

## DAFTAR PUSTAKA

- Adams, M. D., Celniker, S. E., Holt, R. A., Evans, C. A., Gocayne, J. D., Amanatides, P. G., *et al.* 2000. The genome sequence of *Drosophila melanogaster*. *Science*, 287(5461), 2185-2195. doi: 10.1126/science.287.5461.2185
- Arandjelovic, S. and Ravichandran, K. S. 2015. 'review Phagocytosis of apoptotic cells in homeostasis', 16(9), pp. 907–917. doi: 10.1038/ni.3253.
- Chen P, Tu X, FAKdemir, Chew SK, Rothenfluh A and JM Abrams. 2012. Effectors of alcohol-induced cell killing in *Drosophila*. *Cell Death and Differentiation* (2012) 19; doi: 10.1038/cdd.2012.47; Published online 27 April 2012: 1655-1663
- Chyb, S. and Gompel, N. 2013. *Atlas of D.melanogaster Morphology: Wild-type and Classical Mutants*.
- D'Arcy, M. S. (2019) 'c: a review of the major forms of apoptosis, necrosis and autophagy', *Cell Biology International*. John Wiley & Sons, Ltd, 43(6), pp. 582–592. doi: 10.1002/cbin.11137.
- Edwin. 2018. Pengaruh Reseptor Fagositosis Draper Terhadap Kematian *D.melanogaster* Melanogaster Yang Terpapar Alkohol. Skripsi tidak diterbitkan. Makassar. Fakultas Farmasi. Universitas Hasanuddin.
- Elliott, M. R. and Ravichandran, K. S. 2016. 'Review The Dynamics of Apoptotic Cell Clearance', *Developmental Cell*. Elsevier Inc., 38(2), pp. 147–160. doi: 10.1016/j.devcel.2016.06.029.
- Elmore, S. 2007. 'Apoptosis: A Review of Programmed Cell Death', 35(4), pp. 495–516.
- Engel Gregory L, Taber Kreager, Vinton Elizabeth and Crocker Amanda J. 2019. Studying Alcohol Use Disorder Using *Drosophila* Melanogaster in the Era of Big Data. *Behavioraland Brain Functions*. (Online). (<https://doi.org/10.1186/s12993-019-0159-x>, diakses 2019).
- Franc, N. C. *et al.* (1996) 'Croquemort, A Novel *Drosophila* Hemocyte/Macrophage Receptor that Recognizes Apoptotic Cells',

*Immunity*. Cell Press, 4(5), pp. 431–443. doi: 10.1016/S1074-7613(00)80410-0.

Freeman, M. R. *et al.* .2003. 'Unwrapping glial biology: Gcm target genes regulating glial development, diversification, and function', *Neuron*, 38(4), pp. 567–580. doi: 10.1016/S0896-6273(03)00289-7.

Fujita, Y. *et al.* 2012. 'Role of NPxY motif in Draper-mediated apoptotic cell clearance in *Drosophila*', 6(6), pp. 291–297. doi: 10.5582/dtd.2012.v6.6.291.

Gordon, S. and Plüddemann, A. 2018. 'Macrophage clearance of apoptotic cells: A critical assessment', *Frontiers in Immunology*, 9(JAN), pp. 1–9. doi: 10.3389/fimmu.2018.00127.

Guo, R. and Jun, R. 2010. 'Alcohol and aasetaldehyd in public health: From marvel to menace', *International Journal of Environmental Research and Public Health*, 7(4), pp. 1285–1301. doi: 10.3390/ijerph7041285.

Hammer, J. H. *et al.* 2018. *Global status report on alcohol and health 2018, Global status report on alcohol*. doi: 10.1037/cou0000248.

Hochreiter-Hufford, A. and Ravichandran, K. S. 2013. 'Clearing the dead: Apoptotic cell sensing, recognition, engulfment, and digestion', *Cold Spring Harbor Perspectives in Biology*, 5(1), pp. 1–20. doi: 10.1101/cshperspect.a008748.

Kang, H. *et al.* 2020. 'Impaired glycolysis promotes alcohol exposure-induced apoptosis in hei-oc1 cells via inhibition of EGFR signaling', *International Journal of Molecular Sciences*, 21(2), pp. 1–13. doi: 10.3390/ijms21020476.

