

DAFTAR PUSTAKA

- Advani, J., Verma, R., Chatterjee, O., Pachouri, P. K., Upadhyay, P., Singh, R., Yadav, J., Naaz, F., Ravikumar, R., Buggi, S., Suar, M., Gupta, U. D., Pandey, A., Chauhan, D. S., Tripathy, S. P., Gowda, H., & Prasad, T. S. K., 2019. Whole Genome Sequencing of *Mycobacterium tuberculosis* Clinical Isolates From India Reveals Genetic Heterogeneity and Region-Specific Variations That Might Affect Drug Susceptibility. *Frontiers in Microbiology*, 10(309): 1–15.
- Agus, R., Hidayah, N., & Sjafaraenan., 2019. Isolation and Cloning of Rv3204 of *Mycobacterium tuberculosis* to *Escherichia coli* BL21 as Vaccines Tuberculosis : A preliminary Study. *Journal of Physics: Conference Series*, 1341(2).
- Ahsan, M. J., 2015. Recent Advances in the Development of Vaccines for Tuberculosis. *Therapeutic Advances in Vaccines*. 3(3): 66–75.
- Amelia, A., Saleh, D. M., Pramono, H., & Sistina, Y., 2013. Motilitas dan Viabilitas Spermatozoa Itik Lokal *Anas platyrhynchos* Setelah Penyimpanan Refrigerator dalam Ekstender Dikombinasi Berbagai Konsentrasi Krioprotektan Gliserol. *Biologi BIOSFERA*. 3(1).
- Bio Rad. 2017. ELISA Basics Guide. In *Validation of Pharmaceutical Processes, Third Edition*.
- Breed, R. S., Murray, E. G. D., & Smith, N. R., 1957. *Bergey's Manual of Determinative Bacteriology* (Seventh Edition). Baltimore The Williams & Wilkins Company.
- BT Laboratory. 2021. *Human Interleukin 6 Platinum ELISA Kit*. Data Sheet.
- Bunyamin, B., Mulyana, & M, L. A., 2015. Produksi Serum Rabbit Anti-Catfish terhadap Penyakit Motile Aeromonas Septicemia (MAS) pada Ikan Mas Patin Siam (*Pangasius hypophthalmus*). *Mina Sains*. 1(1): 24–33.
- Centers for Disease Control and Prevention. 2015. Epidemiology and Prevention of Vaccine-Preventable Disease 13th Edition. In J. Hamborsky, A. Kroger, & C. Wolfe (Eds.). *Equine Clinical Immunology*.
- Chowdhury, I. H., Choudhuri, S., Sen, A., Bhattacharya, B., Ahmed, A. M., Hazra, A., Pal, N. K., & Bahar, B., 2015. Serum Interleukin 6 (IL-6) as A Potential Biomarker of Disease Progression in Active Pulmonary Tuberculosis Following Anti-Tuberculosis Drug Therapy. *Molecular Immunology*. 63(2): 601–602.
- Choy, E., & Rose-John, S., 2017. Interleukin-6 as a Multifunctional Regulator:

- Inflammation, Immune Response, and Fibrosis. *Journal of Scleroderma and Related Disorders*. 2(2): 51–55.
- Clark, M., & Cameron, D. W., 2006. The Benefits and Risks of Bacille Calmette-Guérin Vaccination Among Infants at High Risk for Both Tuberculosis and Severe Combined Immunodeficiency: Assessment by Markov model. *BMC Pediatrics*. 6(5): 1–12.
- Correia, J. W., Freitas, M. V., Queiroz, J. A., Pereiraperrin, M., & Cavadas, B., 2009. Interleukin-6 Blood Levels in Sensitive and Multiresistant Tuberculosis. *Infection*. 37(2): 138–141.
- Dai, X., Xiong, Y., Li, N., & Jian, C., 2019. Vaccine Types. In V. Kumar (Ed.), *Vaccines*. Intech Open.
- Dinas Kesehatan Makassar. 2020. *Profil Kesehatan Provinsi Sulawesi Selatan*.
- Dunn, J. J., Starke, J. R., & Revell, P. A., 2016. Laboratory Diagnosis of Mycobacterium tuberculosis Infection and Disease. *Journal of Clinical Microbiology*. 54(6): 1434–1441.
- Fernanda, M. A. H., Sa'adi, A., & Sudjarwo., 2019. Verifikasi Linieritas Kurva Baku Testosteron Menggunakan Metode Elisa (Enzyme-Linked Immunosorbent Assay). *Journal of Research and Technology*. 5(1): 59–66.
- Fidhatami, I. I., Agus, R., & Massi, M. N., 2020. Comparison the Concentration of Purification Antigen MTSP11 and MPT63 as Serodiagnostic Active Tuberculosis. *International Journal of Environment, Agriculture and Biotechnology*. 5(1): 63–67.
- Gan, S. D., & Patel, K. R., 2013. Enzyme Immunoassay and Enzyme-Linked Immunosorbent Assay. *Journal of Investigative Dermatology*. 133(9): 1–3.
- Ghazaei, C., 2018. Mycobacterium tuberculosis and Lipids: Insights Into Molecular Mechanisms from Persistence to Virulence. *Journal of Research in Medical Sciences*. 24(1): 1–10.
- Iowa Department of Public Health. 2011. *Iowa Tuberculosis Control Program Annual Report 2011*.
- Jabir, R. A., Rukmana, A., Saleh, I., & Kurniawati, T., 2018. The Existence of Mycobacterium tuberculosis in Microenvironment of Bone. In W. Ribón (Ed.). *Mycobacterium Research and Development*: Intech Open.
- Jiang, W., Cossey, S., Rosenberg, J. N., Oyler, G. A., Olson, B. J. S. C., & Weeks, D. P., 2014. A Rapid Live-Cell ELISA for Characterizing Antibodies Against Cell Surface Antigens of *Chlamydomonas reinhardtii* and Its Use in Isolating Algae from Natural Environments with Related Cell Wall Components. *BMC Plant Biology*. 14(1): 1–12.

