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## Kobe University Academic Research and Education Forum in Indonesia

*Medical and Health Sciences:  
Research Frontiers between  
Kobe University and Universitas Gadjah Mada*

Pre-Conference Abstract, Alumni Profile and Research Activities



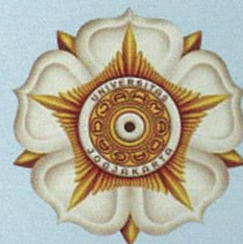
# 2016

## December 21

in *Yogyakarta, Indonesia*



神戸大学



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Organized by: Institute for Promoting International Partnerships, Kobe University  
Co-hosted by: Faculty of Medicine, Universitas Gadjah Mada

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## KOBE University Academic Research and Education Forum in Indonesia

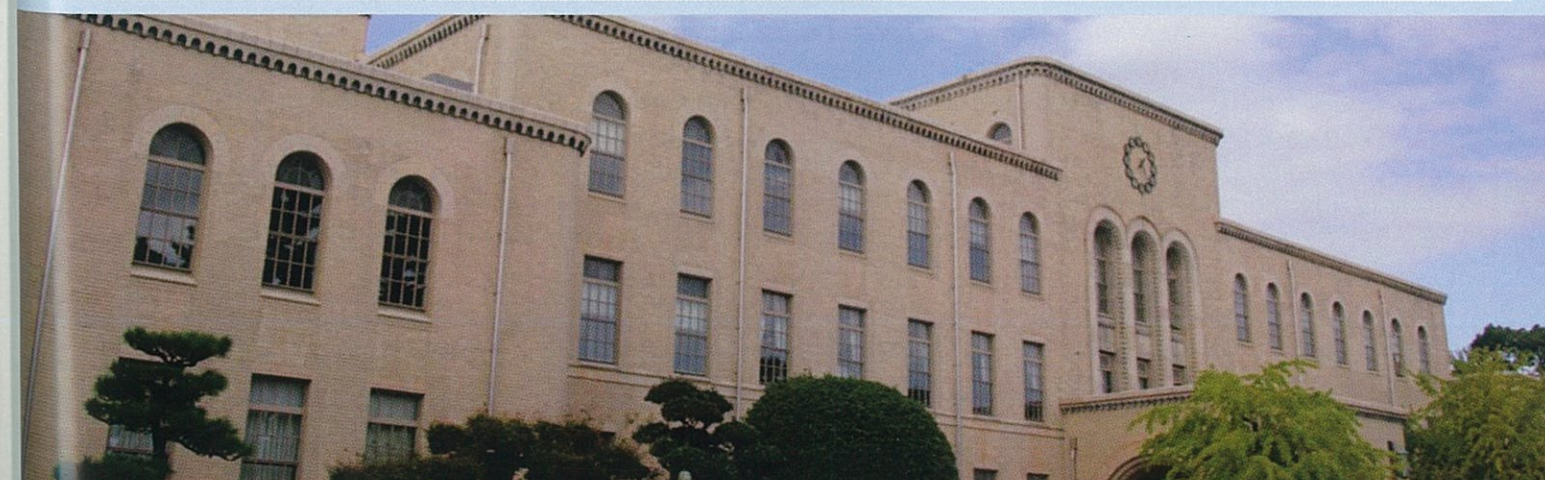
December 21 and 23, 2016

In July 2013, we installed the Center for Asian Academic Collaboration under the Institute for Promoting International Partnerships, which was established to enhance our global competitiveness and develop further as an international hub for education and research. Through the Center, Kobe University is pursuing a strategic approach to international exchange, focusing on Asian countries currently experiencing rapid economic growth which are expected to play increasingly important global roles.

This year we will hold the first Kobe University Academic Research and Education Forum (KUAREF) in Jakarta and Yogyakarta, in Indonesia. This forum, which focuses on research and education, originally started as the Kobe University Global-Link Forum (KUGL) in 2011 in Bangkok, Thailand. KUGL had two main goals: to promote the Kobe University Brand overseas, and to form stronger links with overseas academic associations and the International Alumni Association Network, which provides an invaluable repository of knowledge for the University. KUAREF will inherit the best parts of the KUGL event series and continue to build upon KUGL's achievements.

We believe that the forum will present unique and valuable opportunities for members of leading universities in Indonesia and Japan to gather together, build relationships, and enhance cooperation with each other.

(Institute for Promoting International Partnerships, Kobe University)





## Pre-Conference

Date: Wednesday 21 December 2016 8:30 ~ 16:45

Venue: Auditorium, Faculty of Medicine, Universitas Gadjah Mada

### 8:30-8:50 Opening Remarks

Prof. Noriyuki Inoue (Executive Vice President in charge of International Exchange and Internal Control, Kobe University)

Prof. Ova Emilia (Dean, Faculty of Medicine, Universitas Gadjah Mada)

Prof. Dwikorita Karnawati (President, Universitas Gadjah Mada)

### 8:50-9:05 Seminar Overview

Prof. Satoshi Takada (Graduate School of Health Sciences, Kobe University)

### 9:05-10:45 Session I : Genetic Analysis in the field of child neurology

#### Commentator

#### *Diagnosis of spinal muscular atrophy*

Prof. Hisahide Nishio (Graduate School of Medicine, Kobe University)

#### *Spinal muscular atrophy (SMA): Advances in therapeutic development*

Dr. Nur Imma Fatimah Harahap (Assistant Professor, Graduate School of Medicine, Kobe University)

#### *The role of SCN1A gene in genetic/generalized epilepsy with febrile seizure plus (GEFS+) in Indonesian population*

Prof. Elisabeth S. Herini (Department of Child Health, Faculty of Medicine, Universitas Gadjah Mada)

< Break time : 15 min >

### 11:00-12:40 Session II : Infectious Diseases and Treatments

#### Commentator

#### *Anti-flavivirus compounds from natural resources*

Prof. em. Hak Hotta (Project Professor, Graduate School of Health Sciences, Kobe University)

#### *Molecular Mechanisms of Anti Tuberculosis Drugs Resistance*

Dr. Tri Wibawa (Department of Microbiology, Faculty of Medicine, Universitas Gadjah Mada)

#### *Self-expanding community resilience through well-chained and partnership-based disaster preparedness program.*

Prof. Djoko Legono (Department of Civil and Engineering, Faculty of Engineering, Universitas Gadjah Mada)

### 12:40-13:40 Lunch Break

### 13:40-16:40 Session III: Establishment of UNESCO Chair: Focusing on Gender Aspects of Disaster

#### Commentator

#### *Drawing disaster and recovery: Five years of the Popoki Friendship Story Project*

Prof. Ronni Alexander (Graduate School of International Cooperation Studies, Kobe University)

#### *Disaster and gender; Inquiry in a stricken area*

Dr. Tomoko Nakahara (Assistant Professor, Gender Equality Office, Kobe University)

#### *'Kobe Style' how to share the gender aspects of disaster*

Dr. Junko Okada (Associate Professor, Graduate School of Maritime Sciences, Kobe University)

#### *Interprofessional Teamwork in Community Rehabilitation Affected by Earthquake on May 27th 2006 In Bantul Yogyakarta Indonesia*

Prof. Sunartini (Department of Pediatric, Faculty of Medicine, Universitas Gadjah Mada)

#### *Maternal health in disaster*

Dr. Elsi DH (Department of Pediatric and Maternity Nursing, Faculty of Medicine, Universitas Gadjah Mada)

### 16:40-16:45 Closing Remarks

Prof. Kazunori Uchida (Executive Vice President in charge of Public Relations and Community Cooperation, Kobe University)

## Pre-Conference : Seminar Overview



Kobe University  
Graduate School of Health Sciences

**Prof. Takada Satoshi**

Kobe University has been completing a number of educational collaboration projects in various academic fields in Indonesia. On the other hand, the research platform in medicine and health sciences in Indonesia in place since the 1960s is also continuing. Many graduates of Kobe University have become core researchers in both clinical and basic studies in Indonesian universities including Universitas Gadjah Mada. Currently a project called "Education of medical and health science leaders in the coming generation, in cooperation and collaboration with ASEAN countries" is in progress. Kobe University has played the leading role for this project in collaboration with Universitas Gadjah Mada, the Universitas Indonesia and Airlangga University. J-GRID stands for the Japan Initiative for Global Research Network on Infectious Disease. We have a proud history of collaboration with the Institute of Tropical Disease (ITD) at Airlangga University. Another important project is the Educational Disaster Management undertaken in collaboration with Universitas Gadjah Mada. Kobe University immediately responded after the Central Java Earthquake in 2006. In addition to this, an international seminar on disaster has been held annually for a period of ten years in Yogyakarta. During this pre-seminar we will focus on three topics: genetic analysis in the field of child neurology, infectious diseases and treatments, and gender aspects of disaster. I hope this seminar will provide young students with further stimulation to foster ongoing collaboration.

Dr Takada is a professor of Graduate School of Health Sciences, Kobe University Japan, He received his M.D in 1979, and Ph.D in 1985 from Kobe University. He was trained as a clinical neonatologist, and subsequently as a child neurologist in the same university.

Between 1989 and 2000 he was engaged as Chief of NICU and also as Chief, Division of Child Neurology at Kobe University Hospital. During those days he experienced Hanshin-Awaji earthquake. He worked in collaboration with Kobe City Government for disabled children. In 2000, he was appointed as a professor of Graduate School of Health Sciences. He worked as Dean of the Graduate School of Health Sciences for 3 years.

- Board-certified pediatrician
- Board-certified child neurologist
- Board-certified in pediatric psychiatry
- Board-certified child mental health specialist



## Pre-Conference : Session I

### Genetic Analysis in the field of child neurology



Kobe University  
Graduate School of Medicine

**Prof. Hisahide Nishio, MD, PhD**

### Diagnosis of spinal muscular atrophy

Spinal muscular atrophy (SMA) is a common neuromuscular disorder with an autosomal recessive inheritance trait. SMA is common in children in any region in the world (1: 10,000 live births), but remains an incurable disease.

In 1995, the survival motor neuron gene (*SMN*) was identified as a candidate gene for SMA. *SMN* exists in two nearly identical copies, *SMN1* and *SMN2*. *SMN1* is absent from more than 95% of SMA patients and deleteriously mutated in the remaining patients. Thus, *SMN1* has been recognized as an SMA-causing gene.

On the other hand, *SMN2* was previously considered to be dispensable because approximately 5% of normal individuals do not carry the gene. However, *SMN2* also expresses the same protein, SMN, as *SMN1* does, albeit at considerably lower levels than *SMN1*. A high copy number of *SMN2* can partially compensate for the lack of *SMN1*. Thus, *SMN2* is now considered to be an SMA-modifying gene.

To diagnose SMA and to predict the prognosis, it is necessary to identify the mutation in *SMN1* and determine the copy number of *SMN2*. I will explain the outline of methods for *SMN* gene analysis in my presentation, as well as molecular findings observed in our SMA patients.

#### Professional experience:

2002-present Professor, Kobe University Graduate School of Medicine  
1995-2002 Associate Professor, Kobe University Graduate School of Medicine

#### Education:

1986 Ph.D. Kobe University, Graduate School of Medicine  
1980 M.D. Kobe University, School of Medicine

#### Membership:

The Japan Society of Human Genetics  
The American Society of Human Genetics  
The Japan Pediatric Society  
The Japanese Society of Child Neurology  
The Japan Society of Public Health

## Pre-Conference : Session I

### Genetic Analysis in the field of child neurology



Kobe University  
Graduate School of Medicine

Assistant Professor

**Nur Imma Fatimah Harahap, MD, PhD**

### Spinal muscular atrophy (SMA): Advances in therapeutic development

Spinal muscular atrophy (SMA) is a neuromuscular disorder with autosomal recessive inheritance trait. It is characterized by the degeneration of lower motor neurons leading to muscle weakness. SMA is still an incurable disease.