Katzung, B. G. 2018. *Basic & Clinical Pharmacology, Fourteenth Edition, Basic and Clinical Pharmacology*.

Kementerian Kesehatan RI. 2020. *Farmakope Indonesia edisi VI*. VI, Departemen Kesehatan Republik Indonesia. VI. Jakarta. Available at: [https://perpustakaan.bsn.go.id/index.php?p=show\\_detail&id=14835](https://perpustakaan.bsn.go.id/index.php?p=show_detail&id=14835).

Latada, N.P., 2020. Eksplorasi Efek Etanol Terhadap Sistem Imun Jalur Sinyal Toll Dan Imd Pada Hewan Uji *Drosophila melanogaster*. Universitas Hasanuddin.

Linderman, J. A. *et al.* 2012. 'Infection-Related Declines in Chill Coma Recovery and Negative Geotaxis in *Drosophila melanogaster*', 7(9). doi: 10.1371/journal.pone.0041907.

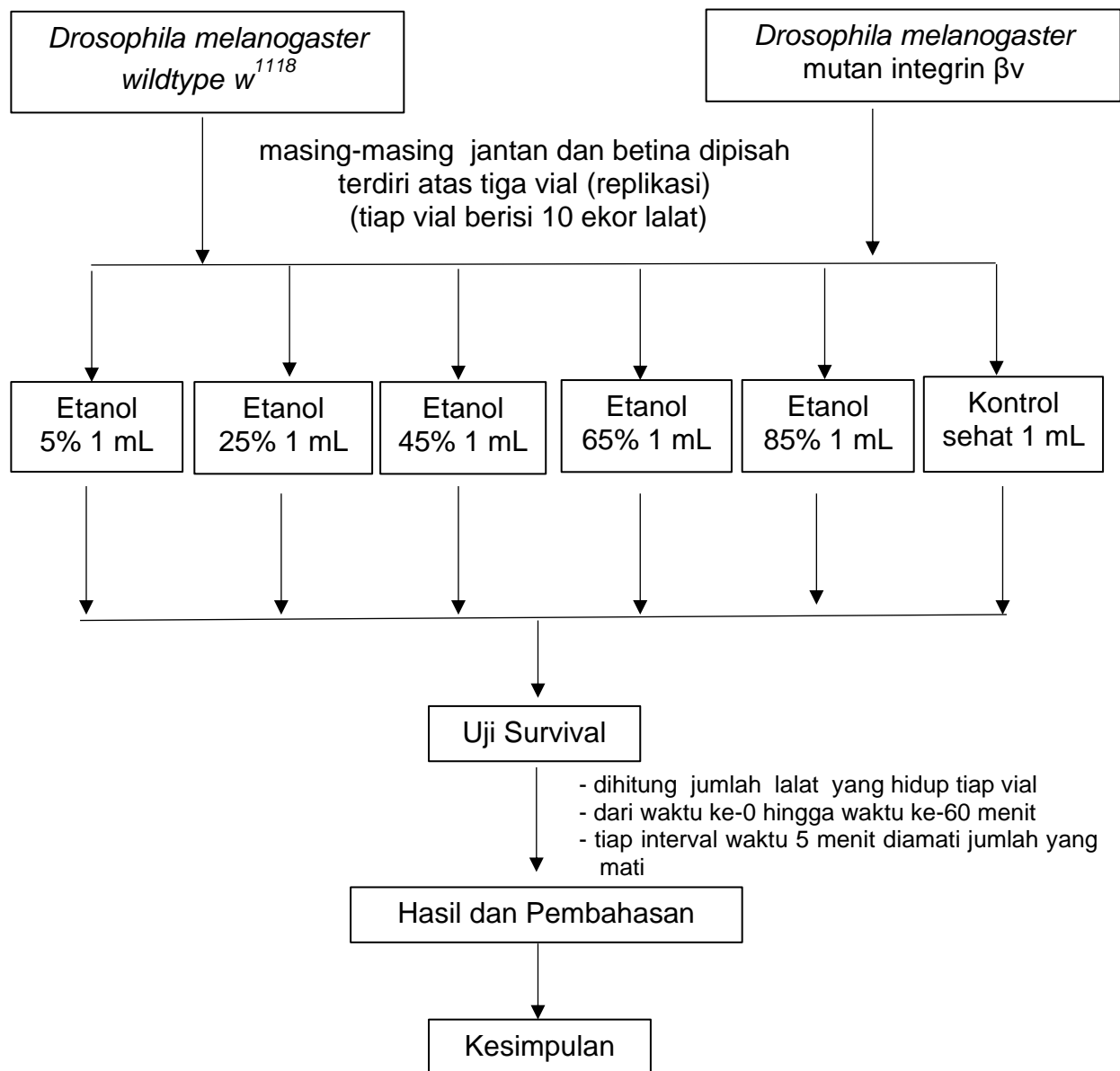
- Luo, B., V. Carman, C. and A. Springer Timothy (2007) 'Structural Basis of Integrin Regulation and Signaling', pp. 619–647.
- Manaka, J. *et al.* (2004) 'Draper-mediated and phosphatidylserine-independent phagocytosis of apoptotic cells by *Drosophila* hemocytes/macrophages', *Journal of Biological Chemistry*, 279(46), pp. 48466–48476. doi: 10.1074/jbc.M408597200.
- Markow. 2015. 'The secret lives of *Drosophila* flies', pp. 1–9. doi: 10.7554/eLife.06793.
- Melcarne, C. and Dkk 2019. 'Phagocytosis in *Drosophila*: From molecules and cellular machinery to physiology', *Insect Biochemistry and Molecular Biology*. Elsevier, 109(March), pp. 1–12. doi: 10.1016/j.ibmb.2019.04.002.
- Mohr, E. and Stepanie .2018 .*First in Fly, D.melanogaster Research and Biological Discovery*. first.
- Nagaosa, K., Okada, R., Nonaka, S., Takeuchi., K., Fujita, Y., Miyasaka , T., Manaka, J., Ando, I. and Nakanishi, Y. 2011. Integrin  $\beta V$  mediated phagocytosis of apoptotic cells in *Drosophila* embryos. *J Biol Chem*. . 286(29): p. 25770-25777.
- Nainu, F., Tanaka, Y., Shiratsuchi, A., & Nakanishi, Y. 2015. Protection of insects against viral infection by apoptosisdependent phagocytosis. *J Immunol*. 195(12), 5696-5706. doi: 10.4049/jimmunol.1500613.
- Nainu, F. (2018) 'Penggunaan *Drosophila melanogaster* Sebagai Organisme Model Dalam Review: Penggunaan *Drosophila melanogaster* Sebagai Organisme Model Dalam Penemuan Obat ( Review : Application of *Drosophila melanogaster* as Model Organism in Drug Discovery )', (March). doi: 10.22487/j24428744.2018.v4.i1.9969.
- Nainu, F., Shiratsuchi, A., & and Nakanishi . 2017 'induction of Apoptosis and Subsequent Phagocytosis of virus-infected Cells As an Antiviral Mechanism'.
- Neckameyer, S., W. and And Bhatt Parag 2016. 'Protocols to Study Behavior in *Drosophila*', *National Library of Medicine .National Center For Biotechnology Information*, pp. 303–320. doi: 10.1007/978-1-4939-6371-3\_19.

