

Site Visit to Hasan Sadikin Hospital by Prof. Dr. Tjandra Yoga Aditama, Sp.P(K).DTM&H, MARS, DTCE

by dr. M. Karyana, Ms. Yanti Triswan, Ms. Novitasari



dr. Rizal is giving explanation for Prof. Dr. Tjandra Yoga Aditama Sp.P(K) DTM&H, MARS

On 29 May 2015, the Chairman of NIHRD, Prof. Dr. Tjandra Yoga Aditama Sp.P(K) DTM&H, MARS, DTCE visited Hasan Sadikin Hospital, Bandung. He was accompanied by Ms. Pretty Multihartina PhD, Director of Center for

Biomedical and Basic Health Technology (Center 1), NIHRD and Dr. Muhammad Karyana, MPH, Head of Communicable Disease Clinical Epidemiology Subdivision, NIHRD. Ms. Yanti Triswan and Ms. Novitasari from the INA-RESPOND Secretariat were also present during the visit.

Hasan Sadikin Hospital is one of the eight sites involved in AFIRE study, and it is also the site for ReDEFINE study. The purpose of the visit was to observe the progress of INA-RESPOND's studies conducted at the site. During the visit, a meeting with the Executive Director of Hasan Sadikin Hospital, Dr. Ayi Djembarsari, MARS was held, including a tour of site's facilities and a discussion with the AFIRE and ReDEFINE study team.

Accompanied by dr. Bacht Alisyahbana, SpPD-KPTI, PhD, INA-RESPOND Steering Committee member/Protocol Co-PI for AFIRE study/Site PI, Prof. Dr. dr. Ida Parwati, SpPK(K), PhD, Head of Clinical Pathology Laboratory, Dr. dr. Ruswana Anwar, SpOG, K-FER, Head of Education and Research, Dr. Arto Yuwono, SpPD, KP, Head of In-Patient Wards, and the site's Research Assistants, Syndi MD and Fritzie MD, the tour of site facilities included the TB DOTS and TB MDR polyclinics, TB meningitis ward, pathology and microbiology laboratories; and BLK (Balai Laboratorium Klinis) which specializes and supported all of the hospital TB clinical research. dr. Rovina Ruslami, SpPD, PhD and dr. H. Ahmad Rizal Ganiem, SpS(K), PhD, PI and Co-PI for the ReDEFINE study were also present during the visit.

[continue to page 3]



June 14 is World Blood Donor Day. The theme of this year's campaign is "Thank you for saving my life". It focuses on thanking blood donors who save lives every day through their blood donations and strongly encourages more people all over the world to donate blood voluntarily and regularly with the slogan "Give freely, give often. Blood donation matters." Related to the World Blood Donor Day, we have an article on how to improve blood safety and availability. Hopefully, after reading this article, we can increase our awareness specifically regarding safety during blood transfusion.

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insight

In our last month's edition, you got to know more about Dr. Bacht (SC member at site 510) and Dr. Gasem (SC member at site 560). This month we will learn more about Prof. Mansyur Arif and Prof. Ketut Tuti Parwati Merati, another two of our dedicated SC members. Let's find out what their views and wishes for the network are from the interview that our research assistants did last month. ☺

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Studies' Progress and Updates