*SMN1* is an SMA-causing gene. *SMN2*, the homologue copy of *SMN1* which always retains in SMA patients, also expresses the same protein, SMN, as *SMN1* does, though with lower levels than *SMN1*. It was shown that a high copy number of *SMN2* can partially compensate for the lack of *SMN1*. Thus, *SMN2* is considered to be an SMA-modifying gene.

Current strategies can be classified into three groups. The first group, “*SMN1*-introduction strategies”, involves strategies to introduce exogenous *SMN1* copies using vector-mediated gene delivery methods and stem cell transplantation methods.

The second group, “*SMN2*-targeting strategies”, involves strategies to increase functional SMN protein using pharmacological compounds (valproic acid, salbutamol, etc.), correct the splicing of *SMN2* mRNA by antisense-oligos or stabilize the SMN protein.

The third group, “Non-SMN-targeting strategies,” involves strategies to protect motor neurons or improve the pathological conditions of non-neuronal tissues including muscles.

In conclusion, we say with confidence that SMA will be able to be treated in the near future.

**Affiliation:** Kobe University Graduate School of Medicine

#### Professional experience:

2016-present Assistant Professor, Kobe University Graduate School of Medicine  
2011-2012 Research Assistant, Pediatric Research Office, Department of Pediatrics, Faculty of Medicine, Universitas Gadjah Mada

#### Education:

2016 Ph.D. Kobe University, Graduate School of Medicine  
2010 M.D. Universitas Jenderal Soedirman

#### Membership:

The Japan Society of Human Genetics



## Pre-Conference : Session I

### Genetic Analysis in the field of child neurology



Universitas Gadjah Mada  
Department of Child Health,  
Faculty of Medicine

**Prof. Elisabeth S. Herini, MD, PhD,  
Pediatrician, Consultant**

### *The role of SCN1A gene in genetic/generalized epilepsy with febrile seizure plus (GEFS+) in Indonesian population*

Genetic/Generalized epilepsy with febrile seizure plus (GEFS+) is the most important familial epileptic syndrome because it links febrile seizure with various other epileptic seizures/syndromes and documents genetic relations between (1) benign and severe and (2) focal and generalized epileptic disorders. GEFS+ was described by Scheffer and Berkovic in 1997 and is currently recognized as one of the epilepsy syndromes by ILAE. This terminology is newer in neurology than epilepsy, which has been known since it was identified in 400 BC by Hippocrates.

Clinical manifestation of GEFS+ spectrum varies from classic febrile seizure to the most severe type which is Dravet Syndrome/ severe myoclonic epilepsy in infancy (SMEI). In our study we have 35 patients consisting of 18 boys (51.4%) and 17 girls (48.6%). The diagnosis of GEFS+ - SMEI spectrum comprised FS+ 9 (25.7%), GEFS+ 11 (31.4%), SMEB 8 (22.9%), and SMEI 7 (20%) cases. This study found four heterozygote mutations of the *SCN1A* gene: A966S, V1612I, C1756G, and G1762 in severe myoclonic epilepsy borderline (SMEB), Dravet Syndrome, SMEB and GEFS+ respectively (Herini et al., 2010a; 2010b; 2010c).

Tonekaboni *et al.* (2013) reported that their genetic testing showed 1 of 3 (33.3%) patients with clinical manifestation had Dravet syndrome and 3 of 20 (15%) patients that were diagnosed with GEFS+ had *SCN1A* mutation.

Nowadays, more than 60 heterozygous pattern *SCN1A* mutations, of which many are de novo mutations, have been detected in Dravet syndrome and GEFS+.

Finally, further research to find the *SCN1A* gene mutation and other genes is still broadly open to GEFS+, which is useful for the development of science in the future.

**Key Words:** GEFS+; Dravet Syndrome; *SCN1A*; Clinical manifestation

#### Education

1977-1984 : Medical Doctor, Faculty of Medicine, Universitas Gadjah Mada  
1993-1997 : Pediatrician, Faculty of Medicine, Universitas Gadjah Mada  
1997-2003 : Consultant of Pediatric Neurology, Faculty of Medicine, Universitas Gadjah Mada and Universitas Indonesia  
2007-2010 : PhD program, Faculty of Medicine, Gadjah Mada University

#### Current Position

Director of medical services and nursing, UGM Hospital  
Head of Neurology Division, Pediatric Department, Faculty of Medicine, UGM  
Staff of Medical Functional Unit, Dr. Sardjito General Hospital, Yogyakarta

## Pre-Conference : Session II

### Infectious Diseases and Treatments



Kobe University  
Graduate School of Health Sciences  
Department of Vaccine and Drug Development,

Endowed Chair and Professor

**Prof. Em. Hak Hotta, MD, PhD**

### *Anti-flavivirus compounds from natural resources*

Dengue virus (DENV) and hepatitis C virus (HCV) belong to the same virus family *Flaviviridae* although the genera they belong to are different from each other. DENV infection causes global health problems, with reportedly more than 100 million patients being infected per year and 2.5 billion people being at risk of infection worldwide. Also, HCV infection is another major global health problem, with an estimated more than 170 million patients being chronically infected, who suffer from chronic hepatitis, liver cirrhosis and hepatocellular carcinoma. Therefore, effective drugs as well as effective vaccines against DENV and HCV are urgently needed to cope with the problems. Natural resources are a good candidate for drug screening. We have been aiming at identifying an antiviral compound(s) against DENV and/or HCV isolated from natural resources, such as medicinal plants, microbes, insects and other animal products. Through bioactivity-guided analysis using HPLC, NMR and LC-MS in combination with antiviral activity assays, we have identified a number of antiviral compounds against DENV and HCV from medicinal plants, microbes and animals. In this symposium, I will present some of the data and discuss the potential use of those substances as seed compounds to develop antiviral drugs against DENV and/or HCV.

#### Present Academic Position

Professor Emeritus, Kobe University (Medicine)  
Professor and Endowed Chair  
Department of Oral Vaccine and Drug Development  
Kobe University Graduate School of Health Sciences  
Biotechnology Research Center, Room 404  
1-5-6 Minatojima-minamimachi, Chuo-ku, Kobe 650-0047, Japan  
Tel +81-78-304-6091; Fax +81-78-304-6019  
Email: hotta@kobe-u.ac.jp; hotta@med.kobe-u.ac.jp

#### Education

M.D. Osaka University (School of Medicine); 1974  
Ph.D. Kobe University (Graduate School of Medicine); 1985



## Pre-Conference : Session II

### Infectious Diseases and Treatments



Universitas Gadjah Mada  
Faculty of Medicine  
Department of Microbiology

**Tri Wibawa, MD, PhD, SpMK**

### *Molecular Mechanisms of Anti Tuberculosis Drugs Resistance*

Tuberculosis is a serious health problem in Indonesia. In recent decades, there was no significant invention of new anti-tuberculosis drugs reported. Tuberculosis therapy relies on conventional drugs such as Isoniazid, Rifampicin, Pyrazinamides, Ethambutol, and Streptomycin. These drugs are the first line drugs for tuberculosis nowadays. In the meantime, there are significant increases in records reporting a significant finding of drug resistance in isolated *M. tuberculosis*. The tuberculosis control is further hampered by the emergence of multidrug resistance (MDR), which is a strain that shows resistance to at least rifampicin and isoniazid, two important drugs in the multidrug treatment strategy for the disease. More recently, severe forms of drug resistant strains known as extensively drug-resistant (XDR) TB have been reported. The advantages of molecular biology techniques are available, mainly supported by the availability of the genome sequence and gene mapping of *M. tuberculosis*. Accumulated data have increased our knowledge of the mechanisms of resistance to the main anti-TB drugs. Better knowledge of the molecular mechanisms of drug resistance in TB will help us to improve current techniques for rapid detection and will also give direction to the exploration of new targets for drug activity and drug development. This mini review aims to describe the molecular mechanism of drug resistance against first line drugs in clinical isolates of *M. tuberculosis*.

#### **Qualification:**

1988-1995: Medical Doctor, Universitas Gadjah Mada  
1996-1998: Research Student in *Molecular Genetics* at Kobe University School of Medicine, Japan (*non degree*)  
1998-2002: PhD in *Molecular Medicine* at Kobe University Graduate School of Medicine, Japan.  
2010-2014: Clinical microbiology specialist, Universitas Gadjah Mada

#### **Research experience and interest:**

1996-2002: Mutation screening of the dystrophin gene in DMD and BMD patients.  
1997-1998: Identification of novel transcript of the dystrophin gene.  
2000-2002: Genetic susceptibility of *Mycobacterium leprae* infection.  
2003-2004: Macrophages apoptosis induced by isoniazid resistant *M. tuberculosis*  
2005-2007: Genetic susceptibility of dengue virus infection.  
2007-2008: Molecular detection of dengue virus. Molecular detection of *M. tuberculosis* resistant to isoniazid.  
2008-2009: Clinical trial of standardized herbal medicine to the dengue virus infected patients.  
2009 : Dengue virus genome library construction.  
2009-2010: Effect of cyclosporine A to the fluconazol resistant *Candida albicans*  
2010-2011: Genotyping and phenotyping of dengue virus to predict the severity and clinical manifestation of dengue virus infection.  
2010-2011: Analysis of NS-1 gene of dengue virus  
2011 : Molecular characterization of pre membrane gene as a toll for dengue virus serotyping  
2011 : Detection of *wolbachia sp* in *Ae. Albopictus*.  
2012-2016: International Research Consortium on Dengue Risk Assessment, Management and Surveillance (research team member)  
2012- 2013: Association of Polymorphisms of DC-SIGN (CD209) Carbohydrate Recognition Domain with Dengue Virus Infection.  
2013- : National Consortium on Dengue Vaccine Development  
2014- : INA-RESPOND: Fever study

#### **Current Position:**

1999-present : Lecturer at Gadjah Mada University School of Medicine  
2009-present : Secretary to the ethical committee (research) of faculty of medicine UGM  
2010-present : Head of Department of Microbiology, Faculty of Medicine, UGM

## Pre-Conference : Session II

### Infectious Diseases and Treatments



Universitas Gadjah Mada  
Faculty of Engineering  
Department of Civil and Environmental  
Engineering

**Prof. Djoko Legono**

### *Self Expanding Resilience through Well-chained and Partnership-based Disaster Preparedness Program*

There are many attempts those have been made to establish the community resilience against possible disasters those might take place at a certain area. Among of them continuous education has become important key that any attempt would meet their effectiveness, efficiency as well as sustainability. Depending upon the nature of the disaster, such attempts should take into account the experience in the past, either the history of the disaster occurrence that took place in the local area or in the neighbouring area. This paper shows the previous experience in developing the community development against the disaster risk preparedness with a particular case of lahar flow disaster at Mt. Merapi area. The well-chained process is applied to provide the concept of the 'working with' rather the 'working for' as stated by previous worker (Salter, et al., 1987). Accordingly, the partnership-based is underlined as a part of self funding and initiative activities and preparedness those become essential factors towards the self expanding activities and therefore also maintain further sustainability of the program.