- Neckameyer, W. S. and Bhatt, P. (2016) 'Protocols to study behavior in drosophila', *Methods in Molecular Biology*, 1478, pp. 303–320. doi: 10.1007/978-1-4939-6371-3\_19.
- Nichols, C. D., Becnel, J. and Pandey, U. B. (2012) 'Methods to Assay *Drosophila* Behavior', *Journal of Visualized Experiments*, (61), pp. 3–7. doi: 10.3791/3795.
- Nonaka, S. *et al.* (2013) 'Integrin  $\alpha$ S3/ $\beta$ -mediated Phagocytosis of Apoptotic Cells and Bacteria in *Drosophila*', *Journal of Biological Chemistry*, 288(15), pp. 10374–10380. doi: 10.1074/jbc.M113.451427.
- Pandey, U. B. and Nichols, C.D. 2011. Human disease models in *Drosophila melanogaster* and the role of the fly in therapeutic drug discovery. *Pharmacological reviews*. American Society for Pharmacology and Experimental Therapeutics, 63(2), pp. 411-36. doi: 10.1124/pr.110.003293
- Perveen, F. K. .2018. 'Introduction to *Drosophila*', *D.melanogaster melanogaster Model for Recent Advances in Genetics and Therapeutics*, pp. 3–14. doi: 10.5772/67731.
- Prastika, J. C. 2020. *Fagositosis Integrin Bv Dan Draper Terhadap Lokomotor Dan Mortalitas D.melanogaster Melanogaster Yang Terpapar Etanol*
- Reiter, L. T. *et al.* 2001. 'A systematic analysis of human disease-associated gene sequences in *Drosophila melanogaster*', *Genome Research*, 11(6), pp. 1114–1125. doi: 10.1101/gr.169101.
- Rodriguez, A. *et al.* 2015. 'Alcohol and apoptosis: Friends or foes?', *Biomolecules*, 5(4), pp. 3193–3203. doi: 10.3390/biom5043193.
- Sandhu, S. *et al.* 2015. 'An inexpensive, scalable behavioral assay for measuring ethanol sedation sensitivity and rapid tolerance in *Drosophila*', *Journal of Visualized Experiments*, 2015(98), pp. 1–9. doi: 10.3791/52676.
- Sari, L. M. 2018. 'Apoptosis: Mekanisme Molekuler Kematian Sel', *Cakradonya Dental Journal*, 10(2), pp. 65–70. doi: 10.24815/cdj.v10i2.11701.
- Steller, H. (2008) 'Regulation of apoptosis in *Drosophila*', *Cell Death and Differentiation*, 15(7), pp. 1132–1138. doi: 10.1038/cdd.2008.50.

