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DAFTAR LAMPIRAN

Lampiran 1. Elisa

Alat dan Bahan:

- 96-well microplate (Corning, #3590)
- Bicarbonate buffer (1.59 g of Na_2CO_3 + 2.93 g of $NaHCO_3$ per 1 l)
- PBS (-)
- PBS-T (PBS, 0.05% Tween 20)
- 1% BSA in PBS
- Cit/phos buffer (0.1 M citrate, 0.2 M disodium phosphate, pH 4.4–4.6)
- SARS-CoV-2 recombinant S1 (Sino Biological, #40591-V08H)
- SARS-CoV-2 recombinant RBD (GenScript, #Z03483)
- Heat-inactivated serum samples (56°C, 30 min)
- Representative serum samples as inter-day reliability control
- Anti-human IgG HRP conjugate (Bio-Rad, #172-1050)
- ABTS (Merck, #A1888)
- H_2O_2

Prosedur:

(Day 0)

1. Coat the microplate with 0.2 µg/50 µl/well of recombinant protein in bicarbonate buffer.
2. Incubate overnight at 4°C.

(Day 1)

3. Aspirate the bicarbonate buffer in the microplate.
4. Add 100 µl/well of 1% BSA in PBS and incubate for 1 h at room temperature (25°C).
5. Dilute serum samples with 1% BSA in PBS (1:100 for S1 and RBD). (These dilution factors roughly correspond to the EC_{50} values for the RayBiotech patient samples)
6. Aspirate the blocking buffer in the microplate.
7. Add 50 µl/well of the diluted samples (duplicates) and incubate for 1 hour at room temperature.
8. Wash the microplate three times with PBS-T and once with PBS.
9. Add 50 µl/well of the diluted anti-human IgG HRP conjugates (1:2000 in 1% BSA/PBS) and incubate for 1 h at room temperature.
10. Prepare the substrate as follows:
    - ABTS: 4 mg
    - cit/phos buffer: 10 ml
    - H2O2: 6 µl (add just before use)
11. Wash the microplate three times with PBS-T and once with PBS.
12. Add 100 µl/well of the substrate and incubate for 30 min (precisely, if possible) at room temperature.
13. Measure the absorbance at 414 nm on a microplate reader.

Lampiran 2. Neutralizing Antibody
Baculovirus Immunized Sera (Mice)

1. Add DMEM-CM (96 well)

Control 2020C 2003							DMEM	Serum		
	#1	#2	#5	#6	#9	#10				
A							260μl	10,8μl	90μl	7-10 times pipetting
B							180μl		90μ	
C									90μl	
D									90μl	
E									90μl	

2. Add 10,8μl serum in "A"
3. serial dilution (90μl ea)
4. prepare white plate:
   A1 B1 C1: 100μl DMEM
   A2 B2 C2: 50μl DMEM
5. SAG-LUC VSV
   200ml/ 5ml DMEM in 15ml falcon tube
6. 50μl/ well VSV (w/o A1 B1 C1)
7. add diluted serum: 50μl/ well
8. 37C 1 hour
9. 293 T/ h ACE2 + hTMPRSS2
   Cell number 200 x2/4= 10^6/well
   Requirement: $2x10^5$/ml
   Dilution: 1:5 2 2mol cell + 9ml B
10. 100μl cells/well
11. incubated 37C over night
12. lysis reagent 400μl in 1,7ml DW
13. discard medium --> A/C
14. 20μl/ well lysis reagent
15. luceferase assay by Glomax

Neutralizing activity of the serum was examined, using a VSV-based pseudovirus, as previously describe. Briefly, the pseudovirus was engineered to express the Wuhan-Hu-1 SARS-CoV-2 Spike protein on the viral surface, in which the luciferase gene was incorporated in the viral genome. The serum was diluted with the medium, and the virus was added by triplicate. Final dilution rate of the serum was 1:100. The mixture of the virus and the serum was incubated with human embryonic kidney (HEK) 293T cells that expressed human ACE2 and human TMPRSS2. The cells were examined by Luciferase Assay System (Promega, Madison, WI, USA) after 24 hours incubation.

