPENEMASE PRODUCING
Escherichia coli
Dina S. Sandhi, Sudarmo, Hapsoro, Santosa, Dody Sugiharto, Heru Agoes Luncur

EFFECTS OF RED PITAYA (*Hylocereus polyrhizus*) ON LIPID PROFILE OF MALE WHITE RATS (*Rattus norvegicus*) RECEIVING HIGH FAT DIET
Pratik P. Patil, Pramod P. Subbarao

COMPARISON OF MICROBIOLOGICAL EXAMINATION BY TEST TUBE AND CONGO RED AGAR
METHODS TO DETECT BIOFILM PRODUCTION ON CLINICAL ISOLATES
Dian Kurniati Putri, Kartika Darmita, Suci Dwi Pratiwi

EFFECTS OF DEXAMETHASONE ON CONTRALATERAL TESTICULAR IMMUNE RESPONSE IN WISTAR STRAIN RATS WITH UNILATERAL TESTICULAR TORSION
Windi Suryati, Jaya Syahidah, Firdausi, Faridah

EFFECTS OF FOLIC ACID INTAKE DURING PREGNANCY WHOSE MOTHER WAS EXPOSED TO CIGARETTE SMOKE TOWARDS BRAIN NEURONS APOPTOSIS INDEX AND QUANTITY OF MICE (*Mus musculus*) OFFSPRING
Dina Fugila Ningrum, Herlina Tri Dewi, Widjati

EFFECTS OF ARAK BALI ADMINISTRATION ON SPERMATOZOA DNA FRAGMENTATION AND TESTOSTERONE LEVEL OF RATS (*Rattus norvegicus*)
Dina Nasar, Uwi Widya, Ni Wayan Sekha Sulisti, Andi Villa Sulisti, Dwi Dwi Pratiwi

ANALYSIS OF METHYLDOPA THERAPY ON sFlt-1 ANTIANGIOGENIC LEVELS IN PATIENTS WITH SEVERE PREECLAMPSIA
Dian Widi Hartini, Purnami, Dwi Sulistyati

ANALYSIS OF DIFFERENCES OF SERUM THROMBOXANE B₂ LEVEL AFTER TAKING ACETOSAL IN ACUTE THROMBOTIC STROKE WITH DIABETES MELLITUS AND NON-DIABETES MELLITUS
Yuli Handayani, Dedi Pramono, Herlina Tri Dewi

ANALYSIS OF ADRENAL SUPPRESSION AFTER HIGH DOSE PREDNISON THERAPY ON CHILDREN WITH STANDARD RISK ACUTE LYMPHOBLASTIC LEUKEMIA IN INDUCTION AND CONSOLIDATION PHASE
Sukmargi Astuti, Dwi Pratiwi, Dwi Lantika, Yulianti

ENHANCED EFFICACY OF SUBLINGUAL IMMUNOTHERAPY IN CHILDHOOD ALLERGIC ASTHMA BY PROBIOTICS
Sriangga Endangita, Dwi Lantika

Review Article:

MANAGEMENT OF PERIOPERATIVE ANESTHESIA IN RIGHT HEART FAILURE
Trias Sudiarta, Herlina Tri Dewi

International Online Distribution by ProQuest™
www.proquest.com

FOLIA MEDICA INDONESIANA

ISSN 2355-8393

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

Prof Dr Suhartono Taat Putra, dr, MS

Deputy Editor-in-Chief

I Dewa Gede Ugrasena, dr, SpA(K)

Editorial Board

Prof Bambang Permono, dr, SpA(K)

Prof Purnomo Suryohudoyo, dr

Prof Dr Doddy M Soebadi, dr, SpB, SpU(K)

Prof Soehartono DS, dr, SpOG(K)

Prof Dr Harjanto, dr, AIF

Dr FM Judajana, dr, SpPK

Prof Soetjipto, dr, MS, PhD

Prof Dr Suharto, dr, MSc, DTM&H, SpPD-KTI

Prof Dr Subijanto Marto Soedarmo, dr, SpA(K)

Prof Dr Kuntaman, dr, MS, SpMK

Dr Anang Endaryanto, dr, SpA(K)

Edhi Rianto, dr, MS

Managing Editor

Ahmad Suryawan, dr, SpA(K)

Dr I Ketut Sudiana, drs, MSI

Dr Nyilo Purnami, dr, SpTHT-KL(K)