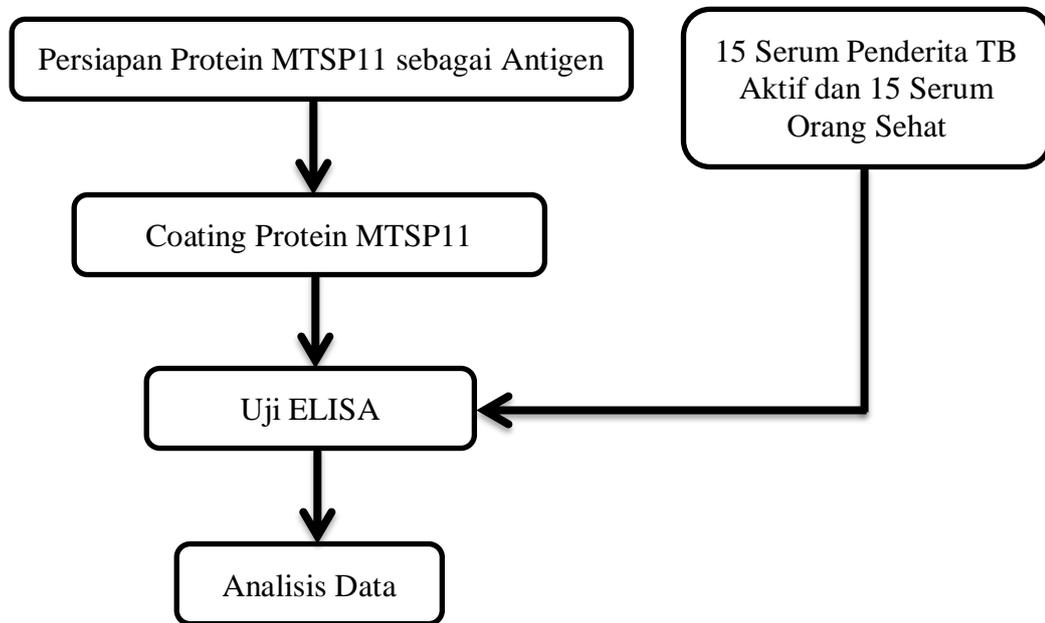
- Joshi, L., Ponnana, M., Sivangala, R., Chelluri, L. K., Nallari, P., Penmetsa, S., Valluri, V., & Gaddam, S., 2015. Evaluation of TNF- α , IL-10 and IL-6 Cytokine Production and Their Correlation with Genotype Variants amongst Tuberculosis Patients and Their household Contacts. *PLoS ONE*. 10(9): 1-15.
- Kaufmann, S. H. E., Evans, T. G., & Hanekom, W. A., 2015. Tuberculosis Vaccines: Time for A Global Strategy. *Science Translational Medicine*. 7(276): 1–3.
- Kaufmann, S. H. E., Weiner, J., & von Reyn, C. F., 2016. Novel Approaches to Tuberculosis Vaccine Development. *International Journal of Infectious Diseases*. 56: 263–267.
- Kementerian Kesehatan RI. 2018. *Infodatin Tuberkulosis 2018*.
- Khaliq, A., Ravindran, R., Hussainy, S. F., Krishnan, V. V., Ambreen, A., Yusuf, N. W., Irum, S., Rashid, A., Jamil, M., Zaffar, F., Chaudhry, M. N., Gupta, P. K., Akhtar, M. W., & Khan, I. H., 2017. Field Evaluation of A Blood Based Test for Active Tuberculosis in Endemic Settings. *PLoS ONE*. 12(4).
- Khare, N., Khare, P., & Singh, D., 2018. A Review: History, Structure, Diagnosis and Treatment of Tuberculosis Disease. *Mycobacterial Diseases*. 8(2): 8–11.
- Labrou, N. E. 2014. *Protein Downstream Processing Design, Development and Application of High and Low-Resolution Methods*. Humana Press.
- Lamichhane, S. R. A. M., & Milic, N., 2018. *Mycobacterium tuberculosis*: Gene and Genome Analysis. *Asian Journal of Microbiology and Biotechnology*. 3(1): 24–33.
- Lim, J. H., Kim, H. J., Lee, K. S., Jo, E. K., Song, C. H., Jung, S. B., Kim, S. Y., Lee, J. S., Paik, T. H., & Park, J. K., 2004. Identification of The New T-cell-Stimulating Antigens from Mycobacterium tuberculosis Culture Filtrate. *FEMS Microbiology Letters*. 232(1): 51–59.
- Lopes, F. H. A., De Assis, L. C., Da Justa Pires Neto, R., Botelho, K. P., Sá, K. M., Frota, C. C., Correia, J. W., & Freitas, M. V. C., 2013. Serum Levels of Interleukin-6 in Contacts of Active Pulmonary Tuberculosis. *Jornal Brasileiro de Patologia e Medicina Laboratorial*. 49(6): 410–414.
- Lubis, F. H., & Annisa, R., 2019. Faktor- Faktor Yang Berhubungan Dengan Penyakit Tbc Pada Nelayan Di Kampung Nelayan Seberang Lingkungan Xii, Kelurahan Belawan I, Medan. *Jurnal Kesehatan Masyarakat & Gizi (Jkg)*. 2(1): 91–100.
- Luo, X., Wu, F., Ma, J., Xiao, H., & Cui, H., 2018. Immunological Recovery in Patients with Pulmonary Tuberculosis After Intensive Phase Treatment. *Journal of International Medical Research*. 46(9): 3539–3551.