- Strangward, P. *et al.* 2020. 'The climbing assay : Learning data analysis through live experiments with fruit flies .. 1 . Background information and explanations of the lesson'.
- Stuart, L. M. and Ezekowitz, R. A. 2008. 'Phagocytosis and comparative innate immunity : learning on the fly', 8(february). doi: 10.1038/nri2240.
- Tabakoff, B. and Hoffman, P. 2000. Animal models in alcohol research', *Alcohol Research and Health*, 24(2), pp. 77–84.
- Takada, Y., Ye, X. and Simon, S. (2007) 'Protein family review The integrins'. doi: 10.1186/gb-2007-8-5-215.
- Thornber, C. W. and Shaw, A. (1977) *Antihypertensive Agents, Annual Reports in Medicinal Chemistry*. doi: 10.1016/S0065-7743(08)61545-6.
- Tritama, T. K. 2015. 'Konsumsi Alkohol dan Pengaruhnya terhadap Kesehatan', 4(November), pp. 7–10.
- Tung, T. T. *et al.* 2013. 'Phosphatidylserine recognition and induction of apoptotic cell clearance by *Drosophila* engulfment receptor Draper', *Journal of Biochemistry*, 153(5), pp. 483–491. doi: 10.1093/jb/mvt014.
- Ulrike Heberlein And, D. J. G. 2002. '*Drosophila melanogaster*, A Genetic Model System For Alcohol Research', 54, pp. 199–228.
- Wong, R. S. Y. 3. 2011. 'Apoptosis in cancer: From pathogenesis to treatment', *Journal of Experimental and Clinical Cancer Research*. BioMed Central Ltd, 30(1), p. 87. doi: 10.1186/1756-9966-30-87.