Keywords: disaster preparedness, community resilience, well-chained, partnership, sustainability

#### **Education and Trainings:**

- Ph.D. : Water Engineering, The City University, London (UK), 1987
- Engineer (Ir) : Civil Engineering, Universitas Gadjah Mada, (Indonesia), 1979
- Training : "Integrated Natural Disaster Management", JICA, Japan, 1999
- Post Doctor : "Debris Flow Modelling", University of Iowa, Iowa City, USA, 1998/1999
- Training : "Water Resources Project Economic", University of Colorado, 1982

#### **Scientific Publications (selected):**

1. Leslie Jamie Cobar, Djoko Legono and Kuniaki Miyamoto, 2016, Modeling of Information Flow for Early Warning in Mt. Merapi Area, Indonesia, *Journal of Disaster Research*, Vol 11 No.1 February 2016.
2. Yulinsa, N., Legono, D., Rahardjo, A.P., 2014, Assessment of Lahar Flow Warning Criteria of Putih River after 2010 Mt. Merapi Eruption, Proceeding of IAHR-APD, Hanoi, 21-25 September 2014, Vietnam.
3. Wardoyo W., Legono D., Jayadi R., Fathani T.F., 2013, Analyzing Sediment Transport Mechanism and Related Hydraulic Structure Damage after Mt. Merapi Eruption in Gendol River, *Journal of Basic and Applied Scientific Research*, 3(1) pp.849-857.
4. Gonda, Y., Legono, D., Santosa, U.B., 2013, Lahar Flows and Flash Floods after the 2010 Eruption of Mt. Merapi, Proceeding of 4th International Seminar of HATHI, 6-8 September 2013, Yogyakarta, Indonesia.
5. Legono, D., Wignyosukarto, B., and Saputra, A., 2011, The Influence of Lahar Flow on Stability of River Structures due to Scour and Impact Forces. Proceeding of International Seminar HATHI Jakarta, 15-16 July 2011.



## Pre-Conference : Session III

Establishment of UNESCO Chair: Focusing on Gender Aspects of Disaster



Kobe University  
Graduate School of International Cooperation  
Studies

**Prof. Ronni Alexander**

### *Drawing disaster and recovery: Five years of the Popoki Friendship Story Project*

The Popoki Friendship Story Project was begun by Ronni Alexander in April 2011, just weeks after the 11 March 2011 triple disaster in northeastern Japan. This project, run by the Popoki Peace Project, began in Sendai, and has included many locations within and outside of Japan, with a particular emphasis on Otsuchi-cho, Iwate Prefecture. In the beginning, it involved stretching a long cloth with a picture of the Project's mascot, the cat Popoki, on one end on whatever space was available in evacuation centers and inviting people to draw freely. As time passed, the project has grown to include workshops, exhibitions and other activities. This presentation will discuss how the Popoki Friendship Story Project has evolved over the past five years. In particular, it will look at: (1) the importance of art-making in the expression of the experience of disaster and recovery; (2) the importance of emotion and feeling safe in narratives of disaster and recovery; and (3) what this project can tell us about gender and disaster. The presentation will conclude with lessons learned and issues for the future.

Ronni Alexander is a scholar, educator, and activist. She is a professor of transnational relations at the Graduate School of International Cooperation Studies, Kobe University, specializing in peace studies and international relations. She holds degrees in psychology (BA, Psychology, Yale, 1977), public administration (MA, Public Administration, ICU) and international relations (PhD, International Relations, Sophia University). Ronni has been living in Japan since 1977 and has been active in community action and education for peace. Her scholarly work has focused on security and gender in Pacific Island Countries, and her current work looks at issues of being and feeling safe, particularly in the context of the military situation on Guam and the 2011 triple disaster in northeastern Japan. In 2006, she began the Popoki Peace Project and conducts a range of activities including continuing work in the areas affected by the 2011 triple disasters in northeast Japan. Ronni's publications include many scholarly works, as well as her picture books, the *Popoki's Peace Book* 1-3 series.

## Pre-Conference : Session III

Establishment of UNESCO Chair: Focusing on Gender Aspects of Disaster

Kobe University  
Gender Equality Office

Assistant Professor

**Dr. Tomoko Nakahara**

### *Disaster and gender ; Inquiry in a stricken area*

This study aims to clarify the present situation in A area which is one of the areas stricken by The Great East Japan Earthquake. I especially pay attention to disaster effects based on gender.

In the previous studies, many have not investigated gender analysis using quantitative data. This study is based on the data from 'Survey for creating future of A area' from April to May 2016 by Professor Katsuro Inokuchi, Kobe University.

Survey questionnaires were distributed to inhabitants in A area aged 15 years or older. About 230 were returned, and the response rate was about 20%. This questionnaire involves questions about the disaster situation, living conditions, work conditions, individual income, household income, health conditions, family relations, hope for the future and so on.

In this study, I divide the data into four groups: women under 60 years old, over 60, men under 60, and over 60. Through this analysis, I would like to show you the difference in damage by gender and generation caused by the earthquake.

Assistant Professor, Gender Equality Office, Kobe University

**Major:** Family Sociology, Home Economics  
2010~ Assistant Professor, Gender Equality Office, Kobe University  
2010 Ph.D. (Nara Women's University)

**Recent study:** 'Hidden Poverty and Quality of Life on Young Women Living with a Partner', *Japan Association For Feminist Economics*, 1, 2016



## Pre-Conference : Session III

### Establishment of UNESCO Chair: Focusing on Gender Aspects of Disaster

Kobe University  
Graduate School of Maritime  
Sciences

Associate Professor

**Dr. Junko Okada**

#### *'Kobe Style' how to share the gender aspects of disaster*

The Great Hanshin Awaji Earthquake was the first one in which women advocated the need for consideration of the gender aspects of disaster in Japan. More than twenty years have passed since then but we cannot solve this problem. We were faced with it in the Great East Japan Earthquake and the Kumamoto Earthquake. The Gender Equality Office of Kobe University decided to establish the UNESCO Chair to focus on this issue in cooperation with researchers from Kobe University and foreign institutions. It is important that we open to the public the knowledge obtained from our research. For this purpose we held seminars to consider the gender aspects of disaster for Kobe citizens and the government officials of some countries in Africa in preparation for the UNESCO Chair. I would like to explain how the Gender Equality Office established the UNESCO Chair focusing on the gender aspects of disaster, especially how to share the concept with the public.

**Associate Professor, Graduate School of Maritime Science, Kobe University**

In addition to her position at Graduate School of Maritime Science, she is **Vice Director of Gender Equality Office of Kobe University**.

**Major:** International Law

2004~ Associate Professor at Graduate School of Maritime Science, Kobe University, Japan.

1993~ Associate Professor at Faculty of Mercantile Marine, University of Kobe Mercantile Marine, Japan.

1989~ Assistant of Professor at School of Law, Nagoya University, Japan.

M.A. in Law from Nagoya University, Japan.

**Recent study:** 'Gender Equality in the international society –Ethic Cleansing in Yugoslavia', in *Hou no Kagaku*, 46, 2015, 'Forming the International Maritime Community through the Port State Control—Consideration from some arguments of International Convention for the Control and Management of Ships' Ballast Water and Sediments', in *Review of the Faculty of Maritime Sciences, Kobe University*, 11, 2014.

## Pre-Conference : Session III

### Establishment of UNESCO Chair: Focusing on Gender Aspects of Disaster



Universitas Gadjah Mada  
Department of Pediatric  
Faculty of Medicine

**Prof. dr. Sunartini, Sp.A(K), PhD**

#### *Interprofessional Teamwork in Community Rehabilitation Affected by Earthquake on May 27th 2006 in Bantul Yogyakarta Indonesia*

**Background:** An earthquake of magnitude 6.2 RC struck Yogyakarta and Central Java on May 27th 2006. It destroyed 5 districts in Yogyakarta: Bantul, Kulon Progo, Gunung Kidul, Sleman, and Yogyakarta city. Of the 79,210 population in Bantul District 4,280 people died; 8,973 people were severely injured; and 3,250 people were fairly injured. More than 17,000 people have been suffering from fractures, head and spinal injuries, followed with neurological, defecation and urination defects. Mental defects such as post traumatic stress disorder (PTSD) were found in children, adults, and elderly people. Community Based Rehabilitation using Mobile Rehabilitation Empowerment of local people was chosen for special reasons such as: 1) the damage to the areas was severe without suitable access 2) no water resources 3) no adequate transportation 4) external aid would not be available for a long period.

**Purposes:** Conducting Mobile Rehabilitation and Trauma Healing provided by Integrated Rehabilitation Teams (nurses, physiotherapists, medical rehabilitation doctors, psychologists, and pediatricians) at sub-district or village level in damaged areas, empowerment of local community for rehabilitating health and social problems and environmental improvement.

**Methods:** Mobile Rehabilitation with interprofessional teamwork empowering the local community to support the victims to improve their own capacity and quality of life.

**Results:** About 3,750 victims received medication, wound care and rehabilitation, physiotherapy, occupational therapy, psychological therapy, trauma healing and training so they can return to daily work.

125 people received handicraft training and special materials or food production training.

387 cadres were trained for daily rehabilitation and 1,000 volunteers were trained with joint simulation of disaster victims. The establishment of Children House Griya Lare Utami in Sewon Bantul as a Center for Integrated Rehabilitation where 50 children joined the trauma healing program.

**Conclusion:** Interprofessional Teamwork was very helpful in carrying out quality activities and prioritizing patient safety.

**Keywords:** Earthquake, Inter-professional Teamwork, Community Based Rehabilitation

#### Education background

1984 : Medical School, Universitas Gadjah Mada, Yogyakarta

1997 : Pediatrician, Universitas Gadjah Mada, Yogyakarta

1993 : Consultant of Pediatric Neurology in Universitas Gadjah Mada, Yogyakarta and Indonesia University, Jakarta

1992 : Graduate from Doctoral Program, ICMR, Kobe University, Japan

**Research Interest:** Japanese encephalitis, autism, cytomegalovirus, DMD and BMD, children with special needs, inter-professional education and team work

#### Selected Publication

1. Elisabeth Siti Herini, Gunadi, Marjan J.A. van Kempen, Surini Yusoff, **Sunartini**, Sutaryo, Suryono Yudha Patria, Masafumi Matsuo, Dick Lindhout, Hisahide Nishio, Novel SCN1A mutation in Indonesian Patients with severe myoclonic Epilepsy in Infancy, *Pediatrics International*, 2010;52:234-239.
2. I Ketut Rutin Pastadita, **Sunartini**, Yudha Patria. Antenatal and postnatal risk factors of obesity in children age 2-5 years old in Yogyakarta District, Indonesia. *J Med Sci, Volume 44, No. 1, March 2012: 84 – 91*
3. Dewi Darmawati, **Sunartini Hapsara**, Suryono Yudha Patria.; Onset of menarche : differences between an urban and a rural community in Tangerang District, Banten Province, Indonesia. *J.Med.Sci* 2012; vol 44;2:222-230
4. Sri Hartini, **Sunartini Hapsara**, Siti E. Herini and Satoshi TakadaI, Verifying the Indonesian version of the Child Behavior Checklist, *Pediatr Int.* 2015 Oct;57(5):936-41. doi: 10.1111/bed.12669. Epub 2015 Aug 26



## Pre-Conference : Session III

Establishment of UNESCO Chair: Focusing on Gender Aspects of Disaster



Universitas Gadjah Mada  
Faculty of Medicine  
Department of Pediatric and Maternity Nursing

**Elsi Dwi Hapsari, BN, MS, DS**

### Maternal Health in Disaster Situation

Health of women during pregnancy, childbirth and postpartum period in Indonesia is still become priority to be improved. In disaster situation, pregnant woman is one of vulnerable population because they are at risk of poor physical, psychological, or social health after disaster. In addition, they may experience the impact sensitivity because of disaster. This presentation will cover the overview of maternal health in Indonesia. After that, maternal health in disaster situation and the use of contraception, especially after Yogyakarta earthquake 2006 and the eruption of Mt. Merapi in 2010, would be discussed. Contraceptive method is a unique aspect in reproductive health of a woman that needs involvement of her partner/husband. In the end of presentation, several efforts are proposed to improve the maternal health in Indonesia especially in disaster situation.