by dr. Anandika Pawitri and dr. Nurhayati

Sepsis Site
Preparation Visit
@ RSCM, Jakarta

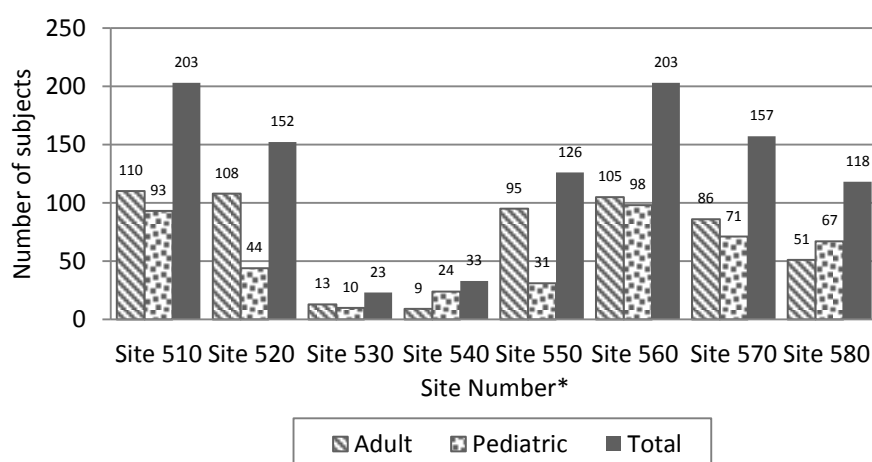


AFIRE STUDY

Next month will be 2 years since the first AFIRE site was activated. Below are the activation dates of the sites:

Site Number / Name	Activation Status Date	First Enrolled Subject Date
Site 520 – RSUP Sanglah	16-Jul-2013	18-Jul-2013
Site 560 – RSUP dr Kariadi	12- Aug-2013	22-Aug-2013
Site 580 – RSUP dr Sardjito	14-Aug-2013	28-Aug-2013
Site 510 – RSUP dr Hasan Sadikin	04-Sep-2013	05-Sep-2013
Site 550 – RSUP dr Wahidin Sudirohusoso	04-Oct-2013	16-Oct-2013
Site 570 – RSUD dr Soetomo	27-Dec-2013	03-Jan-2014
Site 530 – RSUPN dr Cipto Mangunkusumo	06-Nov-2014	27-Nov-2014
Site 540 – RSPI Prof Dr Sulianti Saroso	17-Nov-2014	08-Dec-2014

Enrollment Progress per 24 May 2015



Detailed screening and enrollment progress is available in portal folder:

Studies\INA101\Screening progress.pdf or go to the following link: <https://ina-respond.s-3.com/EdmFile/getfile/797233>

*510– RSUP dr Hasan Sadikin, Bandung
550 – RSUP dr Wahidin, Makassar
520 – RSUP Sanglah, Denpasar
560 – RSUP dr Kariadi, Semarang
530 – RSUPN dr Cipto Mangunkusumo, Jakarta
570 – RSUD dr Soetomo, Surabaya
540 – RSPI Prof Dr Sulianti Saroso, Jakarta
580 – RSUP dr Sardjito, Yogyakarta

For further information on this study, go to <http://www.ina-respond.net/afire-study/>

SEPSIS

Site 41 – RS Cipto Mangunkusumo will be visited by CRA on 8-9 June 2015 for Site Initiation Visit (SIV). The site is currently preparing essential documents needed for the activation. Hopefully, the site can start enrolling subject by the end of June.

Since all sites in Indonesia started later than other sites in Thailand and Viet Nam,

adjustment is made to the enrollment target for Indonesia's sites. Site 41, 42, and 43 will enroll 30, 50, and 50 subjects respectively. This number is based on proportional calculation on the time when the site is activated until December 2015.

	RS dr <u>Wahidin Sudirohudo</u> 42	RS <u>Sardjito</u> 43
Number of screened patients	Adult: 18 Pediatric: 21 Total: 39	Adult: 38 Pediatric: 26 Total: 64
Number of enrolled patients	Adult: 5 Pediatric: 3 Total: 8	Adult: 7 Pediatric: 1 Total: 8
Enrollment expectation	Adult: 25 Pediatric: 25	Adult: 20 Pediatric: 20
No. of day after enrollment	Day 96 (Activation date: Feb 26, 2015)	Day 40 (Activation date: Apr 23, 2015)

Screening and enrollment progress from Sepsis site 42 and 43 up to 1 June 2015

Birthdays and Celebrations!