Viskasari Pintoko Kalanjati, dr, MKes, PhD

Purwo Sri Rejeki, dr, MKes

Dr Gondo Mastutik, drh, MKes

Mia Ratwita Andarsini, dr, SpA

Wita Saraswati, dr, SpOG

Dr Ahmad Yudianto, dr, SpF

Linda Dewanti, dr, MKes, HMsc, PhD

Secretariat

Mochammad Zuhdy, S.Sos

Athfiyatul Fatati, S.Ant

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

TABLE OF CONTENTS

ARTICLES

The Role of HIF-1alpha in Regional Lymph Nodes Metastasis in Colorectal Adenocarcinoma	1-5
 = 10.20473/fmi.v54i1.8042	
Ladyna Rumapar, Sjahjenny Mustokoweni, Alphania Rahniayu	
Analysis of Maspin Expression in Invasive Ductal Carcinoma of the Breast on Stages IIA and IIIB	6-9
 = 10.20473/fmi.v54i1.8043	
Arif Satria Hardika, Dyah Fauziah	
Comparation of Phenotypic and Genotypic Profile of Carbapenemase Producing Escherichia coli	10-15
 = 10.20473/fmi.v54i1.8045	
Silvia Sutandhio, Budiono Budiono, Hardiono Hardiono, Kuntaman Kuntaman, Eddy Bagus Wasito, Maria Inge Lusida	
Effects of Red Pitaya (<i>Hylocereus polyrhizus</i>) on Lipid Profile of Male White Rats (<i>Rattus norvegicus</i>) Receiving High Fat Diet	16-21
 = 10.20473/fmi.v54i1.8046	
Wiwik Werdiningsih, Suhartati Suhartati	
Comparison of Microbiological Examination by Test Tube and Congo Red Agar Methods to Detect Biofilm Production on Clinical Isolates	22-28
 = 10.20473/fmi.v54i1.8047	
Dewi Klarita Furtuna, Kartuti Debora, Eddy Bagus Warsito	
Effects of Dexamethasone on Contralateral Testicular Immune Response in Wistar Strain Rats with Unilateral Testicular Torsion	29-33
 = 10.20473/fmi.v54i1.8049	
Andri Kustono, I Ketut Sudiana, Fikri Rizaldi, Tarmono Tarmono	
Effects of Folic Acid Intake during Pregnancy whose Mother was Exposed to Cigarette Smoke towards Brain Neurons Apoptosis Index and Quantity of Mice (<i>Mus musculus</i>) Offspring	34-40
 = 10.20473/fmi.v54i1.8050	
Nyna Puspa Ningrum, Hermanto Tri Joewono, Widjiati Widjiati	
Effects of Arak Bali Administration on Spermatozoa DNA Fragmentation and Testosterone Level of Rats (<i>Rattus norvegicus</i>)	41-45
 = 10.20473/fmi.v54i1.8051	
Alfiah Hayati, Dwi Winarni, Ni Wayan Sukma Antari, Inne Ninda Resita, Erlyn Nurul Fauziah	
Analysis of Methyldopa Therapy on sFlt-1 Antiangiogenic Levels in Patients with Severe Preeclampsia	46-52
 = 10.20473/fmi.v54i1.8052	
Teri Wina Herwati, Yulistiani Yulistiani, Eddy Zarkaty M	
Analysis of Differences of Serum Thromboxane B2 Level after Taking Acetosal in Acute Thrombotic Stroke with Diabetes Mellitus and Non-Diabetes Mellitus	53-58
 = 10.20473/fmi.v54i1.8053	
Nur Hadiyanti, Didik Hasmono, Mohammad Saiful Islam	
Children with Standard Risk Acute Lymphoblastic Leukemia in Induction And Consolidation Phase	

 = [10.20473/fmi.v54i1.8054](https://doi.org/10.20473/fmi.v54i1.8054)

Adinugraha Amarullah, Didik Hasmono, IGD Ugrasena, Yulistiani Yulistiani

Enhanced Efficacy of Sublingual Immunotherapy in Childhood Allergic Asthma by Probiotics

 = [10.20473/fmi.v54i1.8055](https://doi.org/10.20473/fmi.v54i1.8055)

