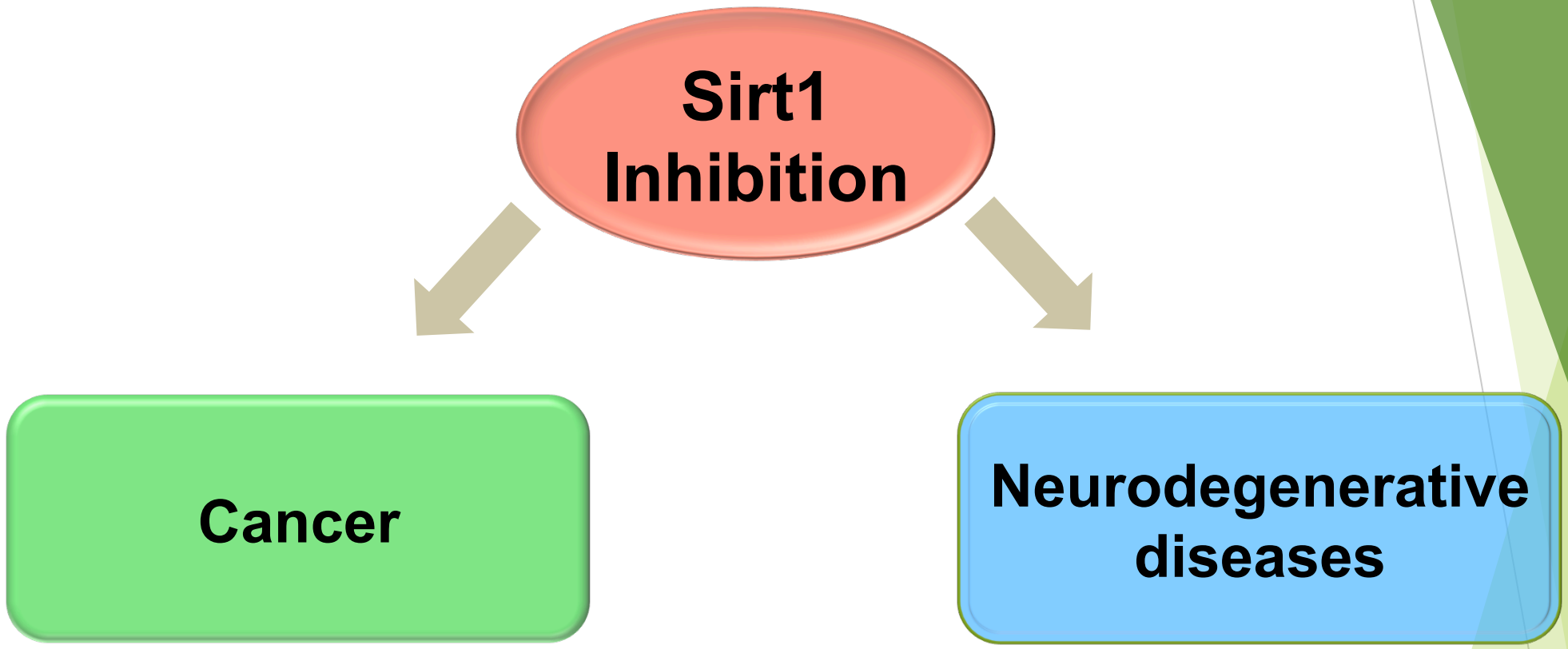
UNIVERSITAS INDONESIA
Veritas, Probitas, Iustitia | Est. 1849
The 29th Pacific Rim Application and Grid Middleware Assembly | PRAGMA 29
Faculty of Computer Science Universitas Indonesia | October 7th - 9th, 2015 www.pragma-grid.net

VIRTUAL SCREENING AND MOLECULER DOCKING OF INDONESIAN HERBAL DATABASE BASED PHARMACOPORE APPROACHED FOR IDENTIFICATION SIRT1 INHIBITOR AS POTENTIAL LIGAND ACTIVE