- Mahdi, A. A., 2018. *ELISA Technical Guide*.
- Martinez, A. N., Mehra, S., & Kaushal, D., 2013. Role of Interleukin 6 in Innate Immunity to Mycobacterium tuberculosis Infection. *Journal of Infectious Diseases*. 207(8): 1253–1261.
- McShane, H., and Davenne, T., 2016. Why Don't We Have An Effective Tuberculosis Vaccine Yet? *Expert Review of Vaccines*. 15(8): 1009–1013.
- Migliori, G. B., Centis, R., Zumla, A., Memish, Z. A., & Raviglione, M. C., 2017. Tuberculosis, Public Health Aspects. In *International Encyclopedia of Public Health* (Second Edition, Vol. 7). Elsevier.
- Munawaroh, A. L., Hidayati, D. Y. N., & Utami, Y. W. 2015. Studi Komparasi Media Kultur Coco Blood Malachite Green (CBM) dengan Lowenstein Jensen (LJ) untuk Diagnosis Cepat, Spesifik, dan Sensitif pada Sputum Pasien Suspek Tuberkulosis. *Majalah Kesehatan FKUB*. 2(2): 79–91.
- Myhr, A. I. 2016. DNA Vaccines: Regulatory Considerations and Safety Aspects. *Current Issues in Molecular Biology*. 22: 79–88.
- Nieuwenhuizen, N. E., & Kaufmann, S. H. E., 2018. Next-Generation Vaccines Based on Bacille Calmette-Guérin. *Frontiers in Immunology*. 9(121):1-16.
- Noviendri, D., & Sugiyono. 2006. Teknik Pemekatan, Purifikasi dan Karakterisasi Protein Rekombinan. *Squalen*. 1(1): 21–27.
- Pai, M., Behr, M. A., Dowdy, D., Dheda, K., Divangahi, M., Boehme, C. C., Ginsberg, A., Swaminathan, S., Spigelman, M., Getahun, H., Menzies, D., & Raviglione, M., 2016. Tuberculosis. *Nature Reviews Disease Primers*. 2.
- Radji, M. 2009. Vaksin DNA: Vaksin Generasi Keempat. *Pharmaceutical Sciences and Research*. 6(1): 28–37.
- Romero-Adrian, T. B., Leal-Montiel, J., Fernández, G., & Valecillo, A., 2015. Role of Cytokines and Other Factors Involved in the Mycobacterium tuberculosis Infection. *World Journal of Immunology*. 5(1): 16.
- Safithri, F., 2011. Diagnosis TB Dewasa Dan Anak Berdasarkan ISTC (International Standard for TB Care). *Saintika Medika*. 7(15): 57–67.
- Sakamoto, K., 2012. The Pathology of Mycobacterium tuberculosis Infection. *Veterinary Pathology*. 49(3): 423–439.
- Sarhan, M. A., 2010. Tuberculosis Vaccine Trials. *The Lancet*. 31(1): 9–13.
- Seyedhosseini, F. S., Mohammadi, S., Ebrahimabad, M. Z., Khodabakhshi, B., Abbasi, A., & Yazdani, Y., 2019. Interleukin-6, Interleukin-17 and Transforming Growth Factor-Beta are Overexpressed in Newly Diagnosed