Anang Endaryanto, Mira Irmawati

Review Article: Management of Perioperative Anesthesia in Right Heart Failure

 = [10.20473/fmi.v54i1.8056](https://doi.org/10.20473/fmi.v54i1.8056)

Fajar Perdhana, Herdono Purnomo

THE ROLE OF HIF-1 α IN REGIONAL LYMPH NODES METASTASIS IN COLORECTAL ADENOCARCINOMA

Ladyna Rumapar, Sjahjenny Mustokoweni, Alphania Rahniayu

Department of Anatomic Pathology, Faculty of Medicine, Universitas Airlangga, Dr. Soetomo Hospital, Surabaya

ABSTRAK

Karsinoma kolorektal memiliki angka morbiditas dan mortalitas yang tinggi di seluruh dunia, dengan >90% merupakan adenokarsinoma. Karsinoma kolorektal merupakan salah satu kanker yang paling sering bermetastasis, terutama ke kelenjar getah bening. Angiogenesis memiliki peranan penting dalam pertumbuhan tumor dan metastasis. Hipoksia merupakan faktor pemicu yang memicu terjadinya angiogenesis. Hypoxia induced factor- 1 (HIF-1) telah diidentifikasi sebagai protein yang penting dan bereaksi langsung terhadap hipoksia. HIF-1 α , salah satu subunit dari HIF-1, merupakan regulator penting dalam angiogenesis. Dilakukan analisis ekspresi HIF-1 α pada adenokarsinoma kolorektal, dengan dan tanpa metastasis ke KGB regional, untuk mengungkap peranan protein tersebut dalam proses metastasis. Penelitian ini bertujuan untuk membuktikan adanya peran HIF-1 α pada proses metastasis KGB regional adenokarsinoma kolorektal. Penelitian observasional analitik dilakukan pada 30 sampel blok parafin adenokarsinoma kolorektal dengan dan tanpa metastasis pada KGB regional di Laboratorium Patologi Anatomi RSUD Dr. Soetomo, Surabaya. Deteksi ekspresi HIF-1 α dilakukan dengan pengecatan imunohistokimia menggunakan antibodi HIF-1 α . Hasil penelitian dianalisis secara statistik menggunakan uji statistik Mann-Whitney dan Kruskal- Wallis. Pada penelitian ini tidak didapatkan perbedaan ekspresi HIF-1 α antara adenokarsinoma kolorektal dengan metastasis KGB dan tanpa metastasis KGB ($p>0,05$). Sebagai simpulan, HIF-1 α tidak berperan dalam metastasis KGB pada adenokarsinoma kolorektal. (FMI 2018;54:1-5)

Kata kunci: Adenokarsinoma kolorektal; HIF-1 α ; KGB regional

ABSTRACT

Colorectal carcinoma has high morbidity and mortality rate worldwide, in which over 90% are adenocarcinoma. Colorectal carcinoma is one of the most cancer that metastasize to the lymph node. Angiogenesis have an important role in tumor growth and metastasis. Hypoxia is the trigger factor for angiogenesis. Hypoxia induced factor- 1 (HIF-1) is one critical protein directly reacting to hypoxia. HIF-1 α , a HIF-1 subunit, is an important regulator of angiogenesis. This study analyzed HIF-1 α expression in colorectal adenocarcinoma with and without regional lymph node metastasis. This study was to prove that HIF-1 α has a role in regional lymph node metastasis in colorectal adenocarcinoma. An analytical observational study was conducted on thirty formalin fixed paraffin-embedded colorectal adenocarcinoma tissues from Anatomic Pathology Laboratory of Dr. Soetomo Hospital. Detection of HIF-1 α expressions were performed with immunohistochemistry method, using HIF-1 α antibody. It were statistically analyzed using Mann-Whitney and Kruskal- Wallis methods. There were no significant differences in the expression of HIF-1 α in colorectal adenocarcinoma with or without lymph node (LN) metastasis ($p>0.05$). As a conclusion, this study showed that HIF-1 α has no role in LN metastasis in colorectal adenocarcinoma. (FMI 2018;54:1-5)

Keywords: Colorectal adenocarcinoma; HIF-1 α ; regional LN

Correspondence: Alphania Rahniayu, Department of Anatomic Pathology, Faculty of Medicine, Universitas Airlangga, Surabaya. Phone: +6281234168612. Email: azkamom@gmail.com