JuNe

- ✚ 6 June – **Dr. dr. Fatmawati**, MPH (SC Member at site 540)
- ✚ 10 June – **dr. Delly Chipta Lestari**, Sp.MK (INA101 Co-PI at site 530)
- ✚ 13 June – **dr. Sudirman Katu**, Sp.PD-KPTI (SEA050 PI at Site 42)
- ✚ 13 June – **dr. Dewi Lokida**, Sp.PK (INA-RESPOND SC Member)
- ✚ 17 June – **dr. Anggraini Alam** (INA101 Co-PI at site 510)
- ✚ 21 June – **dr. I Made Susila Utama**, SpPD-KPTI (INA101 Site PI at site 570)
- ✚ 27 June – **dr. Ni Made Tyas Dwi Arsanti** (INA101 Research Assistant at site 520)
- ✚ 30 June – **Prof. Dr. Usman Hadi**, Sp.PD-KPTI (INA101 Site PI at site 570)

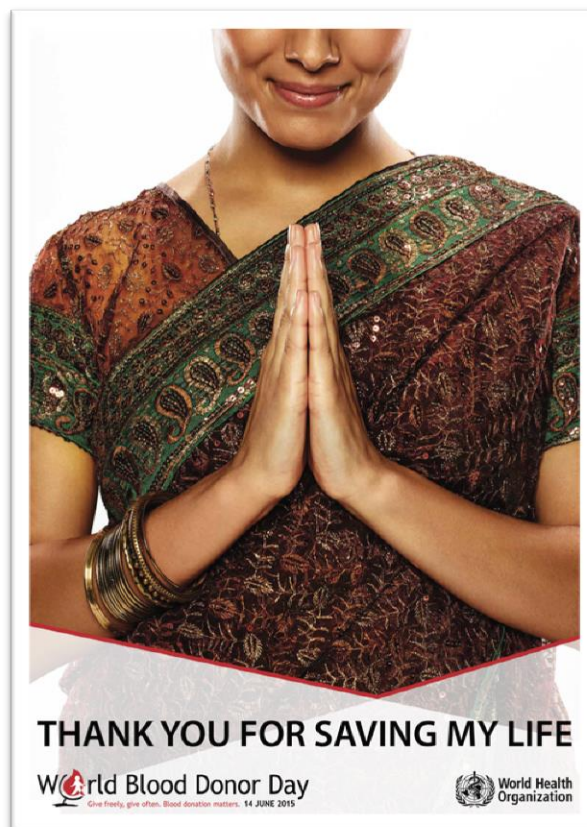
Congratulations to **dr. Ketut Jaya Ningrat** (INA101 RA at site 520) for the birth of your second child! May you cherish this special time, and may the pleasures of parenting warm your heart and fill your life with wonderful memories with your newborn.



[Site Visit to Hasan Sadikin Hospital by Prof. Dr. Tjandra Yoga Aditama, Sp.P(K).DTM&H, MARS]

Prof. Dr. Tjandra Yoga Aditama reiterated two important points that continuously need attention from all partners:

1. The importance of cooperation with foreign countries and to ensure that the cooperation brings benefits for Indonesia's interests, the interests of science, and the interest of researchers in Indonesia.
2. The importance of Material Transfer Agreement (MTA) to ensure the benefits for Indonesia, not to impede.



Save The Date

Manuscript Preparation Meeting

The Manuscript Preparation Meeting will be held on **June 18-19 (adult)** and **25-26 (pediatric)** at NIHRD, Jln. Percetakan Negara no 29, Jakarta Pusat, 10560, Indonesia.