*Keywords: maternal health, reproductive health, disaster*

#### Educational Qualifications

2010 : Doctor of Science (DS), Kobe University Graduate School of Health Sciences

2007 : Master of Science (MS), Kobe University Graduate School of Health Sciences

2000 : Bachelor of Nursing (BN), Universitas Indonesia

#### Publications (last 5 years):

1. Kinkawa M, Hapsari ED, Ueda M, Matsuo H. Current situations, health conditions and challenges in employment of Indonesian nursing/certified care worker candidates based on Economic Partnership Agreement between Indonesia and Japan. *Bulletin of Health Sciences Kobe*, 28:31-40, 2012.
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3. Sugino M, Hapsari ED, Warsini S, Madyaningrum E, Hartanti F, Matsuo H, Takada S. Issues raised by nurses and midwives in a post-disaster in Bantul community. *Disaster Prevention and Management*, Vol. 23 Iss 4 pp. 420 – 436, 2014.
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5. Ernawati H, Hapsari ED, Lusmilasari L. The use of web-based information system in adolescents. *Jurnal Ners*, 9, 2:194-202, 2014.
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7. Choiriyah M, Hapsari ED, Lismidiati W. Tradition and social environment influence breastfeeding support for low birth weight baby at Malang City. *Kesmas: Jurnal Kesehatan Masyarakat Nasional*, Vol. 10, No. 1, Agustus 2015.
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10. Nugraha A, Hapsari ED, Rahmat I. Decision making among farmer couples in deciding ideal family in Bali patrilineal community. *Jurnal Persatuan Perawat Nasional Indonesia* Volume 1/No. 1/April-Juli 2016.



## Profile and Research Activities of Kobe University Alumni in Faculty of Medicine Universitas Gadjah Mada



Assalamu'alaikum wr wb.

Dear colleagues,

The Cooperation between Universitas Gadjah Mada (UGM) and Kobe University has been lasted for more than three decades. One of the results of this cooperation is the Kobe University alumni who participate actively for developing the country, Indonesia. In the science atmospheres, many lessons and knowledges have been learned by the alumni while studying at Kobe University. In the field of medicine and health sciences, until December 2016 Kobe University has graduated 42 alumni from Graduate School of Medicine and Graduate School of Health Sciences that now are working in Faculty of Medicine UGM. With the knowledges and experiences in research gained from the Kobe University, Kobe University alumni who work at the Faculty of Medicine UGM are now actively working to conduct a lot of research to solve health problems that exist in the community.

This book presents alumni profiles and abstracts of the recently research activity from alumni of the Graduate School of Medicine and Graduate School of Health Sciences Kobe University who worked in the Faculty of Medicine UGM. Hopefully, this alumni book has benefit and contribution to the society, other researchers, as well as other stakeholders, including: 1) provide information on the topics of recent research from the alumni; 2) give the possibility for the communication and collaboration for other researchers and other stakeholders for the development of research that can be beneficial for the community; 3) provide the ideas of research topics for students and young researchers.

Last but not the least, we do hope that alumni of the Graduate School of Medicine and Graduate School of Health Sciences Kobe University have contribution to improve health status in the community in Indonesia and are recognized nationally, regionally, and internationally in accordance with the UGM motto: **"Locally Rooted, Globally Respected"**.

Wassalamu'alaikum wr wb.

Arief Budiyo, MD, PhD, Dermatologist  
The Chairman of the Organizing Committee







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8	Dertation or thesis publication	Endothelin-converting enzyme-1 gene ablation attenuates pulmonary fibrosis via CGRP-cAMP/EPAC1 pathway. Am J Respir Cell Mol Biol 2013;48:465-476.
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### Soluble ST2 is Increasing and Predicting Adverse Cardiac Events in Acute Myocardial Infarction with ST-segment Elevation

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**Introduction.** Soluble ST2, a myocardial stretched biomarker, was released during acute myocardial infarction by cardiomyocytes. Its role on adverse outcomes during acute phase needs to be corroborated.

**Aim.** To investigate the role of soluble ST2 on predicting in-hospital adverse outcomes during acute phase of ST-elevation myocardial infarction.

**Method.** A cohort study enrolling 95 consecutive patients with ST-elevation acute myocardial infarction was performed. Soluble ST2 level was measured from peripheral blood taken on admission, before reperfusion procedure commenced, with Aspect-PLUS ST2 rapid test. Follow-up during hospitalisation were performed to detect in-hospital adverse outcomes, i.e. death, acute heart failure, cardiogenic shock and resuscitated ventricular arrhythmia. Two groups were constructed based on soluble ST2 level, i.e. supramedian group and inframedian group. The incidence of adverse outcome between groups was compared. Logistic regression analysis was performed. A p value < 0.05 was statistically significant.

**Results.** The median soluble ST2 level was 152.1 ng/ml. Supramedian group (n=47) had higher incidence of adverse outcome as compared with inframedian (n= 48), i.e. 38.3 % versus 12.5 %, p =0.004. No significant difference of baseline characteristics, such as Killip class, gender, diabetes mellitus, hipertension, previous ischemic heart disease, anterior STEMI, coronary artery disease extent and reperfusion strategy, between groups. Multivariable analysis showed that supramedian ST2 level independently associated with high incidence of adverse outcome (adjusted RR 6.32, 95 CI: 1.41 – 28. 24, p value = 0.02.).

**Conclusion.** High soluble ST2 independently associated with adverse outcomes during acute phase of ST-elevation acute myocardial infarction.

#### Keywords

Soluble ST2, acute myocardial infarction, ST-elevation myocardial infarction, adverse cardiac events

(This abstract is accepted in the 81st Annual Scientific Meeting of the Japanese Circulation Society to be held in Kyoto, Japan 2017)



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8	Dissertation or thesis publication	Budiyo A, Ueda M, Ueda T, Ichihashi M. Formation of cyclobutane pyrimidine dimers and 8-oxo-7,8-dihydro-2'-deoxyguanosine in mouse and organ-cultured human skin by irradiation with broadband or with narrowband UVB. Photochem Photobiol 2002; 76 (4): 397-400.
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### Effects of The Stem Cell Products and Platelet Rich Plasma (PRP) in Acute Wound Healing: In Vivo Comparison Study in The Mice Skin Acute Wound Healing Model

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**Introduction.** Wound healing is the complex processes involving multiple and multistage mechanisms like coagulation, inflammation, extracellular matrix synthesis and depositions, angiogenesis, fibroplasia, epitelization, contraction and remodelling. Various kinds of growth factors are involved in its each stage in order to achieve optimal wound healing. Many studies showed that stem cells (SC) and platelet rich plasma (PRP) generate numerous kinds and enormous amounts of growth factors, for example platelet-derived growth factor (PDGF), vascular endotelial growth factor (VEGF), transforming growth factors (TGF), epidermal growth factor (EGF), fibroblast growth factor (FGF) and others that affect the wound healing processes. Cultivated stem cells can yield various kinds of growth factors in the medium (conditioning medium) that can be termed as stem cells products (SCP).

**Aim.** To make comparison of the clinical and histological effects between stem cells products (SCP) and platelet rich plasma (PRP) in the mice skin wound healing model.

**Method.** The simple quasy experimental method was used in this study involving mice as the subjects. There were 3 groups of mice,: 1) Medium-treated group (Control), 2) PRP-treated group (PRP), and 3) Conditioning medium/ Stem cells products-treated group (SCP). Each group was consisted of 5 mice. Female BALB/C mice age of 8 weeks were used as wound healing models in this study. Mice's back hair were shaved and the dorsal skin were full-thickness excised with size 1x1 cm<sup>2</sup> using surgical scissor to make wounds. Treatment of each group were performed every day until samples were taken for analysis (day 0 until day 8). Platelet rich plasma was made from fresh whole blood with 2 centrifugation step process. Stem cells were isolated and cultivated from Wharton's Jelly in umbilical cord. Explants of Wharton's Jelly were cultured in vitro dan in the forth passage, the cells were grown in 3 dimensional form in order to produce optimal growth factors. After 24 hours cultured the medium was harvested and was used as conditioning medium contain stem cells products. For clinical outcome, wound contraction in mice skin were analized with measuring and comparing the wound size in the day 0, 2 and 8. For histological examination, each wound of the skin mice were biopsied 1,5x1,5 cm<sup>2</sup> along with the wound areas. Hematoksilin-eosin (HE) staining were carried out to evaluate the skin epitelization, granulation and neovascularition in the wound areas.

**Results.** On the second day of wound healing, wound in the control group histologically shows only fibronectin tissues covered the wound without any epithelial cells, whereas in the PRP group exhibits some epithelial cells in the edge of the wound. In the SCP group, epithelial cells are longer covered the edge of the wound in compare with the PRP group. Clinically, wounds in the SCP group are smaller than in PRP group and in PRP group are smaller than in control group. On the 8th day of wound healing, histologically there are granulation tissue consist of new collagen and vascular in the base of the wounds. There are more formation of new vascular in the SCP group in compare with PRP group and control group. Furthermore, on the day 8, in the SCP group shows that wound is completely covered with keratinized epithelial cells. In the PRP group, wound is completely covered with epithelial cells but without any keratinization while in the control group wound is not yet covered completely. Other finding that can be found is that in the day 8 of wound healing, in the stem cell products-treated group there are the formation of new appendices tissue i.e. hair follicles that cannot be found in the other groups. Clinically, wounds in the SCP group and PRP group are already closed completely but in control group are not closed completely yet.

**Conclusion.** This study shows that stem cells products and platelet rich plasma (PRP) accelerate acute wound healing clinically and histologically in compare to control. Between the two modalities, stem cells product accelerate acute wound healing better that PRP. Further experiment is needed using skin chronic wound healing models for example using diabetic mice models.