INTRODUCTION

Colorectal carcinoma (CRC) has high rate of morbidity and mortality worldwide, both in males and females. Over 90% of the CRC is of adenocarcinoma type. CRC is one of the most commonly metastatic cancers, especially to the lymph nodes (LN), liver, and the peritoneum. Adjuvant therapy, such as chemotherapy and radiotherapy, have been widely applied, but late-stage CRC is still difficult to treat. It is therefore necessary to evaluate whether some proteins associated with metastasis can be used as a marker for metastasis in the CRC

(Cao et al 2009, Bosman et al 2010, Wu et al 2010). Rapid proliferation of tumors can lead to hypoxia in the microenvironment. Hypoxia is a triggering factor that induces angiogenesis. Angiogenesis has an important role in tumor growth and metastasis (Cao et al 2009). HIF-1 has been identified as an important protein and reacts directly to hypoxia. HIF-1 α is one subunit of HIF-1. HIF-1 α is important regulator in angiogenesis. (George et al 2001, Nathanson 2003).

The correlation between HIF-1 α expression with regional LN status was reported in colorectal adenocarcinoma.

noma, but there were also studies that reported no correlation between HIF-1 α expression with the regional LN status of colorectal adenocarcinoma. There is not much information about the cellular and molecular mechanisms involved in this lymphatic metastasis (Cao et al 2009, Wu et al 2010, Kwon et al 2010). This study aimed to prove the role of HIF-1 α and VEGF in metastasis to regional LN.

MATERIALS AND METHODS

The research design used was analytic observational with cross sectional approach. The study population were all blocks of paraffin of colorectal adenocarcinoma cases in Anatomic Pathology Laboratory of Dr. Soetomo Hospital, Surabaya, during the period of July 1, 2015 to June 30, 2016. In this period, there were 84 cases of colorectal adenocarcinoma. The samples for the study were taken by random sampling, divided into 15 samples in each group with and without regional LN metastasis. Inclusion criteria were paraffin blocks of surgical specimens, with a minimum amount of 12 regional LN, still having representative tumor cells for immunohistochemical examination, and histopathologic examination results that revealed colorectal adenocarcinoma profile. The diagnosis was established by anatomic pathologist at the Department of Anatomic Pathology, Dr. Soetomo Hospital, Surabaya.

The expression of HIF-1 α was immuno-histochemically examined with monoclonal rabbit antibody HIF-1 α (Biocare) with 1:50 dilution. The expression of HIF-1 α is said to be positive if it is in the cytoplasm. Positive tumor cells were calculated visually with a binocular light microscope, then evaluated on the intensity and percentage of HIF-1 α positively stained cells. The collected data were analyzed statistically. Differences of HIF-1 α expression were analyzed by Mann-Whitney test ($a<0.05$).

RESULTS

Mean age data of the patient in this study was 56.37 ± 10.36 . The youngest patient aged 32 years and the oldest was 80 years. Age grouping was conducted into 5 groups with span of 10 years. The ages of colorectal adenocarcinoma patients were in the range of 51-60 years in as much as 40%. Sex data showed balanced proportion of males and females, with 50% of males and 50% of females. The location of the tumor was mostly in the colon, as much as 50% of the cases, and the least was in the caecum, as much as 6.67% of the cases. Most of the tumor had high degree of differentiation (83.33% of cases), while those with poor differentiation was only 3.33% of cases. The depth of tumor invasion in this study was mostly T3, as much as 23 (76.67%) cases. Mann-Whitney and Kruskal-Wallis tests showed that there was no statistically significant difference in HIF-1 α expression between different age groups, sex, tumor location, degree of differentiation, and depth of invasion, both in colorectal adenocarcinoma with and without regional LN metastasis ($p>0.05$) (Table 1-5).

In this study, HIF-1 α expression was calculated in each group of samples based on the intensity and percentage of positively stained cells. We found median 3 in groups with and without metastasis, for intensity score and cell count as well as the score from multiplication of intensity and cell count (Fig. 1 & Table 6). The expression of HIF-1 α is shown in Fig. 2.

Mann-Whitney statistical analysis showed no difference in HIF-1 α expression between colorectal adenocarcinoma with and without LN metastasis ($p>0.05$), either on the intensity of expression, the number of cells expressing HIF-1 α , or the combined scores of intensity and number of cells expressing HIF-1 α . There was no increase in HIF-1 α expression in colorectal adenocarcinoma with LN metastasis ($p>0.05$) (Table 1).

