3. Menguji Doktor

KODE K13

DESKRIPSI	:	Penyanggah Ujian Doktor Terbuka a.n Mala Kurniati, S.Si., M.Biomed.	Halaman
BUKTI	:	Undangan ……..	02
		SK Dekan FK No 454/UN3.1.1/HK/2021, tanggal 24 Agustus 2021 ……..	03
		bukti kinerja yaitu hal sampul, hal pengesahan dll ……	06

KEMENTERIAN PENDIDIKAN, KEBUDAYAAN,
RISET, DAN TEKNOLOGI
UNIVERSITAS AIRLANGGA
FAKULTAS KEDOKTERAN
Kampus A Jl. Mayjen Prof. Dr. Moestopo 47 Surabaya 60131
Telp. (031) 5020251, 5030252, 5030253 Faks. 5022472
website : http://www.fk.unair.ac.id; email : dekan@fk.unair.ac.id

Nomor : 4850/UN3.1.1/DL/2021 2 Agustus 2021
Lampiran :
Hal : Penyanggah Ujian Akhir Tahap 2 (Terbuka)

Kepada Yth,
Dr. Gondo Mastutik, drh., M.Kes
ditempat

Dengan hormat,

Dengan ini kami mengharap kehadiran Saudara sebagai **Penyanggah** Ujian Akhir Tahap 2 (Terbuka) Prodi Ilmu Kedokteran Jenjang Doktor atas nama **Mala Kurniati, S.Si., M.Biomed** yang akan diselenggarakan pada :

Hari, tanggal : Selasa, 24 Agustus 2021
Pukul : 10.00 – 12.00 WIB
Tempat : Aplikasi Zoom
Meeting ID : 944 3426 2706
Passcode : PascaS3

Demikian untuk diketahui dan atas perhatian Saudara kami sampaikan terima kasih.

a.n. Dekan
Plh. Wakil Dekan I,

Dr. Eighty Mardiyan Kurniawati, dr.,Sp.OG(K)
NIP. 197708142005012001

Catatan
- Dimohon hadir paling lambat 15 menit sebelumnya.
- Pakaian : Pria : Berjas dan berdasi
  Wanita : Menyesuaikan.

KEMENTERIAN PENDIDIKAN, KEBUDAYAAN,
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Telp. (031) 5020251, 5030252-3 Fax. (031) 5022472
Laman : http://www.fk.unair.ac.id e-mail : dekan@fk.unair.ac.id

SALINAN

KEPUTUSAN
DEKAN FAKULTAS KEDOKTERAN
NOMOR 454/UN3.1.1/HK/2021

TENTANG

PENYANGGAH UJIAN DOKTOR TERBUKA PROGRAM DOKTOR
PROGRAM STUDI ILMU KEDOKTERAN FAKULTAS KEDOKTERAN
ATAS NAMA MALA KURNIATI, S.Si.,M.Biomed

DEKAN FAKULTAS KEDOKTERAN,

Menimbang :

a. bahwa ujian disertasi tahap I Jenjang Doktor telah dilaksanakan, selanjutnya mahasiswa yang dinyatakan lulus dari ujian tahap I tersebut berhak mengikuti ujian tahap II yang disebut Ujian Doktor Terbuka;

b. bahwa nama-nama Penyanggah Ujian Doktor Terbuka yang tercantum dalam lampiran Keputusan ini dinyatakan memenuhi syarat dan bersedia untuk ditetapkan sebagai penyanggah Ujian Doktor Terbuka;

c. bahwa berdasarkan pertimbangan sebagaimana dimaksud pada huruf a dan huruf b, perlu menetapkan Keputusan Dekan Fakultas Kedokteran Universitas Airlangga tentang Penyanggah Ujian Doktor Terbuka Program Doktor Program Studi Ilmu Kedokteran Fakultas Kedokteran.

Mengingat :

1. Undang-Undang Nomor 20 Tahun 2003 tentang Sistem Pendidikan Nasional (Lembaran Negara Republik Indonesia Tahun 2003 Nomor 78, Tambahan Lembaran Negara Nomor 4301);
2. Undang-Undang Republik Indonesia Nomor 14 Tahun 2005 tentang Guru dan Dosen (Lembaran Negara Republik Indonesia Nomor 157, Tambahan Lembaran Negara Nomor 4586;
3. Undang-Undang Nomor 12 Tahun 2012 tentang Pendidikan Tinggi (Lembaran Negara Republik Indonesia Tahun 2012 Nomor 158, Tambahan Lembaran Negara Nomor 5336);
4. Undang-Undang Nomor 5 Tahun 2014 tentang Aparatur Sipil Negara (Lembaran Negara Republik Indonesia Tahun 2014 Nomor 06, Tambahan Lembaran Negara Nomor 5494);

5. ...