#### Keywords





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7 Period of study	2006-2011
8 Dissertation or thesis publication	Ardianto B, Sugimoto T, Kawano S, Kasagi S, Jauharoh SN, Kurimoto C, Tatsumi E, Morikawa K, Kumagai S, Hayashi Y. The HPB-AML-I cell line possesses the properties of mesenchymal stem cells. <i>J Exp Clin Cancer Res</i> . 2010; 29: 163.
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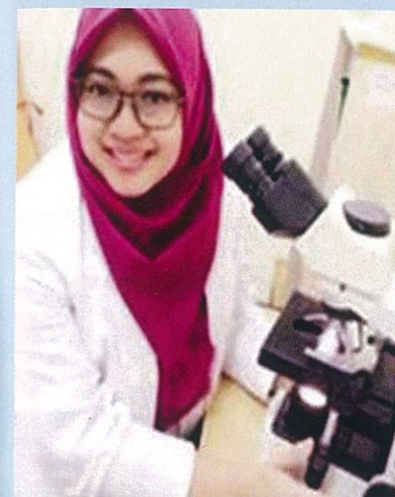
## Role of Immunophenotypes in the Pathogenesis of Febrile Neutropenia in Childhood B-lineage Acute Lymphoblastic Leukemia: A Preliminary Study

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Febrile neutropenia constitutes one of the major challenges in the management of childhood acute lymphoblastic leukemia (ALL). In spite of its consideration as the early sign of bacterial infection, which follows the initiation of cytostatic treatment, recent studies revealed the absence of bacterial growth in more than 40% of febrile neutropenia episodes. These findings indicated the possible involvement of the biological features of leukemic cells in the pathogenesis of febrile neutropenia. A case-control study involved childhood B-lineage ALL (B-ALL) cases with ( $n = 28$ ) and without ( $n = 29$ ) febrile neutropenia, according to the International Diseases Society of America (IDSA) criteria, in the remission-induction phase of cytostatic treatment using the Indonesia-ALL-2006 protocol. These children had been admitted to Dr. Sardjito General Hospital during the period of 2006-2011. The diagnostic immunophenotypes of lymphoblasts were reviewed. In view of the onset, 11 (39%) of 28 cases experienced febrile neutropenia in the first week of remission-induction treatment. There was a decrease in the number of cases, who started to experience febrile neutropenia in the subsequent weeks of treatment. Bivariate analysis disclosed an association between T-lineage antigen coexpression and the absence of febrile neutropenia (OR, 0.31; 95% CI, 0.10-0.96). Our findings, therefore, provided some insights that the pathogenesis of febrile neutropenia might involve the biological characteristics of leukemic cells.



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6 Funding/ scholarship	Monbukagakusho/ MEXT
7 Period of study	2010-2014
8 Dissertation or thesis publication	1. Widasari DI, Yano Y, Utsumi T, Heriyanto DS, Anggorowati N, Rinonce HT, Utoro T, Lusida MI, Soetjipto, Asmara W. Hepatitis E virus infection in two different regions of Indonesia with identification of swine HEV genotype 3. <i>Microbiol Immunol</i> . 2013 Oct;57(10):692-703. 2. Widasari DI, Yano Y, Heriyanto DS, Utsumi T, Yamani LN, Rinonce HT, Wasityastuti W, Lusida MI, Soetjipto, Okada R, Murakami Y, Tanahashi T, Azuma T, Hayashi Y. A deep-sequencing method detects drug-resistant mutations in the hepatitis B virus in Indonesians. <i>Intervirology</i> . 2014;57(6):384-92.
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## A Deep-Sequencing Method Detects Drug-Resistant Mutations in the Hepatitis B Virus in Indonesians

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**Objective.** The long-term administration of a nucleos(t)ide analogue (NA) for the treatment of chronic hepatitis B may encourage the emergence of viral mutations associated with drug resistance. Minor populations of viruses may exist before treatment, but are difficult to detect because of technological limitations. Identifying minor viral quasiespecies should be useful in the clinical management of hepatitis B virus (HBV) infection.

**Method.** Six treatment-naïve Indonesian patients with chronic HBV infection participated in this study. The polymerase region of the HBV genome, including regions with known drug-resistant mutations, was subjected to capillary sequencing and MiSeq sequencing (Illumina). Mutations were analyzed with Genomics Workbench software version 6.0.1 (CLC bio).

**Results.** The mean mapping reads for the six samples was 745,654, and the mean number of amplified fragments ranged from 17,926 to 25,336 DNA reads. Several known drug-resistant mutations in the reverse transcriptase region were identified in all patients, although the frequencies were low (0.12-1.06%). The proportions of the total number of reads containing mutations I169L/M, S202R, M204I/L or N236S were >1.0%.

**Conclusion.** Several known NA-resistant mutations were detected in treatment-naïve patients in Indonesia using deep sequencing. Careful management of such patients is essential to prevent drug-resistant mutations from spreading to other patients.

(This abstract has been published in *Intervirology* 2014; volume 57, issue 6, pages 384-392)





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7	Period of study	2009-2014
8	Dissertation or thesis publication	Dian K. Nurputra, Taku Nakagawa, Yasuhiro, Takeshima, Indra S.K. Harahap, Satoru Morikawa, Toshiyuki Sakaeda, Poh San Lai, Masafumi Matsuo, Yutaka Takaoka, Hisahide Nishio. Paramyotonia congenita: From clinical diagnosis to in silico protein modeling analysis. <i>Pediatr Int</i> 2012; 54(5): 602-612.
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### MxA Protein, A Novel Product of INF-1 Induction, Remains Serving as Potential Biomarker of Viral-Caused Respiratory Infection in Children Despite Suffering from Vitamin-A and Zinc Deficiencies

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**Introduction.** Respiratory tract infection (RTI) takes one of top 10 most common disease of children in Indonesia. Around 60% of RTI are caused by virus. Establishing viral infection in RTI has become major challenge, as bacterial and another pathogen infection deliver similar clinical manifestations. *Myxovirus resistance-A* (MxA) protein, which is selectively induced by type I interferon (INF-1), has become potential candidate for specific biomarker of viral-caused RTI. Interferon activation has been suggested to be modulated by vitamin-A and zinc, thus hypothesize that children with vitamin-A and zinc deficiencies should have lower expression of MxA when they suffer from viral-caused RTI.

**Aim.** To clarify the MxA expression level on children with vitamin-A and zinc deficiencies compared to the children with no deficiency.

**Method.** Subjects with age of 4-11 years old, diagnosed of having RTI on the basis of validated clinical score were included. Bacterial blood culture and RT-PCR of virus from nasopharyngeal swab were performed to confirm the etiological diagnosis. Blood samples were taken and separated into plasma and cell isolates using Ficoll Hipaque technique. Plasma were used for vitamin-A (HPLC), zinc (AAS), and INF-1 (ELISA) examination. Cell isolates were further subjected for MxA protein extraction and analysis (Western Blotting). Subjects were then grouped into deficiency and non-deficiency group. MxA, INF-1 and clinical outcome in each group were compared, respectively.

**Results.** Sixty five subjects were included in this study. Twenty nine subjects were found to have vitamin-A and zinc deficiencies and 46 were into non-deficiency group. Characteristics and clinical outcome on both group were not significantly different. All subjects from deficiency group and 34 from non-deficiency were confirmed of having viral-infection. Bacterial infection were found on remaining 12 subjects from non-deficiency and analyzed separately. MxA examination on deficiency group showed a lower but not statistically different expression (2,12; SD±0,21), compared to the 34 subjects of non-deficiency group (2,51; SD±0,22) ( $p=0,07$  with CI 85-90%). INF-1 measurement showed consistent result, indicating the role of both vitamin-A and zinc in the INF-1 and MxA modulation. Meanwhile, the MxA examination on the 12 subjects showed a significant low expression (0,48; SD±0,37) even when compared to children in deficiency group ( $p=0,02$  with CI 85-90%).

**Conclusion.** MxA protein expression has been found lower in children with vitamin-A and zinc deficiencies compared to children with no deficiency, in which both suffering from viral-caused RTI.



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### Nephroprotective Effect of Centella Asiatica (L.) Urban Extract on renal Fibrosis Rat Model

**Introduction.** Centella asiatica (L.) Urban or pegagan have been used empirically as treatment of many kind of diseases including nephroprotective agent. Its extract also have been marketed as supplement for years. However lack of scientific evidence limit its used as phytopharmaca for nephroprotective agent.

**Aim.** To investigate the nephroprotective effect of pegagan extract in renal fibrosis rat model. **Methods:** In this study, we investigated the nephroprotective effect of pegagan extract on rat with rat model. The histology of the kidney was measured using Periodic Schiff Acid (PAS) staining.

**Result.** Pegagan extract caused a significant ( $p<0.05$ ) decrease in both glomerulosclerosis and tubular fibrosis in a dose-dependent manner in the rat model. The dose of 100 mg/kg and 200 mg/kg of pegagan extract showed significantly ( $p<0.05$ ) lower glomerulosclerosis and tubular fibrosis score compare with those on plasebo groups. The body weight in the end of study was not significantly different ( $P<0.05$ ) between groups.

**Conclusion.** Results of this study showed that pegagan extract have the potential to be used as a nephroprotective agent in rat model. Further study needed to determine its efficacy in another kidney disease model.

**Keywords:** pegagan extract, renal fibrosis, efficacy





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8	Dissertation or thesis publication	Edwin Widyanto Daniwijaya, Yoji Murata, Takenori Kotani, Yasuaki Kitamura, Kemala Isnainiasih Mantilidewi, Shinya Kusakari, Hiroshi Ohnishi, Hideki Okazawa, and Takashi Matozaki. Tyrosine Phosphorylation of Carcinoembryonic Antigen-related Cell Adhesion Molecule 20 and Its Functional Role. Kobe J Med Sci 2013; 59(5): E172-E183
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### Tyrosine Phosphorylation of Carcinoembryonic Antigen-related Cell Adhesion Molecule 20 and Its Functional Role

Edwin Widyanto Daniwijaya<sup>1</sup>, Yoji Murata<sup>1</sup>, Takenori Kotani<sup>1</sup>, Yasuaki Kitamura<sup>1</sup>, Kemala Isnainiasih Mantilidewi<sup>1</sup>, Shinya Kusakari<sup>2</sup>, Hiroshi Ohnishi<sup>2</sup>, Hideki Okazawa<sup>1</sup>, and Takashi Matozaki<sup>1,2</sup>

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Carcinoembryonic antigen-related cell adhesion molecule (CEACAM) 20 is an immunoglobulin-superfamily transmembrane protein that contains an immunoreceptor tyrosine-based activation motif (ITAM) in its cytoplasmic region. However, the mechanism for tyrosine phosphorylation of, or the physiological function of, this protein remains largely unknown. Here we have shown that CEACAM20 is indeed tyrosine-phosphorylated by either treatment with pervanadate or forced expression of c-Src. In addition, Tyr522, Tyr559 or Tyr570, the latter two of which are within the ITAM, is likely important for such tyrosine phosphorylation. Forced expression of Myc-tagged wild-type CEACAM20 promoted the phagocytic activity of cultured cells for microbeads coupled with anti-Myc antibodies. By contrast, such phagocytic activity was markedly reduced when a mutant form of CEACAM20, in which Tyr559 and Tyr570 were substituted with phenylalanine, was expressed. Furthermore, the CEACAM20-mediated phagocytic activity was markedly prevented by the treatment with an inhibitor for either Src family kinases (SFKs), Syk, phosphoinositide 3-kinase (PI3K) or phospholipase C- $\gamma$  (PLC $\gamma$ ). Inhibition of actin polymerization by Cytochalasin D significantly inhibited the CEACAM20-mediated phagocytosis. These results thus suggest that tyrosine phosphorylation of CEACAM20 likely promotes phagocytic activity of the cells. The CEACAM20-mediated phagocytic activity requires the activation of SFKs, Syk, PI3K or PLC $\gamma$ .

**Key words:** Carcinoembryonic antigen-related cell adhesion molecule, Tyrosine phosphorylation, Src family kinases, Immunoreceptor tyrosine-based activation motif, Phagocytosis

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### Acute Inflammatory Response After Colostomi, Posterior Sagital Anorectoplasty and Colostomy Closure In The Treatment of Anorectal Malformation

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**Introduction.** Surgery induces an acute inflammatory response, and many complications can occur in the early postoperative period<sup>1</sup>. Despite advances in surgical techniques and perioperative medicine, excessive surgical stress response can be associated, and even lead, to serious post-operative complications like surgical site infection, sepsis and multiple organ failure<sup>2</sup>. In recent years, the neutrophil-to-lymphocyte ratio (NLR) has been proposed as a simple biological parameter able to stratify the risk of mortality after a major cardiac event and to predict cancer outcome<sup>1,3</sup>. Neutrophil to lymphocyte ratio (NLR) is often used as indicator of subclinical systemic inflammation. Higher NLR early after surgery is related with higher risk of post operative complication.