Andika, Azminah, Linda Erlina, and Arry Yanuar*

Faculty of Pharmacy, University of Indonesia

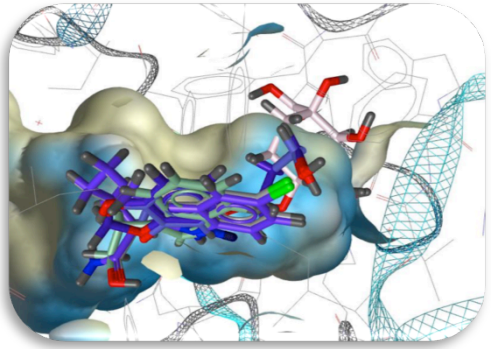


Biological function Sirt1 Inhibition

Work Scheme

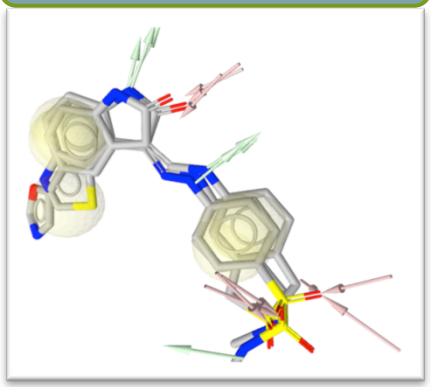
Sirt1 protein (PDB ID : 4I5I) from www.pdb.org