FOR MORE INFORMATION

Please contact Mr. Dedy Hidayat or Ms. Yuyu Nuzulurrahmah at +62 21 42879189 ext. 102 or 112 during office hours (08.00 – 16.00)

PROFILE: Insight To The Network's Steering Committee Member At Sites

by RA from site 520 dr Ketut Jaya Ningrat,
dr Ni Made Tyas Dwi Arsanti,
RA from site 550 dr Fatmawaty Ahmad,
dr Munawir

Makassar – Professor Mansyur Arief was born on 4 November 1964 on Selayar Island, the main island of Selayar Islands which lies off the coast of Cape Bira of South Sulawesi Province. He is one of the INA Respond's Steering Committee (SC) members. Currently, he also serves as the Chairman of the Department of Clinical Pathology, Faculty of Medicine, Hasanuddin University, Makassar, the Chairman of the Functional Medical Staff (SMF) Laboratory of Clinical Pathology, Dr. Wahidin Sudirohusodo Hospital, Makassar, and as an active lecturer of the Department of Clinical Pathology at Hasanuddin University, Makassar.

Prof. Mansyur earned his medical degree in 1989 from the Faculty of Medicine, Hasanuddin University, Makassar. He then received his PhD research course in Hematology and Oncology from Hiroshima University, Japan. After returning from Japan, he took his specialization in Clinical Pathology at Hasanuddin University and earned his Hematology consultant title from the Collegium of Clinical Pathology Indonesia in 2007.

Although he has myriads of jobs, he is still active in organizations. Prof. Mansyur once served as the Chairman of the Indonesian Medical Association, Makassar and the Chairman of Association of Clinical Pathologist, Makassar. He is now a member of Dr. Wahidin Sudirohusodo Hospital Ethics Committee/IRB.

As one of the network SC members and also as the Executive Member of the SEAICRN network, he knows that site 550 Makassar faces many challenges and obstacles. One of the major challenges now is the activation of sepsis study.



Prof. Mansyur Arief
SC Member at Site 550, RS. Wahidin Sudirohusodo, Makassar

This study is a community-based study with a tiered referral system. The patients recruitment becomes even more challenging than other studies mostly because of the ignorance of the society and the cultural differences among the sites. Several attempts have been made, including communicating with colleagues and associates in Public Health Center as well as type C and type B hospitals, so patients presenting sepsis and severe sepsis signs and symptoms can be immediately referred to Dr. Wahidin Sudirohusodo hospital as a research site. Yet, Prof. Mansyur is really proud that Makassar has been selected as the site in the Eastern part of Indonesia, and he is convinced if we retain and increase our quality project, Makassar can develop further; not only in clinical research result but also in human resources.

INA-RESPOND allows us to carry out good clinical research in accordance with the ethics process. In the future, he hopes that Dr. Wahidin Sudirohusodo Hospital, Makassar can maintain its performance and complete the study, showing significant results. Last but not least, he is open handed to collaborate not only in the study field of Infectious Diseases but also in other study fields. Hopefully, Makassar can be one of the role models of clinical research in the eastern part of Indonesia by doing more good clinical research.

Denpasar – Prof. DR. dr. Ketut Tuti Parwati Merati, Sp.Pd-KPTI, FINASIM is the Steering Committee member at site 520 (RSUP. Sanglah, Denpasar.) She was born on 28 December 1948 in Denpasar. Known as an assertive and energetic person, the Leader of Tropic-Infection Division, Internal Medicine, Sanglah Public Hospital obtained her MD from Udayana University School of Medicine in 1976. She completed her studies and got her educational specialist degree in Internal Medicine from Faculty of Medicine, Airlangga University in 1984. In 1992, she joined the training in Research Method in CAPS (Centre for Aids Prevention Studies) in California University, San Francisco, USA. She obtained her Tropic Infection Consultant in 1997, PhD in Biomedical related to HIV AIDS in 2007, and also FINASIM (Fellow of Indonesian Society of Internal Medicine) in 2009.