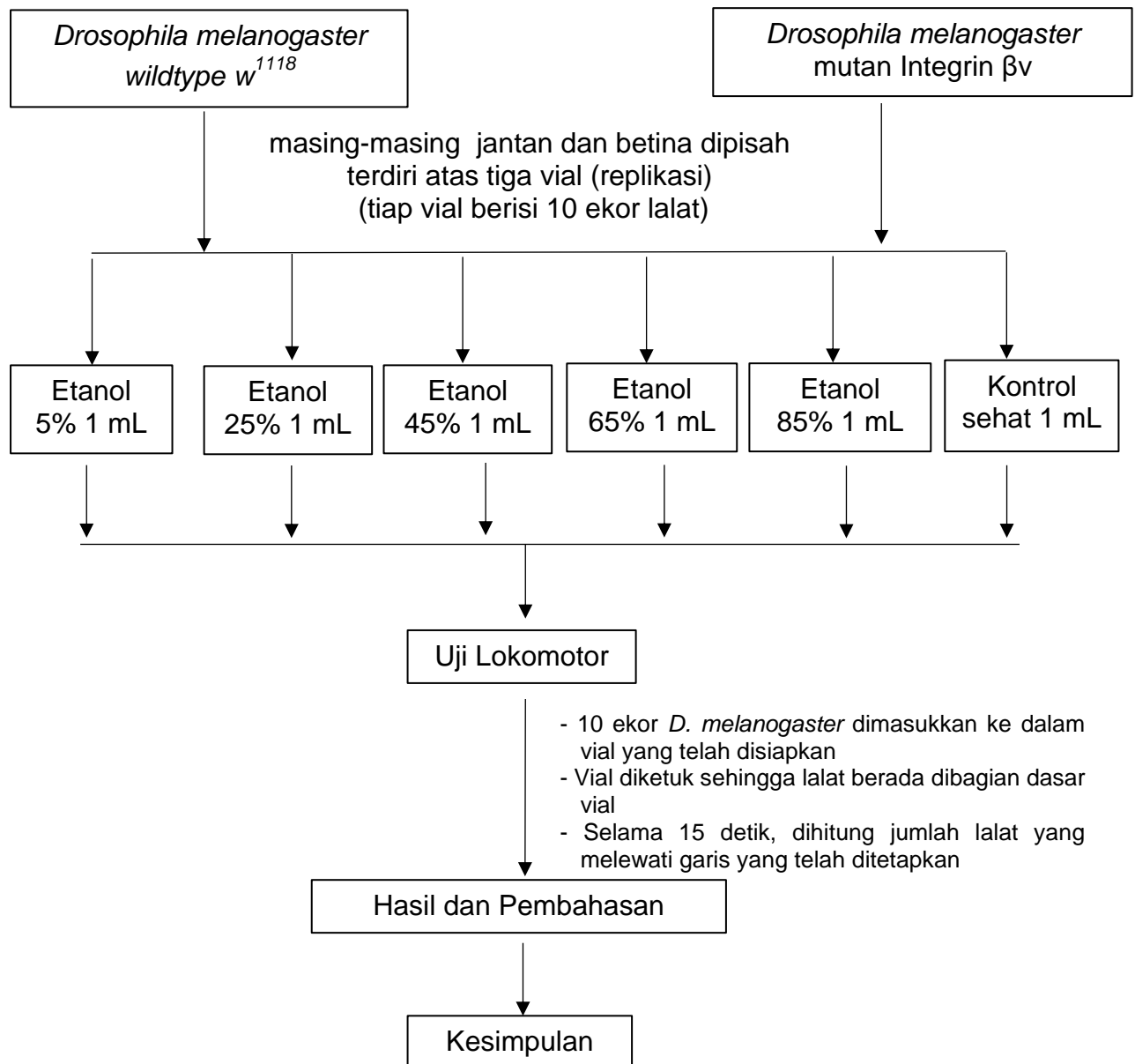
## LAMPIRAN I

### SKEMA KERJA SURVIVAL ASSAY



## LAMPIRAN II

## SKEMA KERJA UJI LOKOMOTOR



### LAMPIRAN III

#### KOMPOSISI FLYFOOD (PAKAN) *Drosophila melanogaster*

##### Bahan Flyfood (per 500 ml):

- Tepung jagung 37,5 g (Tepung Jagung Instan, PT.Lancar Jaya Indonesia)
- Yeast (Ragi) 12,5 g (Nature's Wonder Food Brewers Yeast, Jerman)
- Agar-agar 4,5 g (Swallow Grass Cap Rumput Walet, PT. Agrindo Bogatama,Indonesia)
- Gula pasir 22,5 g (Gulaku)
- Asam Propionat 1,900  $\mu$ l (633 3x)
- Metil Paraben 2,151  $\mu$ l (717 3x)
- Air Steril 500 ml