Compound (.mol2) from www.herbaldb.farmasi.ui.ac.id



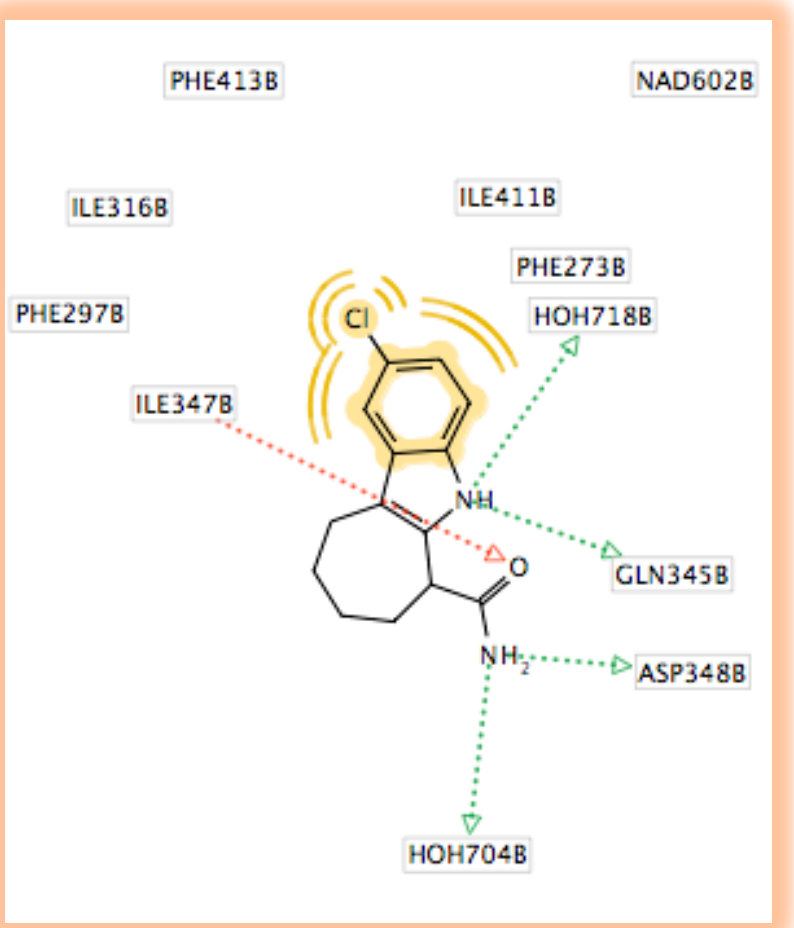
Virtual screening LigandScout 4.0

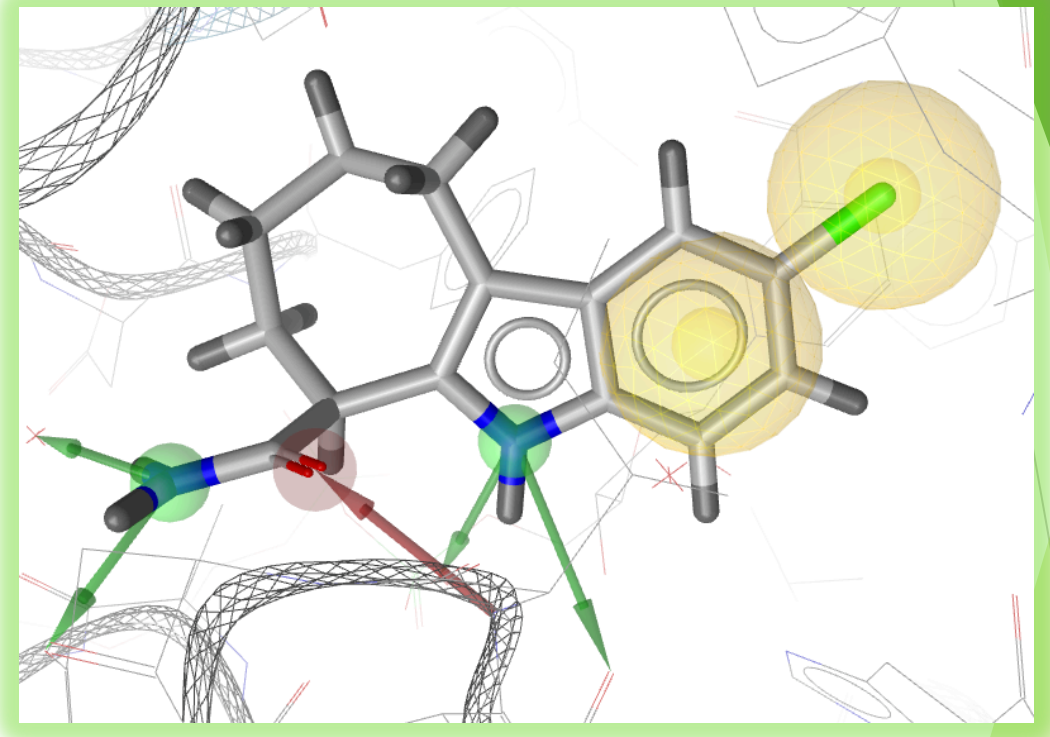
Hit compounds



Re-docking using AutoDock Vina

Pharmacophore feature of Core Molecule 4I5B (2D & 3D)