Prof. DR. dr. Ketut Tuti Parwati Merati is the one who discovered the first HIV/AIDS case at RSUP Sanglah (in April 1987). At that time, she was an Internist working at Sanglah Public Hospital. The first case of HIV was identified in a foreigner from the Netherlands who came to see her because he had cough. At that point, this patient was not really open regarding to his sickness. After conducting a series of checkup procedure, Kaposi Sarcoma was found on his skin. Based on the facts found, she continued checking the patient's blood sample and sent it to NIHRD, as laboratories in Bali were not able to check for HIV/AIDS yet. Later on, the case was announced as the first case of HIV/AIDS in Indonesia by the Ministry of Health, Republic of Indonesia. After that discovery, she became more focused on HIV/AIDS prevention. With the help of Australia and commitment from Indonesian government in the

end of 1987, three doctors including her and three nurses from three different hospitals in Indonesia were funded to go to Sidney, Australia to study HIV/AIDS further. At that time, there were lots of AIDS patients in Sydney.

Her love and dedication to science especially that related to HIV/AIDS are reflected by the number of research she has done in local, national, and international level starting from 1989 until this moment. Her research involves behavior & prevention of HIV/AIDS, clinical researches, treatments and bio molecular which relates to HIV/AIDS. In 1989 she undertook a research regarding the knowledge, attitude, and behavior on five groups at risk for HIV/AIDS: sex workers,

homosexuals, transgender, drug users, and people working in tourism industry. In 1992, she established YCUI (Yayasan Citra Usadha Indonesia), which main activity is to do counseling for those five groups. The difficulty in approaching those groups is the main challenge to train outreach workers. Outreach worker model attracted the attention of HIV/AIDS NGOs worldwide in 1994, and what was happening was featured in



Prof. Ketut Tuti Parwati Merati
SC Member at site 520,
RS Sanglah, Bali

Science magazine: Model Program Take Aim at HIV Rates in Indonesia (science, volume 264, 1 April 1994), and several national and international newspapers such as Worldview: Working Bali Streets (worldview, summer 1994, p 27-29), Innovative Effort Checks AIDS Spread in Indonesia (Boston Globe international newspaper dated 25 April 1994), dr. Tuti Parwati Commits to Fighting HIV/AIDS (The Jakarta Post, February 8, 2007). In 2004 she joined an Asia-Australia researchers' network TAHOD (Treat Asia HIV Observational

Database, and TASER (Treat Asia Study to Evaluate Resistance, 2008-now). The Health Minister of Republic of Indonesia appreciated her dedication in community service and prevention of HIV/AIDS in Indonesia in August 2007. In the same year, she also received an honor from Coordinating Minister for People's Welfare of Indonesia on Pioneer and Dedication That Never Subsides in preventing HIV/AIDS in Indonesia. The Marquis Who's Who Publication Board chose her as one of a few significant figures whose biography was listed on WHO's Biography in WHO in ASIA 1st edition in 2007. In 2010, she was awarded by Minister of Women and Child Protection together with UNESCO National Committee as one of 100 significant women researchers whose biography was published in "One of One Hundred Women Achievers Researchers in Indonesia"

As a Steering Committee at site 520, she has been contributing lots of ideas and feedback for the research involving steps to recruit children subjects as well as character building of Research Assistants in reviewing cases together with internal residents. When she was asked about the challenges she has faced as Steering Committee member, she admitted that it is not easy to maintain the site

internally. According to her the solution of this issue is to emphasize on the communication and commitment aspect. Good intention and clear communication will create a sense of belonging, so all people and sites involved in the research will become close. Commitment is crucial considering the large number of tasks aside from those related to the research. Another challenge that she mentioned is bureaucracy which can potentially obstruct the start of any research. For example, delayed licensing will postpone the start of the research.