**Aim.** To investigate the acute inflammatory response of pediatric patients with anorectal malformation in Indonesia whom undergone colostomy, posterior sagital anorectoplasty (PSARP), and colostomy closure.

**Method.** Cross sectional study during March 2014 until August 2015 we investigated the inflammatory responses in all pediatric patients with anorectal malformation in Indonesia whom undergone colostomy, posterior sagital anorectoplasty (PSARP), and colostomy closure.

**Results.** NLR were significantly higher after PSARP and stoma closure procedures ( $p < 0,05$ ) compare with those before the procedures. Meanwhile NLR was lower after colostomi compare with NLR before the procedure eventhough the difference is not significant statistically. NLR value after PSARP was as high as the NLR after stoma closure procedure. Higher NLR value after PSARP and stoma closure procedures support the acute inflammatory response feature after those procedures. Meanwhile the tendency of NLR value decreasing after colostomy suggest that the procedure was able to improve the condition which is shown by decreasing inflammatory response due to the complication of the anorectal malformation. Interestingly, the NLR after stoma closure procedure was as high as that on PSARP procedure.

**Conclusion.** Based on this result, it suggest that PSARP and stoma closure procedure should be done more meticulously to decrease the risk of complication since higher NLR related to higher risk of complication.

**Keywords**

Acute inflammatory response, neutrophil to lymphocyte ratio, anorectal malformation, colostomy, PSARP





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### Prevalence of Metabolic Syndrome and its Components based on International Diabetes Federation (IDF) Definition in North Sumatra, Indonesia

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**Introduction.** Metabolic Syndrome (MetS) is a group of risk factors including hypertension, dyslipidemia, insulin resistance, and obesity that closely related with cardiovascular disease (CVD) and type 2 diabetes. Almost all studies reported the prevalence of MetS in Indonesia regions were conducted by using Asian modification NCEP-ATP III criteria. Study on the prevalence of MetS using IDF criteria in Indonesia's province have not been conducted yet.

**Aim.** To determine the prevalence of MetS and its components in North Sumatra, Indonesia.

**Method.** This retrospective study was using data involving 627 subjects aged 40 and above from North Sumatra who took part in the Fourth wave of the Indonesian Family Life Survey (IFLS4). MetS was defined according to IDF criteria. The data was analyzed using Stata version 12.0.

**Results.** The prevalence of MetS in North Sumatra was 19.94%. The prevalence of dyslipidemia, hypertension, central obesity, pro-inflammatory state and insulin resistance were 73.37%, 57.74%, 39.87%, 24.24% and 0.80% respectively.

**Conclusion.** The prevalence of MetS in North Sumatra was 19.94% based on International Diabetes Federation (IDF) definition. The most common component found was dyslipidemia.

#### Keywords

Metabolic syndrome (MetS), International Diabetes Federation (IDF), prevalence, North Sumatra, Indonesia.



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### Physical and Psychological Discomforts Experienced by Pregnant Women in their First, Second and Third Trimester of Pregnancy

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**Introduction.** One of the strategies to improve antenatal care quality is by conducting prenatal class in public health centers. In this class, pregnant women need to be informed about physical and psychological discomforts they may experience during the time course of pregnancy and how to adapt with it. However, there is still limited information about those discomforts in Indonesia, especially in Yogyakarta Province.

**Aim.** To identify physical and psychological discomforts experienced by pregnant women in Bantul District, Yogyakarta Province, Indonesia. It was the first step of a study to investigate the effect of prenatal class with using multidiscipline approach to the increase pregnant women's knowledge in Yogyakarta.

**Method.** A cross-sectional study conducted in public health centers located in Bantul District, Yogyakarta Province between April 2015 and January 2016. Number of respondents in the first, second and third trimester of pregnancy were 35, 43, and 90, respectively. A set of questionnaire for physical and psychological discomforts, Measure of Pregnancy-Specific Anxiety, and modification of Pittsburgh Sleep Quality Index were used after the validity and reliability were tested. Data were analyzed with using descriptive statistical techniques. Ethical permission was granted from the Ethic Committee, Faculty of Medicine, Universitas Gadjah Mada.

**Results.** Physical discomfort mostly reported by pregnant women in the first, second, and third trimester of pregnancy were more often to urinate (74.3%, 76.6%, 96.7%, respectively). Psychological discomfort mostly reported by pregnant women in the first, second and the third trimester of pregnancy was anxiety (100%, 100%, 96.7%, respectively). Many respondents did not know how to adapt with the physical and psychological discomforts..

**Conclusion.** These findings suggest that many pregnant women in Yogyakarta experience physical and psychological discomfort during the time course of pregnancy. Prenatal class that includes information of physical and psychological discomfort experienced by Indonesian pregnant women and how to adapt with it is recommended.

#### Keywords





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### Clinicopathologic and Molecular Profile of Duchenne/Becker Muscular Dystrophy in Yogyakarta, Indonesia

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**Introduction.** Duchenne muscular dystrophy (DMD) and Becker muscular dystrophy (BMD) are allelic X-linked recessive diseases caused by mutations in the *dystrophin* gene. Molecular analysis to differentiate DMD and BMD has never been performed in Indonesia.

**Aim.** To elaborate clinicopathologic and molecular profile of DMD/ BMD patients in Yogyakarta, Indonesia.

**Methods.** Eighteen muscle biopsy samples of clinically suspected DMD/BMD patients was analyzed to establish the diagnosis. The corelation of the increased Creatin Kinase (CK) level and histopathological grading with Immunohistochemistry (IHC) result was analyzed statistically. Polymerase chain reaction (PCR) was performed to identify mutation in exon 52.

**Result.** Positive Gower's sign and high serum CK were observed in most of all patients. Two female patients were identified and IHC result of dystrophin suggesting manifesting carrier. Sixteen patients were male, 12 patients showed negative IHC staining, indicating DMD, while 4 patients demonstrated weak expression of dystrophin, indicating BMD. The correlation of increased CK level and IHC result was significant ( $p=0.005$ ), indicating that DMD patients had higher CK level compared to BMD patients. Histopathological grading of muscle biopsy was significantly correlated with diagnosis of DMD/ BMD using IHC ( $p=0.01$ ), showing that DMD patients have more severe tissue damage. Single exon 52 deletion was not found in all patients.

**Conclusion.** This is the first report of clinicopathologic and molecular profile of DMD/BMD in Indonesian population. Serum CK level and histopathological grading of muscle biopsy are useful in distinguishing DMD from BMD in setting where IHC analysis is not available.

#### Keywords

*Dystrophin* gene, DMD, BMD, creatin kinase (CK), Gower Sign's, immunohistochemical (IHC), mutation



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### Transplantation of Melanocyte Stem Cells as a Treatment for Vitiligo

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Vitiligo is an acquired depigmentation disorder characterized by the presence of depigmented macule which is caused by a progressive loss of functioning epidermal melanocytes. Melanocyte precursor came from melanocyte stem cells (MeSCs) that originally located on bulge area of hair follicles. Reactivation of melanocyte precursor along outer root sheath of hair follicle is expected to play important role in repigmentation. Therefore, stem cells are thought to have important implications toward repigmentation and might become a potential promising regenerative therapy for vitiligo. To date there are various methods of surgical intervention for vitiliginous skin, such as hair follicular grafting and mini-punch grafting. The grafts are composed by hair shaft, a part of hair bulge where MeSCs are located, and dermal papilla as niche of mesenchymal stem cells (MSCs) and other epidermal stem cells. Clinical experiments indicated that the transplantation can be performed either by transplantation of extracted follicular units or single cell suspension harvested from this area. By single cell suspension treatment, a 50 cm<sup>2</sup> of vitiliginous skin can be handled by 15 autologous hair follicular units.

In Department of Dermatology and Venereology Dr. Sardjito General Hospital, we have performed multiple mini punch grafts from the left upper thigh skin with vellus hairs and transplanted onto the left eyebrow of segmental vitiligo patient as additional procedure of suction blister grafting. Significant repigmentation appeared a week after the procedure and patient was satisfied with the result.

#### Keywords

Vitiligo, melanocyte stem cells, extracted hair follicular, single cell suspensions





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### Unraveling the Molecular Pathogenesis of Hirschsprung Disease in Indonesia

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**Introduction.** Hirschsprung disease (HSCR) is a heterogeneous genetic disorder characterized by absence of ganglion cells along variable lengths of the intestinal tract, results in functional intestinal obstruction in children. The absence of ganglion cells in HSCR is attributed to a failure migration of enteric neural crest cells through the embryonic intestines between weeks 5-12 of gestation in the developing enteric nervous system (ENS). The molecular pathogenesis of HSCR might involve the compromised of either genes responsible for the gangliogenesis of ENS or the neurotransmitters expressed by the neurons of ENS or their interaction. The *RET*, *NRG1*, and *SEMA3* signaling pathway has been implicated in the survival, proliferation, and migration of enteric neural crest cells in the developing intestines, while the *SK3* down-regulated in the aganglionic intestines results in unopposed cholinergic activity and a tonic hypercontractile state, causing a functional intestinal obstruction in HSCR patients.

**Aim.** We wished to investigate the role of those genes in the molecular pathogenesis of HSCR in Indonesia.

**Methods.** We ascertained 60 HSCR subjects and 124 controls in this study. Seven genetic markers of *RET*, *NRG1* and *SEMA3* genes were examined using TaqMan assay. Subsequently, we genotyped the *RET* rs2435357 variant for an additional 40 HSCR patients and 50 controls using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) method. Furthermore, we performed Sanger sequencing to seek a mutation in the *NRG1* and *SEMA3D* coding sequence in 40 HSCR patients. As for *SK3* mRNA expressions, ten HSCR and five control intestines were collected for quantitative real-time (RT)-PCR.

**Results.** *RET* rs2435357 showed the strongest association with HSCR both by case-control analysis ( $p = 2.5 \times 10^{-8}$ ) and transmission disequilibrium test (TDT) ( $p = 4.2 \times 10^{-6}$ ). *NRG1* rs7835688 was modestly associated with HSCR only by case-control analysis ( $p = 4.3 \times 10^{-3}$ ), whereas *RET* rs2506030 ( $p = 0.042$ ), *NRG1* rs16879552 ( $p = 0.097$ ), *SEMA3* rs12707682 ( $p = 0.06$ ) and *SEMA3* rs1583147 ( $p = 0.023$ ) demonstrated no association. An additional case-control analysis and TDT with a larger number of subjects confirmed that *RET* rs2435357 is significantly correlated with HSCR with p-value of  $2.2 \times 10^{-13}$  and  $1.5 \times 10^{-6}$ , respectively. Two locus analyses of variants showed significant interactions with increased and decreased disease risks of HSCR at *NRG1* but conditional on *RET* rs2435357 genotype. At *SEMA3*, the frequencies of rs11766001 risk allele in HSCR cases and controls were 1.7 and 0.8 % ( $p = 0.48$ ), respectively. Furthermore, we identified one novel missense mutation, c.397G>C, in exon 7, which led to a substitution of valine with leucine (p.V133L) in the *NRG1* protein, respectively, but were unable to find any rare variant in the *SEMA3D*. Moreover, quantitative RT-PCR showed that the *SK3* expressions were significantly lower (64-fold) in aganglionic intestinal group compared to control group ( $10.9 \pm 4.6$  vs.  $4.9 \pm 3.6$ ) with p-value of 0.025 (95% CI = 0.9 – 11.1). The expressions of *SK3* in the ganglionic intestinal group was also lower (21-fold) compared to control group ( $9.3 \pm 5.8$  vs.  $4.9 \pm 3.6$ ), however, did not reach a significant level (p-value = 0.145; 95% CI = -1.7 – 10.6).