Lampiran 3. Form Anamnesis dan Data Pasien

FORM ANAMNESIS DAN DATA PASIEN

ID Pasien :

NO	Pertanyaan	Catatan
1	Nama	
2	Umur	
3	Jenis Kelamin	
4	Alamat	
5	Pekerjaan	
6	Suku	
7	Agama	
8	Tanggal masuk RS/Klinik	
9	Tanggal wawancara	
10	Keluhan Utama	
11	Riwayat Penyakit: - Kapan terdiagnosis? - Dimana? - Riwayat kontak? - Demam? Berapa lama? Frekuensi? Waktu tertentu? Tipe demam (continus, intermitten) - Banyak berkeringat? - Sakit kepala? - Nyeri otot? Di daerah mana? - Gusi bengkak? - Batuk (kering/berdahak)? - Sesak napas? - Nyeri menelan - Nyeri di bagian dada - Penurunan penciuman (bau) - Penurunan pengecapan - Mual/muntah - Diare - Keluhan lain : … - Riwayat rawat inap	
12	Riwayat penyakit sebelumnya? - Riwayat saluran napas - Riwayat alergi (atopi) - Komorbid lain DM/hipertensi - Riwayat malaria	
13	Riwayat keluarga - Apakah ada anggota keluarga yang juga positif COVID 19? - Kapan terakhir kontak dengan penderita sebelum sakit?	
14	Riwayat Pengobatan - Obat apa saja yang telah dikonsumsi?	

- Penggunaan vitamin D
- Riwayat berjemur selama sakit? Frekuensi? Durasi?

Apakah dirawat di ICU? Berapa lama?

15 Riwayat Vaksinasi
- COVID 19 kapan?
- Smallpox (cacar) ya/tidak?

16 Keluhan setelah sembuh:
- Apakah ada keluhan yang masih dirasakan?
- Atau ada keluhan lain yang kira-kira berkaitan?

Lampiran 4. Case Report Form

CASE REPORT FORM

ID Pasien :

No	Pemeriksaan	Tanggal	Hasil
1	Anamnesis: - Keluhan utama - Riwayat penyakit sekarang - Riwayat penyakit dahulu - Riwayat Keluarga		
2	Pemeriksaan fisik: - Keadaan umum - TB/BB - Pemeriksaan kepala-kaki		
3	Pemeriksaan sampel darah - Reaktivitas terhadap protein spike dan nukleokapsid SARS-CoV-2 - Kadar antibody dalam serum		
4	Pemeriksaan penunjang lainnya Radiologi: GGO? Pneumonia? Lab Darah: Trombositopeni? NLR?		

Lampiran 5. Informed Consent

1. PERSETUJUAN SESUDAH PENJELASAN (PSP) untuk orang dewasa (>16 tahun)

Bagian I. Lembar Informasi / Penjelasan kepada Volunteer

Nama saya, …… bekerja di ……..

Kami sedang melakukan riset mengenai penyakit infeksi yang disebabkan oleh virus korona. Penyakit ini biasanya ditandai dengan gejala demam, batuk, sesak napas, hilangnya rasa pengecapan dan penciuman, dan berbagai gejala lainnya.

Kami akan memberikan informasi kepada Bapak/Ibu dan mengundang Bapak/Ibu jika ingin berpartisipasi pada riset ini. Sebelum memutuskan untuk berpartisipasi, Bapak/Ibu dapat berdiskusi dengan seseorang yang Bapak/Ibu percaya. Apabila terdapat kata-kata yang tidak dipahami, silakan bertanya ke saya, dan saya akan menyediakan waktu untuk menjelaskannya. Selain itu jika nanti Bapak/Ibu memiliki pertanyaan, dapat ditanyakan hal tersebut kepada saya, dokter atau petugas yang ditunjuk.

Keikutsertaan Bapak/Ibu dalam riset ini sepenuhnya sukarela. Kalau Bapak/Ibu memilih untuk tidak ikut, Bapak/Ibu tetap mendapatkan layanan kesehatan seperti biasanya. Bahkan, meskipun Bapak/Ibu setuju saat ini, tetapi kemudian berubah pikiran dan menarik persetujuan keikutsertaan Bapak/Ibu, maka layanan yang anda terima dari rumah sakit (RS) di daerah ini tetap dilanjutkan.