Table 1. HIF 1- α expression by age category

Variable	Category	LN metastasis		Total
		+	-	
Age group	≤ 40 years	$2.5 \pm - (2-3)$	-	$2.5 \pm - (2-3)$
	41-50 years	$3.0 \pm - (3-3)$	$2.5 \pm 0.5 (2-3)$	$3.0 \pm 0.5 (2-3)$
	51-60 years	$3.0 \pm 1.0 (0-3)$	$3.0 \pm 0.5 (2-3)$	$3.0 \pm 0.5 (0-3)$
	61-70 years	$2.0 \pm 0.5 (1-3)$	$2.5 \pm - (2-3)$	$2.0 \pm 0.5 (1-3)$
	>70 years	$2.5 \pm - (2-3)$	$1.0 \pm - (1-1)$	$2.0 \pm - (1-3)$
	P	0.504	0.321	0.472

Table 2. HIF 1- α expression by sex category

Variable	Category	LN metastasis		Total
		+	-	
Sex category	Male	2.5 ± 0.5 (0-3)	3.0 ± 0.5 (2-3)	3.0 ± 0.5 (0-3)
	Female	3.0 ± 0.5 (2-3)	2.0 ± 0.5 (1-3)	2.0 ± 0.5 (1-3)
p		0.798	0.171	0.458

Table 3. HIF 1- α expression by tumor location category

Variable	Category	LN metastasis		Total
		+	-	
Location	Colon	2.5 ± 1.0 (0-3)	2.0 ± 0.5 (2-3)	2.0 ± 0.5 (0-3)
	Rectum	3.0 ± - (2-3)	3.0 ± 1.0 (1-3)	3.0 ± 0.5 (1-3)
	Caecum	-	2.5 ± - (2-3)	2.5 ± - (2-3)
	Rectosigmoid	2.5 ± 0.5 (2-3)	3.0 ± - (3-3)	3.0 ± 0.5 (2-3)
p		0.765	0.828	0.873

Table 4. HIF 1- α expression by degree of differentiation category

Variable	Category	LN metastasis		Total
		+	-	
Differentiation	Well	2.5 ± 0.5 (2-3)	3.0 ± 0.5 (1-3)	3.0 ± 0.5 (1-3)
	Moderate	3.0 ± 1.0 (1-3)	-	3.0 ± 1.0 (1-3)
	Poorly	0.0 ± - (0-0)	-	0.0 ± - (0-0)
p		0.187	-	0.159

Table 5. HIF 1- α expression by depth of invasion category (T stage)

Variable	Category	LN metastasis		Total
		+	-	
T Stage	1	-	1.0 ± - (1-1)	1.0 ± - (1-1)
	2	2.0 ± - (2-3)	2.5 ± - (2-3)	2.0 ± 0.5 (2-3)
	3	3.0 ± 0.5 (0-3)	3.0 ± 0.5 (2-3)	3.0 ± 0.5 (0-3)
	4	2.0 ± - (2-2)	-	2.0 ± - (2-2)
p		0.654	0.185	0.267

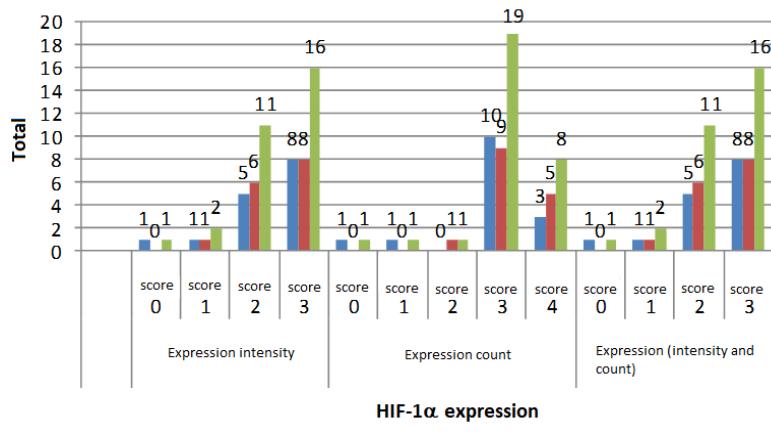


Fig. 1. Distribution of HIF-1 α expression in colorectal adenocarcinoma with and without LN metastasis.