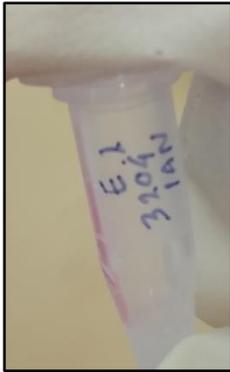
- Tuberculosis Patients; Potent Biomarkers of Mycobacterial Infection. *Archives of Clinical Infectious Diseases*. 14(4): 1–6.
- Shiloh, M. U., 2016. Mechanisms of Mycobacterial Transmission: How does Mycobacterium Tuberculosis Enter and Escape from The Human Host. *Future Microbiology*. 11(12): 1503–1506.
- Singh, P. P., & Goyal, A., 2013. Interleukin-6: A Potent Biomarker of Mycobacterial Infection. *SpringerPlus*. 2(1): 2–9.
- Skwarczynski, M., & Toth, I. 2017. *Micro and Nanotechnology in Vaccine Development* (S. Webber (ed.)). Matthew Deans.
- Soyi, D. S. 2016. Purifikasi Protein Rekombinan dari Klon Gen gag-CA sebagai Kandidat Vaksin Virus Penyakit Jembrana. *Jurnal Ilmiah Sains Dan Teknologi*. 9(2): 74–95.
- Stutz, M. D., Clark, M. P., Doerflinger, M., & Pellegrini, M., 2018. Mycobacterium tuberculosis: Rewiring Host Cell Signaling to Promote Infection. *Journal of Leukocyte Biology*. 103(2): 259–268.
- Sulastriani, S., 2020. Uji Immunoreaktivitas Protein Rekombinan MTSP11 Sebagai Biomarker Tuberkulosis Aktif.
- Tafreshi, S., 2016. BCG Vaccine and Pulmonary Tuberculosis. *Vaccine Research*. 3(8): 36–40.
- Thermo Scientific. 2010. ELISA technical guide and protocols. In *Thermo Scientific* (Vol. 0747, Issue 815).
- World Health Organization. 2013. *Systematic Screening for Active Tuberculosis*.
- World Health Organization. 2013. Vaccine Safety Basics. In *World Health Organization*. WHO Press.
- World Health Organization. 2018. *Weekly Epidemiological Record*.
- World Health Organization. 2020. *Global Tuberculosis Report*.
- Zhu, B., Dockrell, H. M., Ottenhoff, T. H. M., Evans, T. G., & Zhang, Y., 2018. Tuberculosis Vaccines: Opportunities and Challenges. *Respirology*. 23(4): 359–368.
- Zuniga, J., Torres-García, D., Santos-Mendoza, T., Rodriguez-Reyna, T. S., Granados, J., & Yunis, E. J., 2012. Cellular and humoral Mechanisms Involved in the Control of Tuberculosis. *Clinical and Developmental Immunology*. 2012.

LAMPIRAN

Lampiran 1. Skema Kerja



Lampiran 2. Bahan



Protein MTSP 11



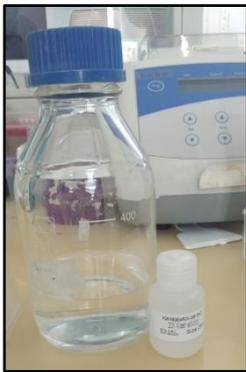
PBS pH 7.2



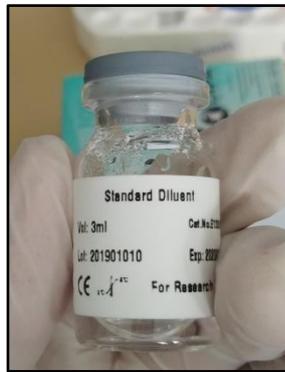
Coating Buffer



Blocking Solution



Wash Buffer



Standard Diluent



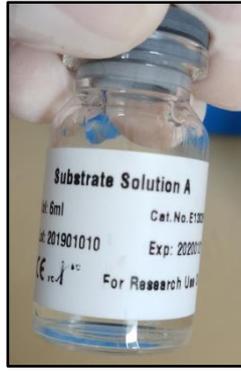
Standard Solution



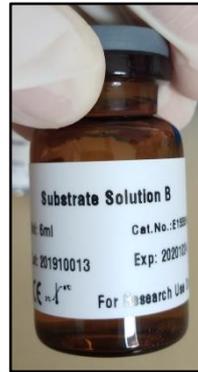
Streptavidin-HRP



Biotin-Conjugate
Antibody



Substrate Solution
A



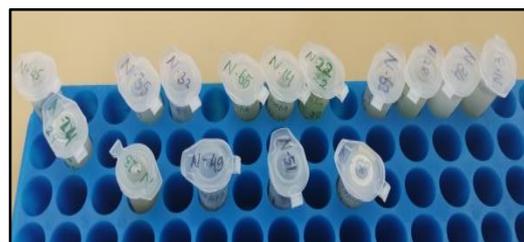
Substrate Solution
B



Stop Solution



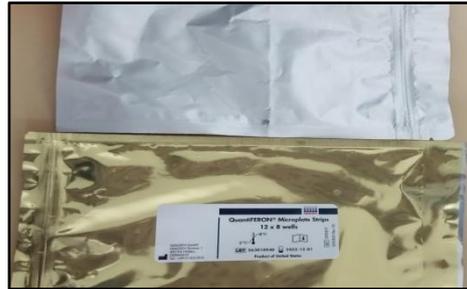
Serum Orang Sehat (Kontrol)