Selama masa riset, darah akan diambil 1 kali, sebanyak +/- 3 ml menggunakan jarum suntik kecil. Hal ini mungkin akan menimbulkan rasa sakit, namun akan kami minimalisir dengan teknik yang sebaik-baiknya. Dalam pengambilan darah ini, kami akan melakukan prosedur bebas-hama untuk menghindarkan Bapak/Ibu dari efek samping infeksi akibat pengambilan darah tersebut dengan menguapkan kapas alcohol sebelum dan setelah memasukkan jarum suntik. Darah Bapak/Ibu akan kami cek apakah mengandung antibody terhadap virus korona. Hal ini penting diketahui karena jika kadar antibody dalam darah Bapak/Ibu tinggi, maka akan memberikan perlindungan terhadap infeksi virus korona di kemudian hari. Namun, jika kadarnya terus menurun, maka data ini akan sangat bermanfaat untuk pembuatan dan pengembangan vaksin. Dengan adanya vaksin, dapat memicu terbentuknya antibody dalam jangka waktu tertentu untuk menghasilkan mekanisme perlindungan dan pertahanan tubuh yang baik terhadap virus korona.

Penerjemah: Saya telah menanyakan Bapak/Ibu bahwa keikutsertaan pada penelitian ini sepenuhnya sukarela: .....(inisial).

Jika Bapak/Ibu memutuskan untuk ikut dalam riset ini, setiap kesakitan yang berkaitan dengan penelitian ini, maka Bapak/Ibu dapat menghubungi dr. Sitti Nurisyah, Sp.P di nomor telepon: 081230308383.

Kami tidak akan memberitahukan identitas Bapak/Ibu di riset ini pada orang lain. Informasi yang kami kumpulkan pada riset ini akan dijaga kerahasiannya. Setiap informasi yang diperoleh tentang Bapak/Ibu akan diberi kode tertentu, tanpa disertai nama Bapak/Ibu. Hanya anggota peniliti yang mengetahui kode Bapak/Ibu dan kami akan menyimpan informasi tersebut dalam laci yang terkunci. Kami akan membagi pengetahuan yang kami peroleh dari riset ini kepada Bapak/Ibu sebelum diumumkan ke public. Informasi rahasia tidak akan dipaparkan. Kami akan menyelenggarakan pertemuan kecil dengan partisipan dan hal ini akan diumumkan. Setelah itu, kami akan mempublikasikan hasil ini dan membuat sedemikian rupa sehingga hasil riset ini dapat berguna bagi orang lain.

Riset ini telah dibahas oleh Komisi Etik Penelitian Kesehatan, Fakultas Kedokteran Universitas Hasanuddin. Kalau saudara ingin mendapat informasi lebih rinci tentang komisi etik tersebut, saudara dapat menghubungi dr. Agussalim Bukhari, M.Med, Ph.D, Sp.GK, Sekretaris Komisi Etik, di nomor: 0411-5780103; 081225704670

Bagian II: Surat Persetujuan Keikutsertaan

Saya telah membaca informasi di atas, atau informasi tersebut telah dibacakan kepada saya. Saya telah diberi kesempatan bertanya dan setiap pertanyaan yang saya ajukan telah dijawab dengan memuaskan. Saya menyetujui secara sukarela untuk berpartisipasi dalam riset ini.

- _Nama Sukarelawan :……..
- _Tanda tangan : ……..
- _Tanggal ..... (Hari/bulan/tahun)

Tanda tangan Saksi : (Tanda tangan Saksi dan cap jari sukarelawan hanya diperlukan bila sukarelawan buta huruf. Jika memungkinkan, saksi adalah seseorang yang dipilih oleh partisipan dan tidak memiliki hubungan dengan tim riset ini).
Saya telah menyaksikan pembacaan secara akurat dari lembar PSP ini ke orang yang mungkin dapat berpartisipasi, yang telah memiliki kesempatan untuk mengajukan pertanyaan. Saya menegaskan bahwa Partisipan telah memberikan persetujuan secara sukarela.

