3. Menguji Doktor

KODE K09

DESKRIPSI	:	Penguji Tertutup a.n Imelda Theodora, dr., SpPA	Halaman
BUKTI	:	Undangan Wadek I ……...	02
		ST WD I FK No 1094/UN3.1.1/DI/2022, tanggal 27 Januari 2022 ……..	03
		Bukti kinerja yaitu hal sampul, hal pengesahan dll …….	04

UNIVERSITAS AIRLANGGA
FAKULTAS KEDOKTERAN
Kampus A.F. Mayjen Prof. Dr. Moestopo, 47 Surabaya 60132 Telp. (031) 5020251 Fax (031) 5022472
Laman : https://fk.unair.ac.id, e-mail : info@fk.unair.ac.id

35-25

Nomor : 1093/UN3.1.1/DL/2022 27 Januari 2022
Lamp : 1 Berkas
Hal : Mohon Kesediaan untuk menjadi Panitia Penguji Disertasi

Yth

1. Dr. Desak Gede A. Suprabawati,dr,Sp.B(K)Onk (Ketua)
2. Prof. Dr. I Ketut Sudiana, Drs.,M.Si
3. Dr. Vicky Sumarki Budipramana, dr., Sp.B-KBD
4. Prof. Dr. Abdurrachman, dr., M.Kes.,PA(K)
5. Dr. Karyono Mintaroem, dr.,Sp.PA
6. Dr. Windhu Purnomo, dr., M.S
7. Dr. Gondo Mastutik, drh., M.Kes
8. Dr. Bambang Purwanto, dr.,M.Kes

Dengan hormat,

Sehubungan dengan selesainya penulisan disertasi peserta Program Doktor angkatan tahun 2014/2015,

Nama : Imelda Theodora, dr., Sp.PA ELPT : 587
NIM : 011417017340
Judul : PERBEDAAN DAN MEKANISME PERKEMBANGAN KARSINOMA KOLOREKTAL MELALUI ANALISIS EKSPRESI *ESTROGEN RECEPTOR β*, INTERLEUKIN-6, STAT3, DAN Ki67

Promotor : Prof. Dr. I Ketut Sudiana, Drs.,M.Si
Ko-Promotor I : Dr. Vicky Sumarki Budipramana, dr., Sp.B-KBD

Ujian Disertasi rencananya diselenggarakan :

Hari, Tanggal : Kamis, 3 Pebruari 2022
Pukul : 09.00 - 12.00 WIB
Tempat : Menguji secara online menggunakan aplikasi Zoom

Maka dengan ini mohon kesediaan Saudara untuk menjadi Ketua / Anggota panitia Penguji Disertasi tersebut, terlampir kami sampaikan pernyataan kesediaan untuk diisi dan dilampirkan pada kami dalam waktu yang tidak terlalu lama guna diproses lebih lanjut.

Demikian atas perhatian Saudara, kami ucapkan terima kasih.

An. Dekan
Wakil Dekan I,

Dr. Achmad Chusnu Romdhoni,dr.,Sp.THT-KL(K).,FICS
NIP. 197609022008011009

Tindasan :
- Kepala Sub. Bagian Keuangan

UNIVERSITAS AIRLANGGA
FAKULTAS KEDOKTERAN
Kampus A Jl. Mayjen Prof. Dr. Moestopo, 47 Surabaya 60132 Telp. (031) 5020251 Fax (031) 5022472
Laman: https://fk.unair.ac.id, e-mail: info@fk.unair.ac.id

SURAT TUGAS

Nomor : 1094/UN3.1.1/DL/2022

Wakil Dekan I Fakultas Kedokteran Universitas Airlangga dengan ini menugaskan :

1.	Dr. Desak Gede A. Suprabawati,dr,Sp.B(K)Onk	Ketua
2.	Prof. Dr. I Ketut Sudiana, Drs.,M.Si	Anggota
3.	Dr. Vicky Sumarki Budipramana, dr., Sp.B-KBD	Anggota
4.	Prof. Dr. Abdurrachman, dr., M.Kes.,PA(K)	Anggota
5.	Dr Karyono Mintaroem, dr ,Sp.PA	Anggota
6.	Dr. Windhu Purnomo, dr., M.S	Anggota
7.	Dr. Gondo Mastutik, drh., M.Kes	Anggota
8.	Dr. Bambang Purwanto, dr.,M.Kes	Anggota

Sebagai Ketua / Anggota Panitia Ujian Tahap Pertama (Tertutup) Program Doktor Fakultas Kedokteran Universitas Airlangga atas nama Imelda Theodora, dr., Sp.PA peserta Program Doktor Program studi Ilmu Kedokteran angkatan tahun 2014/2015 yang diselenggarakan pada tanggal 3 Pebruari 2022.