**Conclusions.** *RET* and *NRG1* genes show a significant impact in the molecular pathogenesis of HSCR in Indonesia. These genes demonstrate that development of HSCR requires epistasis effects of *RET* and *NRG1* early in intestinal development. Moreover, one novel *NRG1* mutation, p.V133L, may lead to the development of HSCR in Indonesian patients. The rarity of the *SEMA3* variant in Indonesian implies that the association of such variant to the disease is restricted to such specific population. Furthermore, this study is the first investigation of the effects of *SEMA3* common and rare variants in Asian ancestry. Nevertheless, the decreased expression of *SK3* in the HSCR intestines suggests that *SK3* also plays a role in the Indonesian HSCR pathogenesis. Unraveling the *RET-NRG1-SEMA3-SK3* functions hold great promise for our understanding of the molecular pathogenesis underlying HSCR, particularly in Indonesia.

**Keywords**



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### Malignant Chondroid Syringoma of The Finger: The First Case Report from Indonesia with A Review of The World Literature

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**Introduction.** Malignant chondroid syringoma (MCS) is an extremely rare cutaneous adnexal neoplasm with only 61 cases reported worldwide in English literature and no previous report from Indonesia. Some previous reviews describe a female predilection of this tumor. Due to its rarity and its similar morphological feature with other neoplasms, MCS may be confused clinically and pathologically with some benign and malignant lesions leading to diagnostic pitfall. We reported the first case of MCS from Indonesia with a diagnostic pitfall due to insufficient biopsy. All cases in the world was also reviewed in order to describe the current clinical characteristic of MCS.

**Case description.** A 34-year-old man came to hospital due to a painless lump in his third finger of the left hand since 7 year. An initial diagnosis of metastatic adenocarcinoma was made based on small incisional biopsy examination. Microscopic examination from amputated finger showed intracutaneous tumor with epithelial and mesenchymal components invading bone tissue, consisting of solid and tubular tumor nest in a myxoid background and atypical chondrocytes proliferation in chondroid matrix. Immunohistochemistry examination showed cytokeratin, vimentin, and S-100 positivity. Diagnosis of MCS was determined.

**Discussion and conclusions.** MCS may be confused with benign or malignant tumor with chondroid differentiation. Both epithelial and mesenchymal component should be found in diagnosing MCS. In our case, only epithelial component can be observed in the small biopsy specimen leading to diagnostic pitfall. MCS should be considered as a differential diagnosis in slowly growing tumor in the skin. Careful morphological examination supported by immunohistochemistry analysis is very important in this case. In addition, our current review of the world literature showed no gender predilection of MCS, different with previous studies.

**Keywords**

Malignant chondroid syringoma, finger, skin, Indonesia





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### Electroencephalography (EEG) Abnormalities Pattern in Brain Tumor and Stroke

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**Introduction.** Electroencephalography (EEG) is commonly used to identify epileptiform discharge confirming the diagnosis of epilepsy. However, EEG is rarely used in brain tumor and stroke patients. The EEG abnormalities in brain tumor and stroke patients are not well determined yet.

**Aim.** To identify the EEG abnormalities pattern in brain tumor and stroke patients.

**Method.** Thirty seven brain tumor patients and 28 stroke patients, during their hospitalization in general neurology ward and stroke unit, underwent the EEG examination at Electromedical Clinic in Sardjito Hospital, Yogyakarta, Indonesia.

**Results.** EEG abnormal result was found in 32 (86.5%) brain tumor patients and 20 (71.4%) stroke patients. The most common type was the abnormalities of both epileptiform discharge and background. It was found in 19 (51,4%) brain tumor and 9 (32,1%) stroke patients. The second common type was the abnormality of background only; 5 (13,5%) brain tumor and 6 (21,4%) stroke patients. More than a half of brain tumor (73%) and stroke (53,6%) patients showed the existence of epileptiform discharge; dominated by sharp wave. The existence of epileptiform discharge may reveal the possibility of functional brain lesion; meanwhile the existence of background abnormality may reveal the possibility of structural brain lesion.

**Conclusion.** EEG in brain tumor and stroke patients showed the same abnormalities pattern, which is the abnormalities of epileptiform discharge and background. It may suggests that there are both structural and fungsional brain lesion in brain tumor and stroke cases.

#### Keywords

Electroencephalography, EEG, brain tumor, stroke, epileptiform, background.



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### Developing Animal Model for Psychiatric Disorders in Indonesia: Experiences and Challenges

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**Introduction.** Modelling psychiatric disorders in animals is difficult due to the subjective nature of many symptoms, the lack of biomarkers and objective diagnostic tests <sup>1,2</sup>. However, developing new treatment strategies for psychiatric disorders require a better understanding of the pathophysiology of the disorders that require the use of animal models to bypass ethical issues. A number of different animal model of psychiatric disorders have been developed, reflecting the various genetic and environmental risk factors and pathophysiological mechanisms associated with the disorders <sup>3</sup>. Reports on the development of animal models require the use sophisticated technology, a major hindrance in developing country such as Indonesia. The limited resource and technology are challenges that need to be overcome.

**Aim.** Our aim was to elaborate the possible development of animal models in developing country with limited resources.

**Methods.** We have developed animal models for simulation of chronic stress exposure and induction of vascular cognitive impairment (VCI). *Chronic mild stressors* protocol was used to induce stress in *Wistar* rats and we observed cognitive impairment, depressive behaviour, and increased anxiety in our models. VCI was induced using *bilateral common carotid artery ligation* in Sprague Dawley rats. Novel object recognition test showed that our models had an impair object recognition and increased impulsive behaviour. We use the animal as assay models for ketamine and antipsychotics exposures. Reports on the results had been published elsewhere. The study was conducted in cooperation with Department of Anatomy and Department of Physiology, Medical Faculty, Universitas Gadjah Mada.

**Results.** We have developed animal models for chronic stress exposure using combination of chronic application of *electric foot shock* and *isolation-restriction* methods. We have also developed animal model for VCI with *bilateral carotid communist artery ligation* techniques. We have exposed our models with ketamine of which results were reported elsewhere.

**Conclusion.** In conclusion, development of animal models for psychiatric disorders is feasible in developing country such as Indonesia. The key success is cooperation with basic medical sciences for both the development and assessment methods





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### Effect of *FTO* rs9939609 Polymorphism on Insulin Resistance In Obese Female Adolescents In Indonesia

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**Introduction.** Polymorphism rs9939609, within intron 1 of *FTO*, has been shown to be associated with obesity and insulin resistance in children in Caucasian populations. However, studies in Asian populations showed inconsistent results.

**Aim.** To investigate an association between *FTO* rs9939609 polymorphism and insulin resistance in obese female adolescents in Indonesia.

**Method.** A total of 78 obese female adolescents were ascertained in this case-control study. The genetic marker was examined using allele-specific polymerase chain reaction (PCR) in genomic DNA for association studies. Insulin resistance was determined based on homeostasis model of assessment for insulin (HOMA-IR)  $\geq 3.14$ .

**Results.** Allele A of the *FTO* gene rs9939609 polymorphism was found in 44.2% obese female adolescents. *FTO* rs9939609 risk allele (A) carriers did not have higher risk of insulin resistance (OR=1.12; 95% CI=0.59-2.12), nor higher fasting insulin concentration ( $p>0.05$ ) and HOMA-IR ( $p>0.05$ ) compared to non-risk allele (T) carriers.

**Conclusion.** Our study suggested that *FTO* rs9939609 polymorphism may not associate with insulin resistance in Indonesian obese female adolescents.

#### Keywords

*FTO*, rs9939609, adolescence, obesity, Indonesia



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### Amniotic Membrane Mesenchymal Stem Cells Support Ex Vivo Generation Of Platelets From Umbilical Cord Blood Hematopoietic Stem Cells

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**Introduction.** Platelet refractoriness is a major problem among patients requiring repeated transfusion, indicated by failure to increase the number of platelet count after transfusion. Production of less immunogenic platelets is a potential approach to overcome this problem. Umbilical cord blood (UCB) is rich in hematopoietic stem cells (HSC) indicated by CD34+. Amniotic membrane is widely known as the best source of mesenchymal stem cells (MSC), which may support the growth of platelet from HSC of UCB.

**Aim.** To generate platelet from CD34+ HSC isolated from UCB, co-cultured with MSC derived from amniotic membrane.

**Methods.** Gradient density separation was performed to obtain mononuclear cells (MN) from 40cc UCB. The isolated MN cells were selected for CD34+ HSC by magnetic sorter beads. CD34+ HSC cells were separated into four 2.5cm plates containing standard medium with addition of TPO, SCF and IL-11 with or without MSC. MSC were isolated from amniotic membrane, cultured in a 5 ml standard medium and harvested on day-5. Formations of platelets were confirmed by flowcytometry after two weeks of culture.

**Results.** We isolated  $1.4 \times 10^6$  sel CD34+ in 2ml medium and divided into 4 plates with final count of CD34+  $3.5 \times 10^5$  cells/flask. The harvested MSC of  $3 \times 10^5$  was divided into 3 of 2.5 cm plates to eventually be mixed with CD34+ cells. Plate 1 of  $3.5 \times 10^5$  CD34+ cells only produced  $2.52 \times 10^2$  platelets. Plate 2, 3 and 4 containing  $3.5 \times 10^5$  CD34+ and  $10^5$  MSC produced  $1.619 \times 10^3$ ,  $2.035 \times 10^3$  and  $4.065 \times 10^3$ , respectively, with mean of  $2.573 \times 10^3$  cells. The ratio of increment between the culture of CD34+ only and with addition of MSC was 1:10,07.

**Conclusions:** There was a greater increment in ex vivo production of platelets in CD34+ HSC isolated from UCB co-cultured with MSC, compared to that of without MSC.

#### Keywords





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## Vitamin D Attenuates Kidney Fibrosis via Reducing Fibroblast Expansion, Inflammation and Epithelial Cell Apoptosis

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**Introduction.** Kidney fibrosis is the common final pathway of Chronic Kidney Diseases (CKD) characterized by myofibroblast formation, inflammation and epithelial architecture damage. Vitamin D is known as a renoprotective agent although the precise mechanism is not well understood.

**Aim.** This study is aimed to elucidate the effect of vitamin D in fibroblast expansion, inflammation and apoptosis in kidney fibrosis.

**Method.** We performed Unilateral Ureteral Obstruction (UUO) model in male Swiss-webster background mice (3 months, 30-40 grams) to induce kidney fibrosis. The mice (n=25) were divided into five groups: UUO, oral Vitamin D treatment with dose: 0.125 µg/Kg (UUO+VD-1), 0.25 µg/Kg (UUO+VD-2) and 0.5 µg/Kg (UUO+VD-3) and Sham operation (SO) with ethanol 0.3% supplementation. We sacrificed the mice in day14 after operation, harvested the kidney, made paraffin section for histological analysis and kept in RNA Later solution for protein and RNA extraction. Tubular injury and fibrosis were quantified based on PAS and Sirius Red (SR) stainings. Immunostaining was done for examination of myofibroblast (αSMA), fibroblast (PDGFRβ), TLR4 and apoptosis (TUNEL). Reverse Transcriptase PCR (RT-PCR) was done for measuring MCP-1, ICAM-1, TLR4, and Collagen1 expression. TGFβ1 level was quantified using ELISA.