5. Peraturan Pemerintah Republik Indonesia Nomor 57 Tahun 1954 tentang Pendirian Universitas Airlangga Di Surabaya sebagaimana telah diubah dengan Peraturan Pemerintah Nomor 3 Tahun 1955 tentang Pengubahan Peraturan Pemerintah Nomor 57 Tahun 1954. (Lembaran Negara Republik Indonesia Tahun 1954 Nomor 99 Tambahan Lembaran Negara Nomor 695 juncto Lembaran Negara Republik Indonesia Tahun 1955 Nomor 4 Tambahan Lembaran Negara Nomor 748);
6. Peraturan Pemerintah Nomor 4 Tahun 2014 tentang Penyelenggaraan Pendidikan Tinggi dan Pengelolaan Perguruan Tinggi. (Lembaran Negara Republik Indonesia Tahun 2014 Nomor 16, Tambahan Lembaran Negara Nomor 5500);
7. Peraturan Pemerintah Nomor 30 Tahun 2014 tentang Statuta Universitas Airlangga. (Lembaran Negara Republik Indonesia Tahun 2014 Nomor 100, Tambahan Lembaran Negara Nomor 5535);
8. Peraturan Rektor Universitas Airlangga Nomor 38 Tahun 2017 tentang Peraturan Pendidikan Universitas Airlangga;
9. Peraturan Rektor Universitas Airlangga Nomor 21 Tahun 2014 tentang Pedoman Pendidikan Program Doktor (S3) Universitas Airlangga;
10. Keputusan Rektor Universitas Airlangga Nomor 1947/H3/KR/2011 tentang Penetapan Ruang Lingkup Program Studi dalam Kategori Monodisiplin, Interdisiplin dan Multidisiplin untuk Pengelolaan Program Magister dan Program Doktor;
11. Keputusan Rektor Universitas Airlangga Nomor 762/UN3/KR/2020 tentang Pengangkatan Dekan Fakultas, Direktur Sekolah Pascasarjana, dan Direktur Rumah Sakit Periode 2020-2025.

MEMUTUSKAN :

Menetapkan : KEPUTUSAN DEKAN FAKULTAS KEDOKTERAN TENTANG PENYANGGAH UJIAN DOKTOR TERBUKA PROGRAM DOKTOR PROGRAM STUDI ILMU KEDOKTERAN FAKULTAS KEDOKTERAN ATAS NAMA MALA KURNIATI, S.Si.,M.Biomed

PERTAMA: ...

PERTAMA : Menetapkan Penyanggah Ujian Doktor Terbuka Program Doktor Program Studi Ilmu Kedokteran Fakultas Kedokteran atas nama Mala Kurniati, S.Si.,M.Biomed yang dilaksanakan pada tanggal, 24 Agustus 2021 dengan susunan nama sebagai berikut:

1. Prof. R.M. Coen Pramono D., drg.,SU.,Sp.BM(K)
2. Dr. Agung Sosiawan, drg.,M.Kes.
3. Prof. Dr. Indri Safitri Mukono, dr.,MS
4. Prof. Sri Agus Sudjarwo, Ph.D
5. Dr. Gondo Mastutik, drh.,M.Kes.
6. Dr. Bambang Purwanto, dr.,M.Kes.
7. Dr. Lynda Hariani, dr.,Sp.BP-RE(K)
8. Prof. Dr. Harianto Notopuro, dr.,MS
9. Prof. Dr. Budi Santoso, dr., Sp.OG(K)

KEDUA : Dalam menjalankan tugasnya sebagaimana dimaksud dalam diktum PERTAMA, berpedoman pada peraturan dan ketentuan yang berlaku serta mempertanggungjawabkan tugasnya kepada Dekan Fakultas Kedokteran.

KETIGA : Biaya untuk keperluan tersebut dibebankan pada dana Rencana Kegiatan dan Anggaran Tahunan (RKAT) Fakultas Kedokteran.

KEEMPAT : Keputusan ini mulai berlaku pada tanggal ditetapkan.