Surat tugas ini diterbitkan sementara untuk menunggu keluarnya Surat Keputusan dari Dekan Fakultas Kedokteran Universitas Airlangga.

Surabaya, 27 Januari 2022

An. Dekan
Wakil Dekan I,

Dr. Achmad Chusnu Romdhoni,dr.,Sp.THT-KL(K),FICS
NIP. 197609022008011009

Diterbitkan untuk Ujian Akhir Tahap 1 (Tertutup)

DISERTASI

PERBEDAAN DAN MEKANISME PERKEMBANGAN KARSINOMA KOLOREKTAL MELALUI ANALISIS EKSPRESI *ESTROGEN RECEPTOR β*, INTERLEUKIN-6, STAT3, DAN Ki67

IMELDA THEODORA

PROGRAM STUDI ILMU KEDOKTERAN JENJANG DOKTOR
FAKULTAS KEDOKTERAN UNIVERSITAS AIRLANGGA
SURABAYA
2022

PERBEDAAN DAN MEKANISME PERKEMBANGAN KARSINOMA KOLOREKTAL MELALUI ANALISIS EKSPRESI *ESTROGEN RECEPTOR β*, INTERLEUKIN-6, STAT3, DAN Ki67

DISERTASI

Untuk memperoleh Gelar Doktor

Dalam Program Studi Ilmu Kedokteran Jenjang Doktor

pada Fakultas Kedokteran Universitas Airlangga

dan dipertahankan di hadapan Panitia Ujian Akhir Tahap 1 (Tertutup)

Oleh :

IMELDA THEODORA

011417017340

PROGRAM STUDI ILMU KEDOKTERAN JENJANG DOKTOR

FAKULTAS KEDOKTERAN UNIVERSITAS AIRLANGGA

SURABAYA

2022

LEMBAR PENGESAHAN

DISERTASI

PERBEDAAN DAN MEKANISME PERKEMBANGAN KARSINOMA KOLOREKTAL MELALUI ANALISIS EKSPRESI *ESTROGEN RECEPTOR β*, INTERLEUKIN-6, STAT3, DAN Ki67

YANG TELAH DISETUJUI

PADA TANGGAL 26 JANUARI 2022

Oleh

Promotor

Prof. Dr. I Ketut Sudiana, Drs., MSi.

NIP. 195507051980031005

Ko-Promotor

Dr. Vicky Sumarki Budipramana, dr., SpB-KBD

NIP.195509112016016101

Mengetahui,

Koordinator Program Studi Ilmu Kedokteran Jenjang Doktor

Fakultas Kedokteran Universitas Airlangga

Prof. Dr. Hendy Hendarto, dr., SpOG(K)

NIP. 196198172016016101

Disertasi ini telah disetujui untuk diuji dan dinilai

oleh panitia penguji Ujian Tahap 1 (Tertutup)

pada tanggal 3 Februari 2022

Panita penguji:

Ketua : 1. Prof. Dr. I Ketut Sudiana, Drs.,M.Si

Anggota : 2. Dr. Vicky Sumarki Budipramana, dr., Sp.B-KBD

3. Prof. Dr. Abdurrachman, dr., M.Kes.,PA(K)

4. Dr. Windhu Purnomo, dr., MS

5. Dr. Desak Gede A. Suprabawati,dr,Sp.B(K)Onk

6. Dr. Bambang Purwanto, dr.,M.Kes

7. Dr. Gondo Mastutik, drh., M.Kes

8. Dr. Karyono Mintaroem, dr., SpPA

SUMMARY

Colorectal carcinoma is the third most common malignancy worldwide, and second most leading cause of death in the United States. In Indonesia, it is one of the five malignancy with the most incidence. Therapy for colorectal carcinoma's keep involving and tend to be more personalized, using new regiments those are more specific for each individu.

Previous studies suggest that sex steroids influence colorectal cancer (CRC) carcinogenesis. Estrogen receptor β is the most predominant ER expressed in CRC. A number of studies show decline in ERβ expression and increase in IL-6 expression in colorectal carcinoma. Estrogen receptor β is known to have genomic and non genomic effect on cells proliferation, but which effect is more dominant in colorectal carcinoma needs further investigation.