Table 6. HIF-1 α expression based on metastatic status

HIF-1 α expression	Metastasis	Median	Interquartile deviation	Min	Max	p
Intensity	+	3	0.5	0	3	0.853
	-	3	0.5	1	3	
Count	+	3	0	0	4	0.331
	-	3	0.5	2	4	
Intensity & count	+	3	0.5	0	3	0.853
	-	3	0.5	1	3	

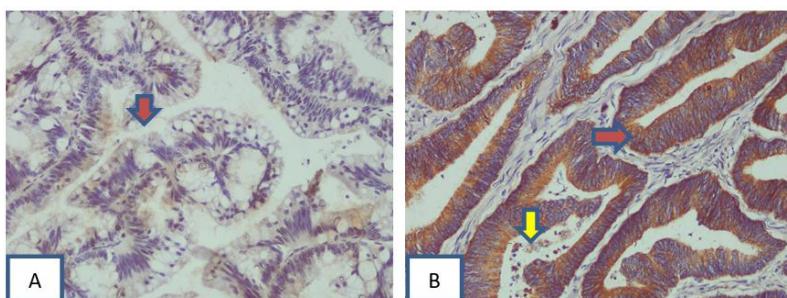


Fig. 2. Expression of HIF-1 α . A. Tumor cells stained with HIF-1 α antibody in the cytoplasm, with an intensity score of 1+ (red arrow) (IHC, 400x). B. Tumor cells stained with HIF-1 α antibody in the cytoplasm, with an intensity score of 3+ (red arrow). Neutrophils also appear in this antibody (yellow arrow) (IHC, 400x).

DISCUSSION

Colorectal carcinoma is one of the most common cancers in the world, ranked fourth in males, after lung, prostate, and gastric carcinoma; and ranked third in women, after breast and cervical cancer. The histologic type of adenocarcinoma was studied in this study because more than 90% of colorectal carcinomas were adenocarcinomas. Its association with regional LN status was studied because metastasis in LN had an independent prognostic interest for colorectal carcinoma

(Hamilton & Aaltonen 2000, Shepherd et al 2013). Colorectal adenocarcinoma patients mostly have an age range of 51-60 years. This is consistent with a previous study suggesting that the incidence of colorectal carcinoma increases with age, and rarely before age 40 (Hamilton & Aaltonen 2000). In this study, we found balanced proportion of males and females, each of them was 15. This is in accordance with another study that adenocarcinoma in colorectal cancer can be found in both sexes (Shepherd et al 2013). Most prevalent location of the tumor is in the colon and the rectum. The

results of this study are in accordance with that of Cao et al (2009) who found that the location of tumors in populations with high incidence rates is more common in the colon and the rectum than in other sites. The dominant tumor depth of invasion (T stage) was T3, which is in accordance with previous study conducted by Kwon et al (2010).

In this study we also assessed the HIF-1 α expression on several clinicopathologic parameters like age, sex, tumor location, differentiation grade, and the depth of invasion (T stage). The result showed that in all of those clinicopathologic parameters, there were no differences in HIF-1 α expression, whether in group with or without lymph nodes metastasis, and also in overall group ($p>0,05$). In the matter of age group, this study is in accordance to the study by Cao et al (2009), Kwon et al (2010), Decastel et al (2014), Wincewicz et al (2007), and Wu et al (2010), who also found that there was no correlation between HIF-1 α expression and patient age group ($p>0,05$) (Cao et al 2009, Kwon et al 2010 Decastel et al 2014, Wincewicz et al 2007, and Wu et al 2010).

Mann-Whitney statistical results showed that there was no difference in HIF-1 α expression between colorectal adenocarcinoma with and without LN metastasis ($p>0,05$). This is in accordance with a study conducted by Kwon et al (2010) who found no significant correlation between HIF-1 expression and clinicopathologic parameter, one of the LN metastasis parameters. This may be due to the complicated correlation between HIF-1 α and mutations which occur in the suppressor gene tumor, one of which is p53. One of the HIF-1 α regulatory mechanisms is the Mdm pathway, in which HIF-1 α binds to p53, and ubiquination is taking place mediated by Mdm2 (mouse double minute 2 homologue), resulting in HIF-1 α degradation by Mdm2 (Kwon et al 2010, Powis & Kirkpatrick 2004, Masoud & Li 2015).