**Results.** We observed a significantly lower level of fibrosis (p<0.001), tubular injury score (p<0.001) and myofibroblast area (p<0.001) in group treated with vitamin D compared to UUO group. The TGFβ1 level and the fibroblast quantification were also significantly lower in the former group. However, we didn't find any significant difference among Vitamin D treated groups. Concerning the dose independent effect, we only compared the UD-1 group and found that UD-1 had a significantly lower number of epithelial cell apoptosis by TUNEL assay. RT PCR analysis showed lower expression of collagen1 as well as inflammation mediator expression (MCP-1, ICAM-1, TLR4) in UD-1 group compare to SO group.

**Conclusion.** Vitamin D reduces kidney fibrosis through inhibition of fibroblast activation and ameliorate epithelial cell architecture.

### Keywords

Kidney fibrosis, vitamin D, fibroblast, inflammation, apoptosis, TGFβ1



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## Differential White Blood Cell and Platelet Counts in Obese Adolescents: Sex Difference and Their Correlation with Insulin Resistance

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**Introduction.** Subclinical increase of white blood cell counts have been reported as signs of low grade chronic inflammation in obese individuals. Higher white blood cells and also platelet counts have been correlated with insulin resistance. However, there is limited data on differential blood cells and platelet counts in obese adolescents of different sex.

**Aims.** This study aims to compare differential white blood cell and platelet counts in obese and non-obese boys and girls in correlation with their obesity and insulin resistance status.

**Methods.** The subjects of this study were high school students, consisted of 131 obese boys, 76 non-obese boys, 98 obese girls and 98 non-obese girls. White blood cell differential counts and thrombocyte count were obtained using automatic hematological analyzer and neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) were calculated. HOMA-IR was calculated from fasting blood glucose (GOD-PAP) and fasting serum insulin (ELISA) level. The data was analyzed using ANOVA and linear regression methods. The level of significance was defined at 95%.

**Results.** Non-obese girls had higher WBC, neutrophil count, platelet count, NLR and PLR than non-obese boys (p<0.05), while monocyte, basophil and eosinophil counts were similar in both sex (p>0.05). However, in the obese groups, boys had higher monocyte, basophil and eosinophil counts than girls (p<0.05) while the boy's WBC reached the obese girl's WBC level (p=102). In girls, obesity resulted in higher WBC, neutrophil and lymphocyte counts (p<0.05) while other indices remained similar to the level of the non-obese counterparts (p>0.05). On the contrary, all of the counts were higher in obese boys compared to the non-obese group, except for basophil count, NLR and PLR. Obese boys had the lowest level of PLR (p<0.05) and PLR was negatively correlated with HOMA-IR (adjusted R<sup>2</sup> 0.018; unstandardized coefficient -0.026 (95%CI -0.049- -0.003); p=0.029). In boys, monocyte count was the strongest predictor of HOMA-IR among other white blood cells and platelet counts (adjusted R<sup>2</sup> 0.111; unstandardized coefficient 0.010 (95%CI 0.006- 0.014); p<0.001) and strengthened waist circumference as the strongest predictor of HOMA-IR (adjusted R<sup>2</sup> 0.366; unstandardized coefficient 0.005 (95%CI 0.001- 0.008); p<0.001).

**Conclusion.** There are sex differences in differential white blood cell and platelet counts in obese adolescents. Higher monocyte count in obese boys may reflects higher degree of tissue inflammation and metabolic risk.

### Keywords

Obesity, adolescents, differential white blood cell count, platelet, insulin resistance





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### Association Between ACE Gene Polymorphism with Severity and Outcome of Acute Ischemic Stroke

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**Introduction.** ACE gene insertion / deletion polymorphism (ACE I / D) is known to be associated with the occurrence of ischemic stroke through its effect on pathogenesis of atherosclerosis and hypertension.

**Aim.** This study aimed to examine the relationship between this polymorphism with severity and outcome of ischemic stroke in Indonesian population.

**Method.** This is a cross sectional study in a population of patients with acute ischemic stroke in the Stroke Unit of DR Sardjito Hospital in Yogyakarta, Indonesia. Demographic data, stroke risk factors, comorbidities, and stroke severity (NIHSS) were assessed at admission. The clinical outcome (NIHSS) and functional outcome (Barthel Index) were assessed when the patients were discharged from the hospital. ACE I / D genotype of the patients were identified by PCR.

**Result.** Of the 67 patients included in this study, 43 patients (64.2%) had II polymorphism, 23 patients (34.3%) had ID polymorphism, and 1 patient (1.5%) had a DD polymorphism in the ACE gene. The mean NIHSS on admission was  $8.1 \pm 7$ . There was no significant difference in stroke severity assessed with NIHSS on admission among patients with II polymorphisms and patients with ID polymorphisms (mean NIHSS on admission were 7.8 and 7.7 respectively;  $p = 0.789$ ). There was no significant difference in the clinical outcome of patients with II and ID polymorphisms (mean NIHSS at discharge were 4.6 and 4.3 respectively;  $p = 0.91$ ). There was also no significant difference between the functional outcome of patients with II and ID polymorphisms (mean Barthel index at discharge were 62.4 and 56.1 respectively;  $p = 0.335$ ).

**Conclusion.** This study showed that there was no significant association between ACE gene polymorphism with severity and outcome of acute ischemic stroke in Indonesian population.

#### Keywords

Acute ischemic stroke, ACE gene polymorphism, outcome.



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### Usefulness of CBC/6-18 to Evaluate Emotional and Behavioral Problems in Indonesian Autism Spectrum Disorder Children

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**Introduction.** The Child Behavior Checklist (CBCL) has been widely utilized to estimate emotional and behavioral problems in children in the USA and Europe. Although the Indonesian version of the CBCL/6-18 was proven to have good validity and internal consistency in children with typical development (TD) in Indonesia, it has not been utilized for children with autism spectrum disorder (ASD).

**Aim.** To investigate the usefulness of CBCL/6-18 for detecting emotional and behavioral problems in Indonesian ASD children.

**Method.** One hundred and eight mothers of children with ASD and with TD were enrolled in this study. The diagnosis of ASD in Indonesia was made by expert child neurologists based on DSM-IV-TR. Mothers of children aged 6-18 years completed the Indonesian version of the CBCL.

**Results.** The scores of total problems, internalizing, and externalizing were significantly higher in the ASD group than the TD group. Children with ASD scored significantly higher in seven of the eight CBCL subscales (except somatic complaints) compared with TD children.

**Conclusion.** The CBCL/6-18 Indonesian version could be considered as a useful tool for detecting emotional and behavioral problems in children with ASD in Indonesia in Muslim populations.

#### Keywords

Autism spectrum disorder, Child Behavior Checklist, emotional and behavioral problem, Indonesian children.





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## Structural Equation Modelling on Demographic Factors of Nurses' Disaster Preparedness

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Disaster preparedness is a vital component to reduce the impacts from natural or man-made disasters. Nurses perform many important activities in disaster preparedness phase including both planning and capacity building activities. Their disaster preparedness level could be influenced by the internal or demographic factors and external factors. This study investigates the influence of internal factors to nurses' disaster preparedness. The purpose of this study was to investigate a predictive model that could explain the demographic influences factors of nurses' disaster preparedness. The study, using a set of four questionnaires: 1) demographic information; 2) self-efficacy related to disaster preparedness; 3) the Disaster Preparedness Evaluation Tool (DPET) with permission; and 4) information regarding disaster preparedness activities, was conducted with 285 registered nurses from 4 hospitals in Yogyakarta, Indonesia. The data were analyzed using R Software and SEM package for R software. Based on the constructed model from all demographic factors, we found that age, work experience, and education level were have indirect effect on nurses' DPET score and self-efficacy related to disaster preparedness score. Fit indices were acceptable for the conceptual model. The model revealed an excellent fit (AGFI = 0.99; CFI = 1.00; and RMSEA = 0.00). This study is a structural equation model that explains the related demographic factors and their relationship with nurses' disaster preparedness. Findings from this study can be used to develop strategies to enhance nurses' disaster preparedness.

**Keywords:** structural equation modeling, disaster preparedness, disaster nursing



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8	Desertation or thesis publication	Different Variants in Reverse Transcriptase Domain Determined by Ultra-deep Sequencing in Treatment-naïve and Treated Indonesian Patients Infected with Hepatitis B Virus. 2016. Wasityastuti W, Yano Y, Widasari DI, Yamani LN, Ratnasari N, Heriyanto DS, Okada R, Tanahashi T, Murakami Y, Azuma T, Hayashi Y. Kobe J Med Sci. 62 (1): E1-8
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## Lower linkage disequilibrium of Human Leucocyte Antigen (HLA)-DP gene among Indonesian

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**Introduction.** Human leucocyte antigen (HLA) which regulate immune response is widely reported be associated with disease susceptibility. In genetic mapping studies of complex traits, polymorphism which abundant and occur 1/1000 base pair is an important marker. A tight gene linkage provide benefit for genetic marker selection and association study. However, the degree of linkage disequilibrium among populations are varies.

**Aim.** To measure the linkage disequilibrium of 3 single nucleotide polymorphisms (SNPs, rs3077C>T, rs3135021G>A, and rs9277535G>A) of HLA-DP gene among Indonesian and be compared with Japanese population.

**Method.** Six hundred and eighty-six Indonesian and 80 Japanese subjects involved in this study. Genotyping for SNP genotype determination was performed using the allelic discrimination assay on a 7500 Real-Time PCR System. The linkage disequilibrium of the polymorphisms were examined using Haploview software.

**Result.** The three SNPs with physical distance 27 kilo base pair were successfully genotyped at rates of >97.5%. The linkage disequilibrium between two SNPs in Indonesian population were lower (0.07–0.60) than in a Japanese population (0.76–0.93).

**Conclusion.** The linkage disequilibrium of 3 SNPs on HLA-DP among Indonesian population were weak (<0.80). Therefore, a tag SNP cannot represent a specific set of SNPs of HLA-DP gene.





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### A Case Report of Sibling Relationship Determination

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**Introduction.** DNA fingerprint is a method of forensic identification, which has high accuracy, is very important to solve personal identity problem, including determining the sibling relationship among children. In this study, we report a case of sibling determination. A single female, whose husband died several years before, has two sons and a daughter came to our institution for DNA test. In the beginning of their marriage, they entrusted the first and second children to her uncle, and became their uncle's family based on administration (*kartu keluarga/C1*). But the youngest child was included in their own family adminsitration. They never changed the administration status of their children until the uncle and her husband died. To prevent the conflict of inheritance, she need a DNA test to show the evidence that all of the children are their biological offspring.

**Aim.** To determine sibling relationship among three children.

**Methods.** DNA analysis was performed from a mother and three children, without the father, using 20 loci of autosomal STR and 23 loci of Y-chromosomal STR, followed by statistical analysis of sibling.

**Results.** All of the 20 loci of chromosomal STR DNA showed that all of the children have half allele of the mother, indicated that they have the same mother. The 23 Y-chromosomal STR loci of the sons share the same allele, indicated that they have the same paternal line. Statistical analysis of the sibling relationship among the sons is 97.97%, indicated that they are sibling. Analysis of the daughter and 2<sup>nd</sup> son are 99.99% indicated that they are sibling. The daughter and 3<sup>rd</sup> son are sibling based on statistical analysis result is 97.97%.

**Conclusion.** We concluded that they came from the same father and mother.

#### Keywords

Sibling; STR ;Y-chromosom



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