This is an cross sectional, analitic observational study designed to investigate the difference and mechanism of ERβ and IL-6 in colorectal carcinoma development. Forty paraffin blocks of colorectal carcinoma cancer were obtained from Anatomical Pathology Installation RSU Dr. Soetomo Surabaya, and were subjected to immunohistochemistry staining using antibody to ERβ, IL-6, *Signal Transducer and Activator of Transcription 3* (STAT3), and Ki-67 to analyse the cell proliferation. Percentage of immunoreactive tumor cell per 1000 cells was recorded. Tumor differentiation was graded according to the WHO 2010 criteria, into well (>95% glandular formation), moderate (50-95% glandular formation), and poor differentiation (<50% glandular formation). Tumor infiltration was grouped based on AJCC TNM Staging 8th edition.

Our result shows the average age for CRC is 54.13 years with no gender difference. There is a significant difference and correlation in ERβ and IL-6 expression to the tumor differentiation, without significant difference in tumor infiltration. No difference found in Ki67 expression in each tumor differentiation, but there is significant difference in tumor infiltration. From the path analysis, our study sees that ERβ and IL-6 effect on tumor differentiation is not related to cell proliferation.

We observe a negative correlation of ERβ expression with tumor differentiation (p = 0,018 r = -0,371), but not to tumor infiltration. Interleukin-6 is correlated the tumor differentiation, higher expression of Interleukin-6 is associated with worse tumor differentiation (p = 0,035). IL-6 is correlated with STAT-3 expression, but not related to cell proliferation. The novelty of this study is ERβ and IL-6 is related to the tumor differentiation, but not to tumor infiltration, but there is no significant correlation between ERβ and IL-6 in human colorectal cancer speciments. IL-6 expression has a significant correlation with STAT-3 expression in colorectal carcinoma. Our results suggest that low expression of ERβ and high expression of IL-6 was a negative risk factor in colon cancer

ABSTRACT

Background: Colorectal carcinoma (CRC) is the third most common malignant disease worldwide, and second most leading cause of death in the United States. In Indonesia, it is one of five malignancy with the most incidence. Colorectal carcinoma's therapy become more personalized, with new regiments which becoming more specific for each individu. As it grows, colorectal carcinoma is known to have correlation with Estrogen Receptor β (ERβ) and Interleukin 6. A number of studies show decline in ERβ expression and increase in IL-6 ekspresion in colorectal carcinoma correlated with worse prognosis in CRC. Estrogen receptor β is known to have genomic and non genomic effect on cells proliferation, but which effect is more dominant in colorectal carcinoma is no yet known.

Objective: to analyze the difference and mechanism of ERβ and IL-6 in colorectal carcinoma.

Method: This is an analitic observational study with cross sectional design using forty paraffin blocks of colorectal carcinoma cancer obtained from Anatomical Pathology Installation RSU Dr.Soetomo Surabaya. Estrogen Receptor β, Interleukin-6, Signal Transducer and Activator of Transcription 3 (STAT3), and Ki-67 were investigated by immunohistochemical staining of formalin fixed, paraffin-embeded tissue sections from 40 CRCs. Percentage of immunoreactive tumor cell per 1000 cells was recorded. Tumor differentiation was graded according to the WHO 2010 criteria, and tumor infiltration was defined based on AJCC 8th edition TNM staging. In this study we grouped the tumor into T1-T2 group and T3-T4 group.

Result: The average age for the sample is 54.13 years with no gender difference. We observe a negative correlation of ERβ expression with tumor differentiation (p = 0,018 r = -0,371), but not to tumor infiltration. Interleukin-6 is correlated with the tumor differentiation, higher expression of Interleukin-6 is associated with worse tumor differentiation (p = 0,035). IL-6 is correlated with STAT-3 expression (p = 0,001 β = 0,511), but not related to cell proliferation. From the path analysis, our study sees that ERβ and IL-6 effect on tumor differentiation is not related to cell proliferation.

Conclusion: The higher IL-6 expression and the lower ERβ expression, the worse the tumor differentiation. High expression of IL-6 is correlated with STAT-3 expression, but not to cell proliferation. The novelty of this study is ERβ and IL-6 is related to the tumor differentiation, but not to tumor infiltration, but there is no significant correlation between ERβ and IL-6 in human colorectal cancer speciments. IL-6 expression has a significant correlation with STAT-3 expression in colorectal carcinoma *in vivo*.

Keywords: Colorectal carcinoma, ERβ, IL-6, STAT3, Ki67, differentiation, tumor infiltration.