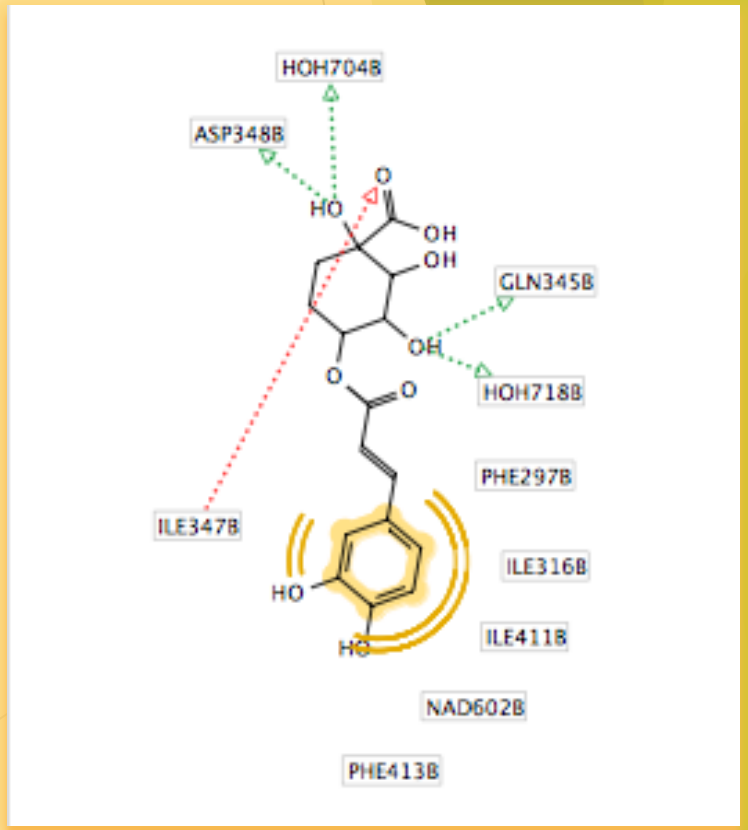




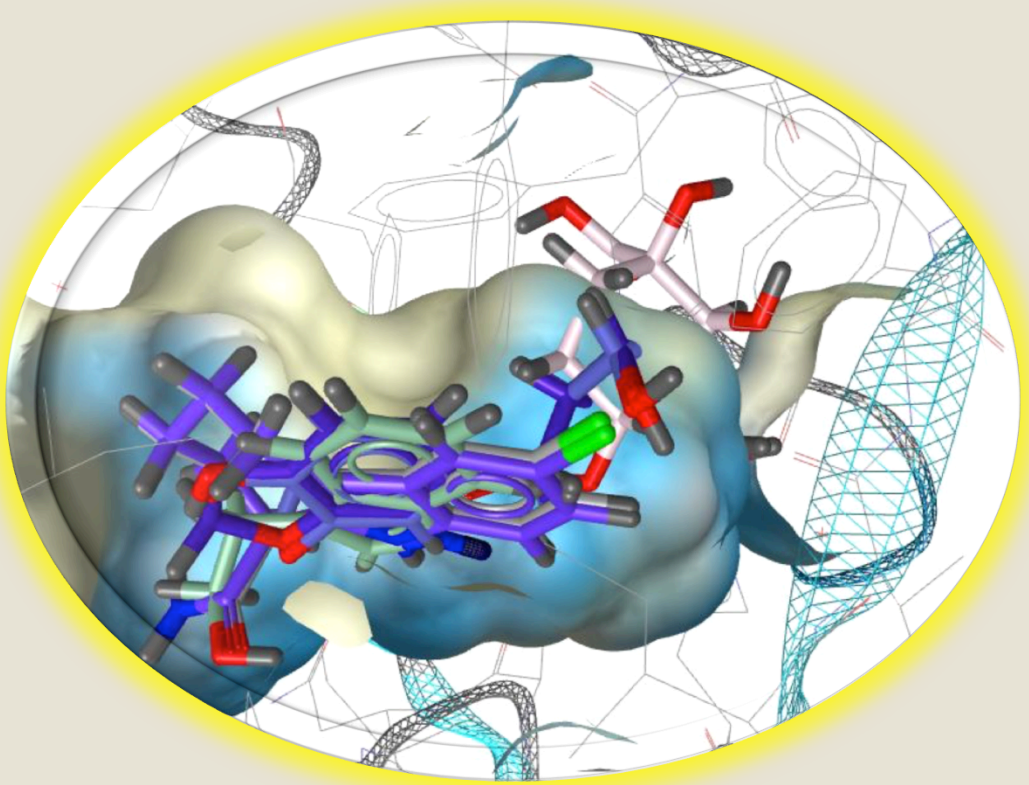
Hit Compounds from virtual screening Herbaldb

Name	Pharmacophore-Fit Score	Score	Best Match
Chlorogenic acid.mol	67.23	67.2311	(4I5I) [B] 4I5601
(-)-Dihydrocubebin.mol	66.07	66.0661	(4I5I) [B] 4I5601
(-)-Secoisolariciresinol.mol	66.06	66.0647	(4I5I) [B] 4I5601
Indole-3-ethanol.mol	63.48	63.4836	(4I5I) [B] 4I5601