Serum TB Aktif



Tip (Axygen)

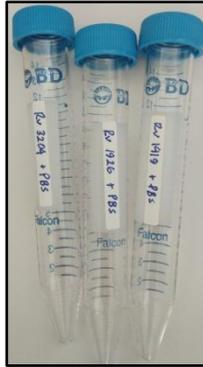


Microplate Strips

Lampiran 3. Alat



Mikropipet
(Bio Rad)



Tabung Falcon



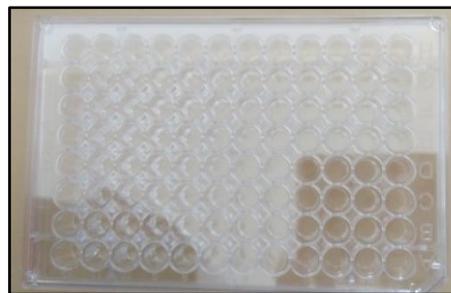
Tabung Eppendorf



Wadah



Inkubator Shaker



ELISA Plate



ELISA Reader



Tabung Vakum



Rak Tabung Eppendorf

Lampiran 4. Prosedur Kerja



Coating Protein MTSP11

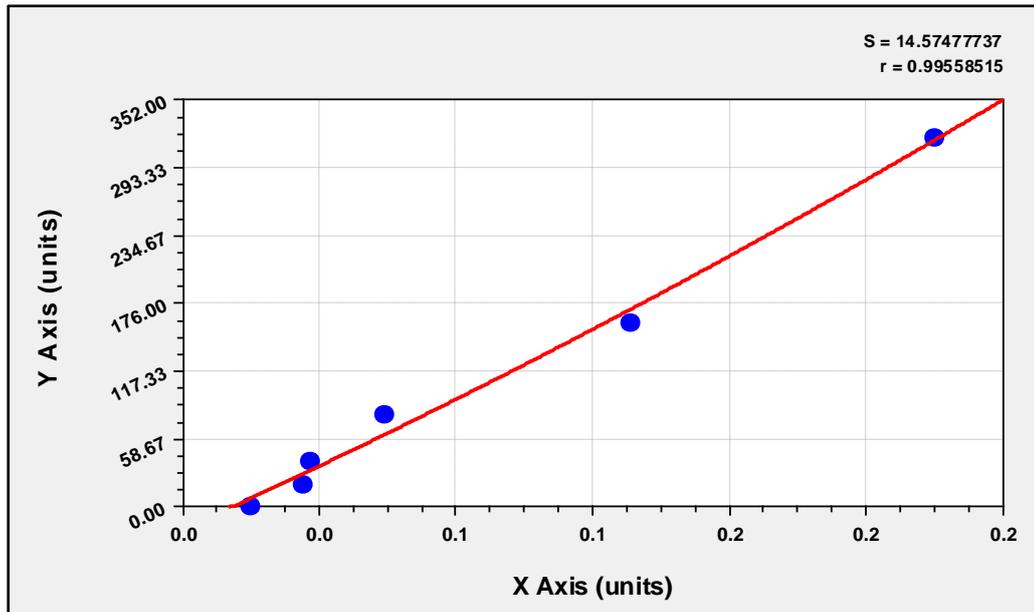


Proses ELISA



Pembacaan Hasil ELISA

Lampiran 5. Kurva Larutan Standar ELISA



Lampiran 6. Hasil Uji Statistik

One-Sample Test						
	Test Value = 0					
	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
Nilai Absorbansi (450 nm)	6.779	29	.000	.0980867	.068492	.127682
Konsentrasi IL-6 (pg/mL)	4.420	29	.000	121.18633	65.1069	177.2658