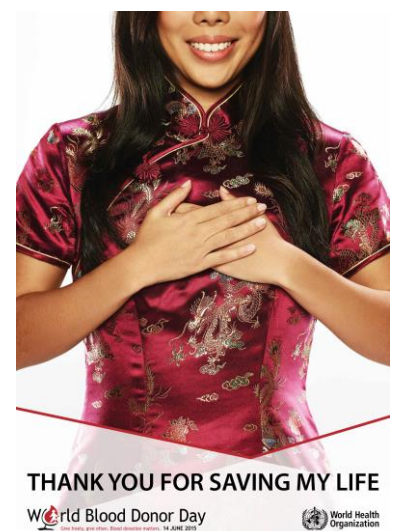
She appreciates the existence of INA-RESPOND Network as the network is the embryo of future multicenter research. This comment was also shared during the NSC meeting in Bandung (2014), where according to her, the hospitals involved in the AFIRE study have received benefits of the network existence. "As researchers, the doctors can learn how to carry out a good clinical research. And in the meantime, the site itself can learn about standards of care implemented by other sites. She hopes that this network can grow further by building up communication and mutual interest between involved parties.

World Blood Donor Day: How to Improve Blood Safety and Availability

by Ms. Neneng Aini

Since 2004, to raise awareness of the need for safe blood and blood products, every 14 June countries around the world celebrate World Blood Donor Day. This date is also commemorated to thank blood donors for their voluntarism that can help patients suffering from life-threatening conditions live longer or get higher quality of life, and support complex medical and surgical procedures. Although blood transfusions are life saving, they are not without risks. Infections were once the main risk. Multiple critical steps have been taken to minimize the risk; however, this risk can never be entirely eliminated.

Bacteria or viruses may be transmitted through transfusion in 2 ways. The first way is through the contamination of blood or its components during blood collection or packing. Besides this, bacteria and virus can also be transmitted when the donors



experience asymptomatic infections. Viruses which are potential to become a threat to the blood supply include HIV, West Nile virus, dengue viruses, chikungunya virus, and hepatitis particularly Hepatitis B and C. Both gram-positive and gram-negative organisms have also shown to cause transfusion-associated sepsis. Other pathogens, such as *Plasmodium malariae* and *Trypanosoma cruzi* (Chagas disease), remain a risk for transfusion-transmissible disease.⁽¹⁻⁵⁾

There is a lack of comprehensive guidance for transfusion service and clinical staff on how to best recognize transfusion transmissible infections (TTI), but we should note, it is important that practitioners have the responsibility to prevent this infection. To improve blood safety and availability, WHO has recommended the following integrated strategy⁽⁶⁾:

1. Establishment of a national blood system with well-organized and coordinated blood transfusion services, effective evidence-based and ethical national blood policies with the goal of achieving self-sufficiency, and legislation and regulation, that can provide sufficient and timely supplies of safe blood and blood products to meet the transfusion needs of all patients.
2. Collection of blood, plasma, and other blood components from low-risk, regular, voluntary, unpaid donors through the strengthening of donation systems, the phasing out of family/replacement donation, the elimination of paid donation, and effective donor management. Identification of donor population at low risk needs a special concern from blood center or transfusion service physician. Assessment of the donor's history of disease should be done thoroughly and decision to accept or postpone a donor with history of infectious disease must be made carefully.
3. Quality-assured screening of all donated blood for transfusion transmissible infections, including HIV, hepatitis B, hepatitis C and syphilis, confirmatory testing of the results of

all donors screen reactive for infection markers, blood grouping and compatibility testing, and systems for processing blood into blood products (blood components for transfusion and plasma derived-medicinal products), as appropriate, to meet health care needs.

4. Rational use of blood and blood products to reduce unnecessary transfusions and minimize the risks associated with transfusion, the use of alternatives to transfusion, where possible, and safe and good clinical transfusion practices, including patient blood management.