- _Nama Saksi : ……..
- _Tanda tangan Saksi : ……..
- _Tanggal ..... (Hari/bulan/tahun)

Cap Jempol Partisipan :
Tanda Tangan Peneliti : Saya telah membacakan atau bersaksi mendengarkan pembacaan lembar informasi PSP pada calon partisipan yang memiliki kesempatan untuk bertanya. Saya menegaskan bahwa partisipan telah memberikan persetujuannya secara sukarela

- _Nama Peneliti :……
- _Tanda tangan Peneliti : ……..
- _Tanggal .....(Hari/bulan/tahun)

Salinan dari lembar persetujuan ini akan diberikan kepada Partisi

Lampiran 6. Hasil Analisis Normalitas Data S1, RBD dan NP

Tests of Normality[b,d,e,f,g,h,i,j,k]

	group	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
S1_0	A	.227	13	.065	.854	13	.032
	B	.180	39	.003	.886	39	.001
	C	.226	35	.000	.740	35	.000
RBD_0	A	.199	13	.167	.903	13	.147
	B	.169	39	.007	.940	39	.037
	C	.119	35	.200*	.935	35	.040
NP_0	A	.139	13	.200*	.921	13	.258
	B	.119	39	.173	.915	39	.006
	C	.174	35	.009	.915	35	.010
S1_30	A	.211	13	.116	.793	13	.006
	B	.131	39	.087	.939	39	.035
	C	.263	35	.000	.698	35	.000
RBD_30	A	.235	13	.048	.805	13	.008
	B	.125	39	.130	.968	39	.320
	C	.134	35	.114	.946	35	.085
N_30	A	.151	13	.200*	.914	13	.207
	B	.111	39	.200*	.933	39	.023
	C	.104	35	.200*	.974	35	.572
S1_90	A	.209	13	.125	.851	13	.030
	B	.100	39	.200*	.969	39	.345
	C	.154	35	.036	.921	35	.016
RBD_90	A	.129	13	.200*	.927	13	.310
	B	.092	39	.200*	.970	39	.364
	C	.127	35	.170	.935	35	.041
N_90	A	.181	13	.200*	.909	13	.175
	B	.089	39	.200*	.957	39	.138
	C	.075	35	.200*	.959	35	.211

Hasil analisis Normalitas Data neutralizing

Tests of Normality

	Kelompok	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Internalization 0 day	B	.254	12	.032	.840	12	.028
	A	.186	12	.200*	.893	12	.127
	C	.170	12	.200*	.906	12	.191
Internalization 30 day	B	.272	12	.014	.813	12	.013
	A	.175	12	.200*	.912	12	.223
	C	.224	12	.099	.802	12	.010
Internalization 90 day	B	.270	12	.016	.818	12	.015
	A	.219	12	.115	.798	12	.009
	C	.233	12	.071	.872	12	.069

*. This is a lower bound of the true significance.

a. Lilliefors Significance Correction

Untuk uji Normalitas data, data dikatakan normal jika hasil statistik menunjukkan nilai p> 0,05, dari tes normality menunjukkan bahwa kelompok data yang normal yaitu nilai RBD hari ke-0 pada kelompok A ; NP pada hari ke-0 pada kelompok A; RBD hari ke-30 pada kelompok B dan C; NP pada hari ke-30 pada kelompok C; nilai S1 hari ke-90 pada kelompok C; RBD hari ke-90 pada kelompok A dan B ; NP pada hari ke-90 pada kelompok A,B,C

Sedangkan pada data neutralizing hanya kelompok A dan C hari ke-0 dan kelompok A hari ke-30 yang berdistribusi normal.

Untuk melakukan uji statistik parametrik seperti Uji t Dependent/ Ujit t Independent atau Uji One way Anova, kelompok yang akan diuji semuanya harus terdistribusi normal, jika ada salah satu kelompok saja yang tidak normal, maka sebaiknya menggunakan uji non patametrik. Melihat hasil uji normalitas data yang ada, disarankan untuk melakukan uji non-parametrik