Ditetapkan di Surabaya
pada tanggal 24 Agustus 2021

DEKAN,

ttd

Budi Santoso
NIP. 196302171989111001

Salinan sesuai dengan aslinya
Kepala Bagian Tata Usaha,

Basuni
NIP. 196501021987011001

SALINAN disampaikan Yth.
1. Rektor Universitas Airlangga
2. Yang bersangkutan

DISERTASI

PERAN *SINGLE NUCLEOTIDE POLYMORPHISM* (SNP) GEN BMP2 rs235768 DAN GEN BMP4 rs17563 PADA KEJADIAN CELAH BIBIR DAN ATAU PALATUM NON SINDROMIK BERDASARKAN PENDEKATAN GENOMIK

MALA KURNIATI

PROGRAM STUDI ILMU KEDOKTERAN JENJANG DOKTOR
FAKULTAS KEDOKTERAN UNIVERSITAS AIRLANGGA
SURABAYA
2021

PERAN *SINGLE NUCLEOTIDE POLYMORPHISM* (SNP) GEN BMP2 rs235768 DAN GEN BMP4 rs17563 PADA KEJADIAN CELAH BIBIR DAN ATAU PALATUM NON SINDROMIK BERDASARKAN PENDEKATAN GENOMIK

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 I (Tertutup)

Oleh:

Mala Kurniati
NIM : 011717017335

PROGRAM STUDI ILMU KEDOKTERAN JENJANG DOKTOR
FAKULTAS KEDOKTERAN UNIVERSITAS AIRLANGGA
SURABAYA
2021

LEMBAR PENETAPAN PANITIA PENGUJI

Disertasi ini telah disetujui untuk diuji dan dinilai oleh panitia penguji Ujian Tahap I (Tertutup)

Pada tanggal 18 Juni 2021

Panitia Penguji :

Ketua : Prof. Dr. Harianto Notopuro, dr., MS

Anggota : Prof. R.M. Coen Pramono D, drg., S.U., Sp.BM(K)., FICS

Dr. Agung Sosiawan, drg.,M Kes

Prof. Dr David S.Perdana Kusuma, dr., Sp.BP-RE(K)

Dr. Ni Wajan Tirthaningsih, dr., MS., PA(K)

dr. Hidayat Sujuti, Ph.D.,Sp M

Dr. Hari Basuki Notobroto, dr., M.Kes

Andra Rizqiawan, drg.,Ph D.,Sp BM(K)

Ditetapkan dengan Surat Keputusan
Dekan Fakultas Kedokteran Universitas Airlangga
Tentang Panitia Penguji Disertasi
No : 3517/UN3.1.1/DL/2021
Tanggal : 4 Juni 2021

SUMMARY

THE ROLE OF SINGLE NUCLEOTIDE POLYMORPHISM (SNP) OF THE BMP2 rs235768 GENE AND THE BMP4 rs17563 GENE IN THE OCCURRENCE OF NON-SYNDROMIC CLEFT LIP AND/OR PALATE BASED ON GENOMIC APPROACH

A cleft lip with or without palate (CL/P) refers to orofacial deformity conditions in which an abnormal opening or fissure is formed in the lip or palate. There are three main types of abnormal CL/P: cleft lip (CL), gap palate (GP), and cleft lip and palate (CLP). The factor influencing the emergence of CL/P is multi-factor influenced by genetic and non-genetic factors. Bone Morphogenetic Protein (BMP) is a superfamily of TGF β functioning in the process of developing and forming various craniofacial elements, including neural cranial crest, as well as the facial, dental, labial, and palatal primordia. The BMP family genes forming the palate are BMP2 and BMP4 genes; the genes function to control the development of the facial primordia. Some studies conclude that the investigation on genes triggering the occurrence of CL/P is still contradictory because they employ different populations and races. Therefore, further research is necessarily conducted to discover or prove a gene that can affect the occurrence of CL/P.

This study aimed to: (1) analyze the frequency of genotypes and allele of the SNP of the BMP2 rs235768 A>T gene and the BMP4 rs17563 T>C gene on the incidence of CL/P; (2) analyze the relationship between the SNP of the BMP2 rs235768 A>T gene and the BMP4 rs17563 T>C gene on the incidence of CL/P and control; (3) analyze the relationship between the SNP of the BMP2 rs235768 A>T gene and the BMP4 rs17563 T>C gene with the types of abnormality on the incidence of CB/P; (4) analyze the relationship between the types of abnormality on the incidence of CB/P and gender, family history, and a mother's age during childbirth; (4) analyze the description of the combined genotype of the BMP2 rs235768 A>T gene and the MP4 rs17563 T>C gene on the patient's family on the incidence of CL/P; and (5) analyze the effect of mutations of the BMP2 rs235768 A>T gene and the BMP4 rs17563 T>C gene on the function of the protein and changes in the conformation of three-dimensional proteins.