These strategies tend to improve transfusion safety and appropriateness. From research area, there is a hope from pathogen-reduction methods although such methods are not yet available for all blood components and there is no extensive validation. Ongoing efforts and collaboration will be required to further improve patient outcomes.^(4, 7)

REFERENCES

1. Screening Donated Blood For Transfusssion-Transmissible Infections: Recommendation. Geneva: World Health Oragnization, 2009.
2. Dodd RY. Emerging pathogens in transfusion medicine. Clinics in laboratory medicine. 2010;30(2):499-509.
3. Stramer SL, Hollinger FB, Katz LM, Kleinman S, Metzger PS, Gregory KR, et al. Emerging infectious disease agents and their potential threat to transfusion safety. Transfusion. 2009;49 Suppl 2:1S-29S.
4. Allain JP, Bianco C, Blajchman MA, Brecher ME, Busch M, Leiby D, et al. Protecting the blood supply from emerging pathogens: the role of pathogen inactivation. Transfusion medicine reviews. 2005;19(2):110-26.
5. Alter HJ, Stramer SL, Dodd RY. Emerging infectious diseases that threaten the blood supply. Seminars in hematology. 2007;44(1):32-41.
6. Aide-mémoire: Blood safety. Geneva: World Health Organization, 2002.
7. Blajchman MA. Protecting the blood supply from emerging pathogens: the role of pathogen inactivation. Transfusion clinique et biologique : journal de la Societe francaise de transfusion sanguine. 2009;16(2):70-4.

Latest News: A Glance of Research Progress in the World

by dr. Herman Kosasih

“One-Stop Shopping” To Detect Complete History of Virus Infections in an Individual

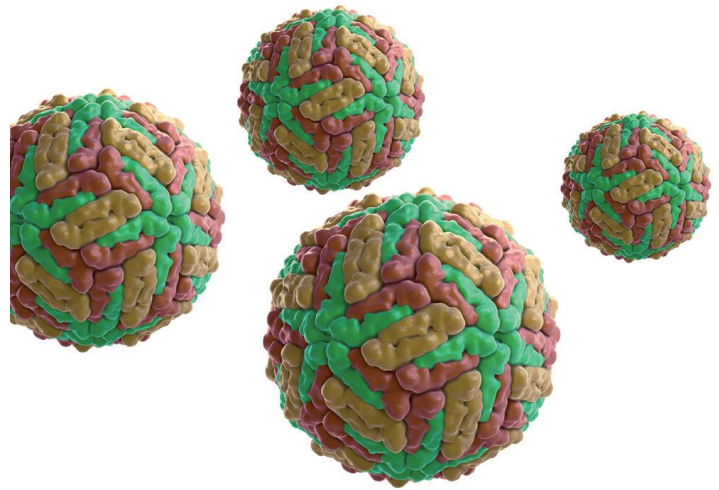
In the near future, we may be able to know all the viruses that have infected our body in just only 2-3 days. It is fast, because we do not have to test for one individual virus at a time, instead we can assay all of these at once. A novel diagnostic platform called VirScan uses 93,904 synthesized 200-mer oligonucleotides that comprise a reference library of 206 viruses known to infect humans. The library is cloned into bacteriophage, and incubated with a serum sample. Antibodies within the serum that bind to bacteriophage are then sequenced and identified.

This platform has been tested in serum samples collected from 569 people living in several countries. According to the results, two individuals experienced 84 virus infections and five individuals had 62 previous virus infections. On average, every individual recorded 10 virus species infections. The sensitivity and specificity was analyzed by comparing the results of VirScan and ELISA and Western-Blot assays in HIV or HCV infected sera and revealed approximately 95%.

Further reading: Comprehensive serological profiling of human populations using a synthetic human virome. *Science* 5 June 2015: Vol. 348 no. 6239 aaa0698 DOI:10.1126/science.aaa0698

Dengue Vaccine, Close to Approval?

The most advance dengue (DEN) vaccine is the live attenuated, tetravalent DEN vaccine (CYD-TDV). This vaccine utilizes the licensed yellow fever17D vaccine as backbone, with the premembrane (prM) and envelope (E) genes are replaced with those of each DEN virus representing serotypes 1 to 4. Three clinical trials have been conducted and all shows



(Asher Mullard, 2014)

consistent performance, wide variation in serotype-specific efficacy, the lowest to DEN-2, and the highest to DEN-3 and DEN-4. As it shows modest overall efficacy (56.5%-60.8%) and reduces the risk of severity of illness and hospitalization rate, this vaccine should have a substantial public health impact. However, since the efficacy is significantly higher in vaccine recipients that already have immunity to DEN than in those who have never been infected, the usefulness for travelers is doubtful. It might have implications for the schedule of vaccine introduction as this vaccine boosts and broadens pre-existing immunity rather than raising protective immunity. Besides these issues, other remaining problem that should be solved is the lower efficacy against serotype 2.