Lampiran 7. Titik Persentase Distribusi t (df = 1 - 40)

Pr df	0.25 0.50	0.10 0.20	0.05 0.10	0.025 0.050	0.01 0.02	0.005 0.010	0.001 0.002
1	1.00000	3.07768	6.31375	12.70620	31.82052	63.65674	318.30884
2	0.81650	1.88562	2.91999	4.30265	6.96456	9.92484	22.32712
3	0.76489	1.63774	2.35336	3.18245	4.54070	5.84091	10.21453
4	0.74070	1.53321	2.13185	2.77645	3.74695	4.60409	7.17318
5	0.72669	1.47588	2.01505	2.57058	3.36493	4.03214	5.89343
6	0.71756	1.43976	1.94318	2.44691	3.14267	3.70743	5.20763
7	0.71114	1.41492	1.89458	2.36462	2.99795	3.49948	4.78529
8	0.70639	1.39682	1.85955	2.30600	2.89646	3.35539	4.50079
9	0.70272	1.38303	1.83311	2.26216	2.82144	3.24984	4.29681
10	0.69981	1.37218	1.81246	2.22814	2.76377	3.16927	4.14370
11	0.69745	1.36343	1.79588	2.20099	2.71808	3.10581	4.02470
12	0.69548	1.35622	1.78229	2.17881	2.68100	3.05454	3.92963
13	0.69383	1.35017	1.77093	2.16037	2.65031	3.01228	3.85198
14	0.69242	1.34503	1.76131	2.14479	2.62449	2.97684	3.78739
15	0.69120	1.34061	1.75305	2.13145	2.60248	2.94671	3.73283
16	0.69013	1.33676	1.74588	2.11991	2.58349	2.92078	3.68615
17	0.68920	1.33338	1.73961	2.10982	2.56693	2.89823	3.64577
18	0.68836	1.33039	1.73406	2.10092	2.55238	2.87844	3.61048
19	0.68762	1.32773	1.72913	2.09302	2.53948	2.86093	3.57940
20	0.68695	1.32534	1.72472	2.08596	2.52798	2.84534	3.55181
21	0.68635	1.32319	1.72074	2.07961	2.51765	2.83136	3.52715
22	0.68581	1.32124	1.71714	2.07387	2.50832	2.81876	3.50499
23	0.68531	1.31946	1.71387	2.06866	2.49987	2.80734	3.48496
24	0.68485	1.31784	1.71088	2.06390	2.49216	2.79694	3.46678
25	0.68443	1.31635	1.70814	2.05954	2.48511	2.78744	3.45019
26	0.68404	1.31497	1.70562	2.05553	2.47863	2.77871	3.43500
27	0.68368	1.31370	1.70329	2.05183	2.47266	2.77068	3.42103
28	0.68335	1.31253	1.70113	2.04841	2.46714	2.76326	3.40816
29	0.68304	1.31143	1.69913	2.04523	2.46202	2.75639	3.39624
30	0.68276	1.31042	1.69726	2.04227	2.45726	2.75000	3.38518
31	0.68249	1.30946	1.69552	2.03951	2.45282	2.74404	3.37490
32	0.68223	1.30857	1.69389	2.03693	2.44868	2.73848	3.36531
33	0.68200	1.30774	1.69236	2.03452	2.44479	2.73328	3.35634
34	0.68177	1.30695	1.69092	2.03224	2.44115	2.72839	3.34793
35	0.68156	1.30621	1.68957	2.03011	2.43772	2.72381	3.34005
36	0.68137	1.30551	1.68830	2.02809	2.43449	2.71948	3.33262
37	0.68118	1.30485	1.68709	2.02619	2.43145	2.71541	3.32563
38	0.68100	1.30423	1.68595	2.02439	2.42857	2.71156	3.31903
39	0.68083	1.30364	1.68488	2.02269	2.42584	2.70791	3.31279
40	0.68067	1.30308	1.68385	2.02108	2.42326	2.70446	3.30688