## LAMPIRAN IV

### DOKUMENTASI PENELITIAN



**Gambar 15.** Mikroskop Zoom Stereo untuk memisahkan *D.melanogaster* jantan dan betina



**Gambar 16.** Tabung gas CO<sub>2</sub> untuk pembiusan *D.melanogaster*



**Gambar 17.** Magnetic stirrer untuk pembuatan pakan *D.melanogaster*



**Gambar 18.** Bahan pakan *D.melanogaster* yang telah ditimbang



**Gambar 19.** Proses pembuatan pakan *D.melanogaster*



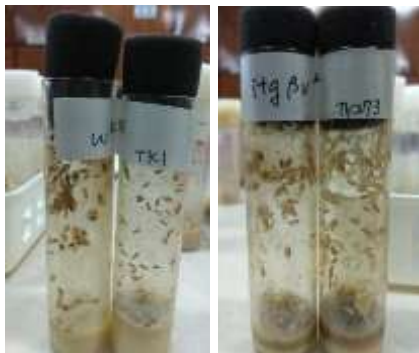
**Gambar 20.** Pakan *D.melanogaster* yang siap digunakan



**Gambar 21.** Etanol PA 96% yang akan diencerkan dalam beberapa konsentrasi



**Gambar 22.** Etanol yang telah diencerkan menjadi beberapa konsentrasi, 85%,65%,45%,25%, dan 5% untuk digunakan dalam pengujian mortalitas dan lokomotor



**Gambar 23.** *D. melanogaster*  $w^{1118}$  (Wildtype) dan mutan integrin  $\beta v$  yang dikultur



**Gambar 24.** *D. melanogaster*  $w^{1118}$  (Wildtype) dan mutan integrin  $\beta v$  umur 4-7 hari



**Gambar 25.** Pemisahan *D. melanogaster* jantan dan betina dibawah Mikroskop Zoom Stereo



**Gambar 26.** *D. melanogaster*  $w^{1118}$  (Wildtype) dan mutan integrin  $\beta v$  jantan dan betina dibawah pembesaran Mikroskop Zoom Stereo



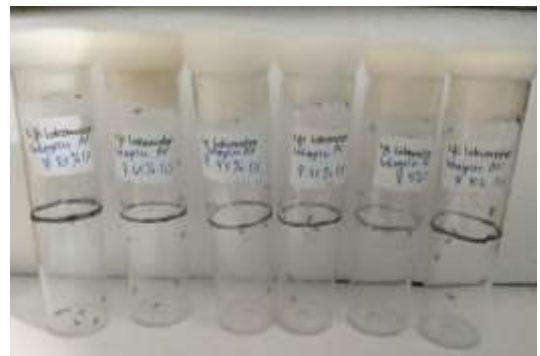
**Gambar 27.** Pengamatan uji Survival *D.melanogaster*  $w^{118}$  (Wildtype)



**Gambar 28.** Pengamatan uji Survival *D. melanogaster* mutan integrin  $\beta$



**Gambar 29.** Pengamatan uji Lokomotor *D.melanogaster*  $w^{118}$  (Wildtype)



**Gambar 30.** Pengamatan uji Lokomotor *D.melanogaster* mutan integrin  $\beta$

## LAMPIRAN V

### DATA STATISTIK

**Tabel 2. Hasil data survival etanol konsentrasi 85%, 65%, 45%, 25%, 5% dan kontrol sehat *Drosophila melanogaster*  $w^{1118}$  (wildtype) jantan**

Survival Curve comparison		A	B	C	D
1	Comparison of Survival Curves				
2					
3	<b>Log-rank (Mantel-Cox) test (recommended)</b>				
4	Chi square	88.96			
5	df	5			
6	P value	<0.0001			
7	P value summary	****			
8	Are the survival curves sig different?	Yes			
9					
10	<b>Logrank test for trend (recommended)</b>				
11	Chi square	75.11			
12	df	1			
13	P value	<0.0001			
14	P value summary	****			
15	Sig. trend?	Yes			
16					
17	<b>Gehan-Breslow-Wilcoxon test</b>				
18	Chi square	74.99			
19	df	5			
20	P value	<0.0001			
21	P value summary	****			
22	Are the survival curves sig different?	Yes			
23					

**Tabel 3. Hasil data etanol konsentrasi 85%, 35%, 45%, 25%, 5% dan kontrol sehat *Drosophila melanogaster*  $w^{1118}$  (wildtype) betina**