Further reading: Wilder-Smith, Dengue vaccines: dawning at last? *Lancet*. 2014 Oct 11;384(9951):1327-9; Capeding, et al. Clinical efficacy and safety of a novel tetravalent dengue vaccine in healthy children in Asia: a phase 3, randomised, observer-masked, placebo-controlled trial. *Lancet* 2014; 384: 1358–65; Villar, et al. Efficacy of a tetravalent dengue vaccine in children in Latin America. *N Engl J Med*. 2015 Jan 8;372(2):113-23.

Vaccine, a New Malaria Intervention?

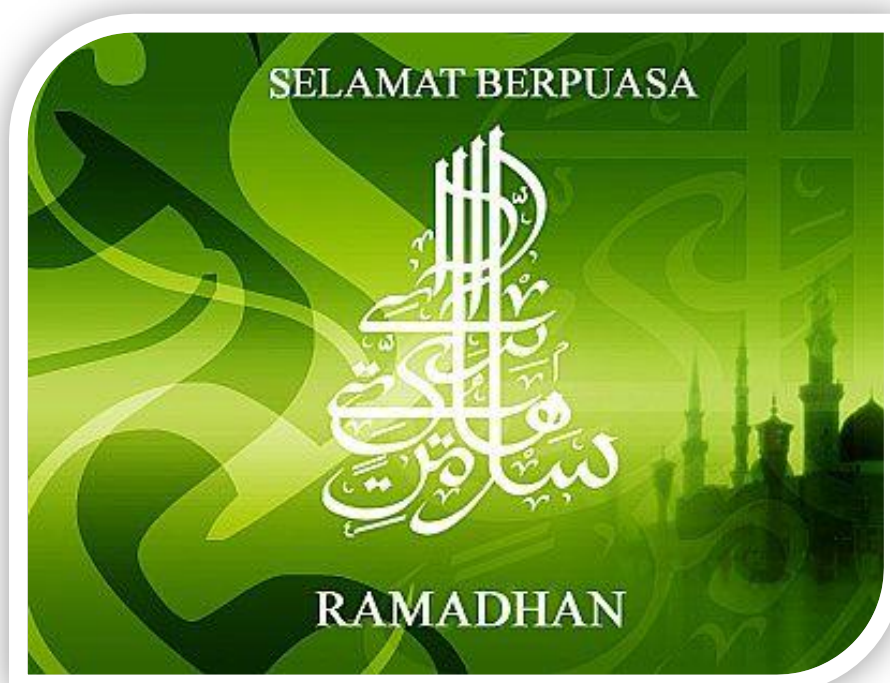
Developing malaria vaccine is really hard due to the complexities of the parasite lifecycle and host immune response. It has taken 30 years to get to the RTS, S vaccine, currently being reviewed by the European Medicines Agency for approval. In this vaccine epitopes from the parasite

circumsporozoite protein are combined with elements designed to evoke an immune response to prevent hepatocyte infection, and thereby block progression to red blood cells and clinical malaria. In children age 5-17 months group, protection against malaria was observed in 36.3%, while in children aged 6-12 weeks, protection was 25.9%. Although apparent protection is modest, since

vaccine would be used alongside with complementary interventions such as bednets and effective artemisin-combination treatments and other WHO recommended control measures, this protection could prove to be beneficial and a vaccine rollout program deserves our support.

Further reading: The Lancet, vol 385, April 25, 2015

The INA-RESPOND network wishes you



**INA-RESPOND
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