The research was conducted from September 2019 to October 2020 and involved 70 research subjects, consisting of 34 patients (48.6%) with the incidence of CB/P and 36 normal people (51.4%) as a control. The research subjects were selected from two hospitals: the Regional General Hospital (RSUD) Bima, West Nusa Tenggara in October 2019 and NU Hospital, Tuban, East Java in February 2020. The DNA of 70 blood samples derived from the CL/P patients and the control group was isolated. The PCR technique was conducted to amplify

the DNA of the targeted regions of exon 3, the BMP2 rs235768 A>T gene, and exon 4 of the BMP4 rs17563 T>C gene. The statistical analysis employed Fisher's exact test to determine the relationship between SNP of BMP2 rs235768 A>T gene and the BMP4 rs17563 T>C gene with the incidence of CL/P. The determination of conformation of three dimensions employed two programs, while the determination of mutation effects employed seven bioinformatics programs.

This study discovered five major points. First, the SNP of the BMP2 rs235768 A>T gene was good on the incidence of CL/P and the control. Second, SNP of BMP4 rs17563 T>C gene did not exist on the incidence of CL/P and the control. Third, there was a relationship between family history and the types of abnormality on the incidence of CL/P. Fourth, there were three other variants on the sequencing results of the BMP2 gene in exon 3. They were variant 1 of 10642G>A heterozygous genotype (AG), variant 2 of 10810G>A heterozygous genotype (AG), and variant 3 10843 C>T heterozygous genotype (CT). The mutating BMP2 rs235768 A>T gene and BMP4 rs17563 T>C gene influenced the functions of the protein using an *in-silico* way and the changes in the conformation of the three-dimensional proteins between wild-types and mutants.

ABSTRACT

The Role of Single Nucleotide Polymorphism (SNP) BMP2 rs235768 Gene and BMP4 rs17563 Gene in the Occurrence of Non-Syndromic Cleft Lip and/or Palate based on Genomic Approach

Mala Kurniati

Cleft lip with or without palate (CB/P) is a condition of orofacial deformity, that is the formation of an unnatural opening or gap in the lip or palate. There are three types of CB/P disorders, which are cleft lip (CB), cleft palate (CP), and cleft lip and palate (CBP). Factors that influence the occurrence of CB/P are multifactorial, influenced by genetic factors and non-genetic factors. The purpose of this study was to analyze the relationship between Single Nucleotide Polymorphism (SNP) BMP2 rs235768 A>T gene and BMP4 rs17563 T>C gene on the incidence of CB/P.

This research involved 70 research subjects, consisting of 34 CB/P patients and 36 for the controls. DNA isolation was performed on the research subjects, followed by genotyping analysis by PCR-RFLP. Determination of 3-dimensional conformation was done using 2 bioinformatics programs and determination of mutation effects employed 7 bioinformatics programs.

The results showed that there was a relationship between the SNP BMP2 rs235768 A>T gene in the incidence of CB/P and controls (p=0.0498). There was no SNP relationship between BMP4 rs17563 T>C gene and control (p=0 935) in the incidence of CB/P. There was a relationship between family history and the type of abnormality in the incidence of CB/P (p=0.011). Three other variants were found in the results of BMP2 gene sequencing in exon 3, which were variant 1; 10642G>A heterozygous genotype (AG), variant point 2; 10810G>A heterozygous genotype (AG), and variant 3; 10843 C>T heterozygous genotype (CT). There is an effect of mutation in BMP2 rs235768 A>T and BMP4 rs17563 T>C genes on protein function in silico and changes in the three-dimensional conformation of proteins between wild type and mutants.

There is a relationship between the SNP BMP2 rs235768 gene A>T in CB/P events and controls. There was no relationship between the SNP of the BMP4 rs17563 T>C gene in CB/P events and controls. There is an effect of mutation in BMP2 rs235768 A>T and BMP4 rs17563 T>C genes in silico and a three-dimensional conformational change of protein between wild type and mutants.

Keywords: SNP, BMP2 Gene, BMP4 Gene, CB/P, Protein Conformation