CONCLUSION

In colorectal adenocarcinoma, HIF-1 α do not play a role in LN metastasis. Thus, it cannot serve as a marker of metastasis in this cancer.

REFERENCES

- Bosman FT, Carneiro F, Hruban R.H, Theise N.D (2010). Carcinoma of the colon and rectum. World Health Organization Classification of Tumours of the Digestive System. Lyon, IARC, 134-138
- Cao D, Hou M, Guan Y, Jiang M, Yang Y, Gou H (2009). Expression of HIF-1 α and VEGF in colorectal cancer: association with clinical outcomes and prognostics implications. BMC Cancer 9, 432
- Decastel M, Andrea AM, Lubeth M (2014). Inflammatory and cell adhesion protein markers in colorectal cancer in patient seen at the teaching hospital of Guadalupe: Role of NF kappaB and P-selectin. J Cytol Histol 5, 276
- George ML, Tutton MG, Janssen F (2001). VEGF-A, VEGF-C and VEGF-C in colorectal cancer progression. Nature publishing group, 420-427
- Hamilton SR, Aaltonen LA (2000). Pathology and Genetics of tumor of the Digestive System. Lyon, IARC Press, p 103-119
- Kwon HC, Kim SH, Oh SY (2010). Clinicopathological significance of nuclear factor-kappa B, HIF-1 α , and vascular endothelial growth factor expression in stage III colorectal cancer. Japanese cancer association 101, 1557-1561
- Masoud GN, Li W (2015). HIF-1 α pathway: role, regulation and intervention for cancer therapy. Acta Pharmaceutica Sinica B
- Nathanson SD (2003). Insights into the mechanism of lymph node metastasis. American Cancer Society, 413-423.
- Powis G, Kirkpatrick L (2004). Hypoxia inducible factor-1a as a cancer drug target. Molecular Cancer Therapeutics, p.647-654
- Shepherd NA, Warren BE, Williams GT (2013). Morson and Dawson's Gastrointestinal Pathology, 5th ed.. New Jersey, Blackwell Publishing Ltd., p 685-715
- Wincewicz A, Sulkowska M, Koda M (2007). Clinicopathological Significance and Linkage of the Distribution of HIF-1 α and GLUT-1 in Human Primary Colorectal Cancer. Pathology Oncology Research vol 13, no.1, 15-20
- Wu Y, Jin M, Xu Z (2010). Clinicopathologic Significance of HIF-1 α , CXCR4, and VEGF Expression in Colon Cancer. Hindawi Publishing Corporation, p 1-10

FOLIA MEDICA INDONESIANA
UNIVERSITAS AIRLANGGA
P-ISSN : 23558393 <> E-ISSN : 2599056X ◀ Subject Area : Education

0
Impact Factor

962
Google Citations

S2
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

S2 Journal

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

S2 Journal

Citation Per Year By Google Scholar



Journal By Google Scholar

	All	Since 2017
Citation	962	723
h-index	14	12
i10-index	28	21



**KOMITE ETIK PENELITIAN KESEHATAN
RSUD DR. SOETOMO SURABAYA**

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

659 / Panke.KKE / XI / 2016

KOMITE ETIK RSUD Dr. SOETOMO SURABAYA TELAH MEMPELAJARI SECARA SEKSAMA RANCANGAN PENELITIAN YANG DIUSULKAN, MAKA DENGAN INI MENYATAKAN BAHWA PENELITIAN DENGAN JUDUL :

" Ekspresi Protein HIF-1 α dan VEGF pada Adenokarsinoma Kolorektal : Hubungannya dengan Status KGB Regional "

PENELITI UTAMA : Ladyna Rumapar, dr

**PENELITI LAIN : 1. Sjahjenny Mustokoweni, dr., Sp. PA (K), MIAC
2. Alphania Rahniayu, dr., Sp. PA**

UNIT / LEMBAGA / TEMPAT PENELITIAN : RSUD Dr. Soetomo Surabaya

DINYATAKAN LAIK ETIK

SURABAYA, 17 NOV 2016



KETUA

**(Dr. Elizens Hanindito, dr., Sp.An, KIC,KAP)
NIP. 19511007 197903 1 002**