Survival Curve comparison		A	B	C	D
1	Comparison of Survival Curves				
2					
3	<b>Log-rank (Mantel-Cox) test (recommended)</b>				
4	Chi square	76.22			
5	df	5			
6	P value	<0.0001			
7	P value summary	****			
8	Are the survival curves sig different?	Yes			
9					
10	<b>Logrank test for trend (recommended)</b>				
11	Chi square	67.40			
12	df	1			
13	P value	<0.0001			
14	P value summary	****			
15	Sig. trend?	Yes			
16					
17	<b>Gehan-Breslow-Wilcoxon test</b>				
18	Chi square	66.37			
19	df	5			
20	P value	<0.0001			
21	P value summary	****			
22	Are the survival curves sig different?	Yes			
23					

Tabel 4. Hasil data survival etanol konsentrasi 85%, 65%, 45%, 25%, 5% dan kontrol sehat *Drosophila melanogaster* mutan integrin  $\beta v$  jantan

Survival Curve comparison					D
1	Comparison of Survival Curves				
2					
3	Log-rank (Mantel-Cox) test (recommended)				
4	Chi square	91.80			
5	df	5			
6	P value	<0.0001			
7	P value summary	****			
8	Are the survival curves sig different?	Yes			
9					
10	Logrank test for trend (recommended)				
11	Chi square	74.42			
12	df	1			
13	P value	<0.0001			
14	P value summary	****			
15	Sig. trend?	Yes			
16					
17	Gehan-Breslow-Wilcoxon test				
18	Chi square	78.98			
19	df	5			
20	P value	<0.0001			
21	P value summary	****			
22	Are the survival curves sig different?	Yes			
23					

Tabel 5. Hasil data survival etanol konsentrasi 85%, 65%, 45%, 25%, 5% dan kontrol sehat *Drosophila melanogaster* mutan integrin  $\beta v$  betina

Survival Curve comparison		A	B	C	D
1	Comparison of Survival Curves				
2					
3	Log-rank (Mantel-Cox) test (recomm				
4	Chi square	102.7			
5	df	5			
6	P value	<0.0001			
7	P value summary	****			
8	Are the survival curves sig different?	Yes			
9					
10	Logrank test for trend (recommende				
11	Chi square	77.29			
12	df	1			
13	P value	<0.0001			
14	P value summary	****			
15	Sig. trend?	Yes			
16					
17	Gehan-Breslow-Wilcoxon test				
18	Chi square	91.53			
19	df	5			
20	P value	<0.0001			
21	P value summary	****			
22	Are the survival curves sig different?	Yes			
23					

Tabel 6. Hasil data survival etanol konsentrasi 85%, 65%, 45%, 25%, 5% dan kontrol sehat *Drosophila melanogaster w<sup>1118</sup>* (*wildtype*) dan mutan integrin  $\beta$ v jantan

Survival Curve comparison		A	B	C	D
1	<b>Comparison of Survival Curves</b>				
2					
3	<b>Log-rank (Mantel-Cox) test (recommended)</b>				
4	Chi square	189.9			
5	df	11			
6	P value	<0.0001			
7	P value summary	****			
8	Are the survival curves sig different?	Yes			
9					
10	<b>Logrank test for trend (recommended)</b>				
11	Chi square	24.83			
12	df	1			
13	P value	<0.0001			
14	P value summary	****			
15	Sig. trend?	Yes			
16					
17	<b>Gehan-Breslow-Wilcoxon test</b>				
18	Chi square	163.0			
19	df	11			
20	P value	<0.0001			
21	P value summary	****			
22	Are the survival curves sig different?	Yes			
23					

Tabel 7. Hasil data survival etanol konsentrasi 85%, 65%, 45%, 25%, 5% dan kontrol sehat *Drosophila w<sup>1118</sup>* (*wildtype*) dan mutan integrin  $\beta$ v betina

Survival Curve comparison		A	B	C	D
1	<b>Comparison of Survival Curves</b>				
2					
3	<b>Log-rank (Mantel-Cox) test (recommended)</b>				
4	Chi square	180.0			
5	df	11			
6	P value	<0.0001			
7	P value summary	****			
8	Are the survival curves sig different?	Yes			
9					
10	<b>Logrank test for trend (recommended)</b>				
11	Chi square	27.62			
12	df	1			
13	P value	<0.0001			
14	P value summary	****			
15	Sig. trend?	Yes			
16					
17	<b>Gehan-Breslow-Wilcoxon test</b>				
18	Chi square	156.1			
19	df	11			
20	P value	<0.0001			
21	P value summary	****			
22	Are the survival curves sig different?	Yes			
23					