Pharmacophore features 2D chlorogenic acid



The docking result of hit compounds



Name	Affinity (kcal/mol)
(4I5I) [B] 4I5601 [1]	-11
Chlorogenic acid.mol [1]	-10.9
Chlorogenic acid.mol [2]	-10.8
(4I5I) [B] 4I5601 [2]	-10.2
Chlorogenic acid.mol [3]	-10.2
Chlorogenic acid.mol [4]	-10
Chlorogenic acid.mol [5]	-10
(-)-Dihydrocubebin.mol [1]	-10
(-)-Dihydrocubebin.mol [2]	-10
Chlorogenic acid.mol [6]	-9.9
(-)-Dihydrocubebin.mol [3]	-9.7
Chlorogenic acid.mol [7]	-9.6
Chlorogenic acid.mol [8]	-9.6
Chlorogenic acid.mol [9]	-9.5
(-)-Dihydrocubebin.mol [4]	-9.4
(-)-Dihydrocubebin.mol [5]	-9.3
(4I5I) [B] 4I5601 [3]	-9.2
(-)-Secoisolariciresinol.mol [1]	-9.2
(-)-Secoisolariciresinol.mol [2]	-9.2
(-)-Dihydrocubebin.mol [6]	-9
(-)-Secoisolariciresinol.mol [3]	-9
(-)-Secoisolariciresinol.mol [4]	-9
(-)-Secoisolariciresinol.mol [5]	-8.9
(-)-Secoisolariciresinol.mol [6]	-8.9
(-)-Secoisolariciresinol.mol [7]	-8.9
(4I5I) [B] 4I5601 [4]	-8.8
(-)-Secoisolariciresinol.mol [8]	-8.8
(-)-Secoisolariciresinol.mol [9]	-8.8
(4I5I) [B] 4I5601 [5]	-8.7
(-)-Dihydrocubebin.mol [7]	-8.6
(-)-Dihydrocubebin.mol [8]	-8.6
(-)-Dihydrocubebin.mol [9]	-8.6
(4I5I) [B] 4I5601 [6]	-8.3
(4I5I) [B] 4I5601 [7]	-8.1
Indole-3-ethanol.mol [1]	-7.1
Indole-3-ethanol.mol [2]	-7.1

CONCLUSION

- There were 4 hit compounds in Indonesian Herbal database from virtual screening with PDB ID : 4I5I based pharmacophore approached
- The best docking result : Chlorogenic acid, (-)-Dihydrocubebin, (-)-Secoisolariciresinol, Indole-3-ethanol.
- The 4th hit compounds in Indonesian Herbal database have potential ligand active as inhibitor sirt1 and need to do further research.

References

- 1. Ruijter, A. J. M. D. E., Gennip, A. H. V. A. N., Caron, H. N., Kemp, S., & Kuilenburg, A. B. P. V. A. N. (2003). Histone deacetylases (HDACs): characterization of the classical HDAC family, *749*, 737–749.
- 2. Sauve, A. A., Wolberger, C., Schramm, V. L., & Boeke, J. D. (n.d.). The Biochemistry of Sirtuins. http://doi.org/10.1146/annurev.biochem.74.082803.133500
- 3. Liu, T., Liu, P. Y., & Marshall, G. M. (2009). The Critical Role of the Class III Histone Deacetylase SIRT1 in Cancer, (5), 1702–1706. http://doi.org/10.1158/0008-5472.CAN-08-3365
- 4. Alcaín, F. J., & Villalba, J. M. (2009). Sirtuin inhibitors, 283–294.
- 5. Bendix, F., Wolber, G., & Seidel, T. (2010). 3D Pharmacophore Elucidation and Virtual Screening Strategies for 3D pharmacophore- based virtual screening. http://doi.org/10.1016/j.ddtec.2010.11.004
- 6. Mukesh, B., & Rakesh, K. (2011). ISSN 2229-3566 Review Article MOLECULAR DOCKING: A REVIEW Bachwani Mukesh *, Kumar Rakesh, *2*(6), 1746–1751.
- 7. Yanuar A, Mun A, Bertha A, Lagho A, Syahdi RR, Rahmat M, et al. Medicinal Plants Database and Three Dimensional Structure of the Chemical Compounds from Medicinal Plants in Indonesia. 2011;**8**(5):180–3

THANK YOU
TERIMA KASIH