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# Human Breast Cancer Cell Line MCF-7

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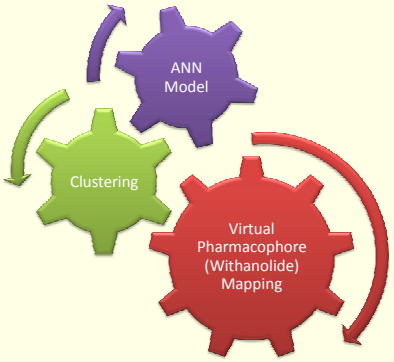
## INTRODUCTION

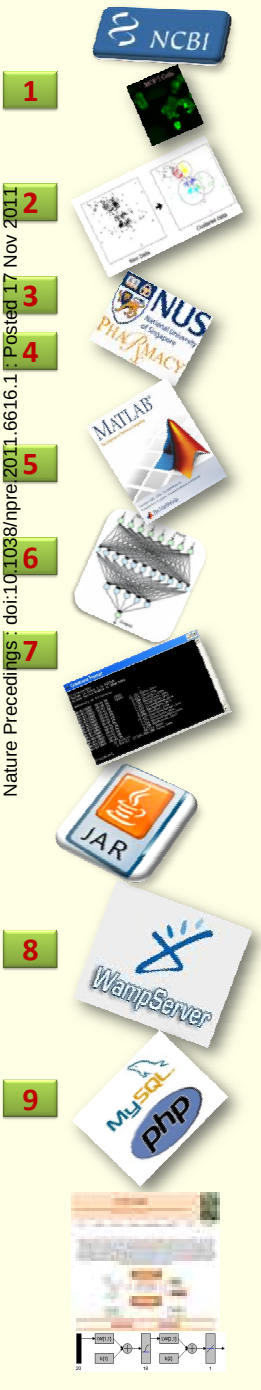
Withanolides are a group of natural C-28 steroids built on an ergostane skeleton and classified into two major groups according to their structural skeleton: (a) compounds with a beta-oriented side chain and (b) compounds with a alpha-oriented side chain. Withanolide E represents one of the members of the later group. Classification of active compounds on the basis of pharmacophore against specific cancer cell line poses a serious concern at the primary stage of virtual screening. To overcome this problem we have developed an artificial neural network based virtual screening model for discriminating active and non-active Withanolide-E like derivatives or analogs against human breast cancer cell line MCF-7. In the present work, a 2D chemical descriptors ensemble pharmacophore has been modelled on the basis of withanolide E structural featured molecules. The ANN structure activity based classification model could be useful for identification of active withanolides analogs as anticancer leads against MCF-7. Model can be used for predicting possible growth inhibitory concentration (logGI50) against breast cancer cell line MCF-7. The virtual screening tool "CanWithaANN" can be accessed at local network of CIMAP.




## THEME

Establishing relationship between '**Virtual Pharmacophore Consensus**' and '**bioactivity**' at cell line level

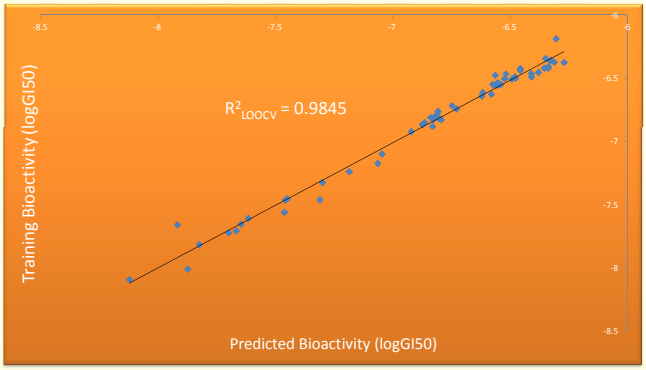





## RESULTS

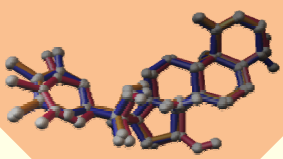
[http://192.168.17.28/canwithaann/indexx.html]

1. Web-application implementing model
2. ANN model, capturing the 'virtual Pharmacophore' for Withanolide-E against human breast cancer cell line MCF-7.
3. Clustered molecules (Analogs) other than Withanolide similar structures which participate actively against MCF-7.
4. Revealed unexplored Withanolide's active derivatives against MCF-7.



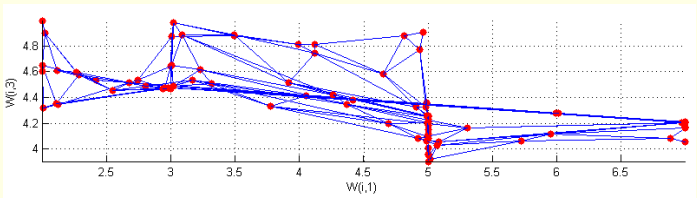

## METHODOLOGY

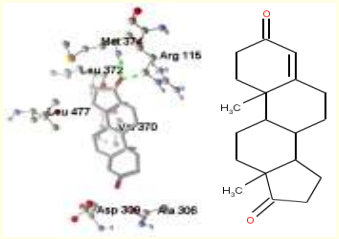
1. Data (Molecules active against MCF-7 cell line)
2. Withanolide-E centered clustering or mapping (SOM / K-means)
3. 2D-Descriptor calculation for molecules (PaDEL)
4. Descriptor selection (Correlation matrix / PCA)
5. ANN based SAR model for clustered molecules
6. Decision making for activeness of new coming Withanolide structures
7. Evaluation of model developed
8. Server-side (WAMP) implementation of model developed
9. Web-application of model developed(php + mySQL), including user account management [http://192.168.17.28/canwithaann/indexx.html]



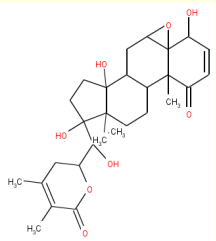
| S.No. | NCBI CID | logGI50_M | Target cell line |
|---|---|---|---|
| 1. | 276293 | -9.119 | MCF-7 |
| 2. | 401678 | -8.75 | MCF-7 |
| 3. | 24202596 | -8.112 | MCF-7 |
| 4. | 388300 | -8.02 | MCF-7 |
| 5. | 122736 | -8 | MCF-7 |
| 6. | 407582 | -7.886 | MCF-7 |
| 7. | 282304 | -7.785 | MCF-7 |
| 8. | 314799 | -7.823 | MCF-7 |
| 9. | 4605 | -7.788 | MCF-7 |
| 10. | 390666 | -7.725 | MCF-7 |
| 11. | 286106 | -7.624 | MCF-7 |
| 12. | 222156 | -7.602 | MCF-7 |
| 13. | 373676 | -7.475 | MCF-7 |
| 14. | 222154 | -7.523 | MCF-7 |
| 15. | 417553 | -7.426 | MCF-7 |
| 16. | 417451 | -7.382 | MCF-7 |
| 17. | 222160 | -7.426 | MCF-7 |
| 18. | 3061 | -7.384 | MCF-7 |
| 19. | 281990 | -7.301 | MCF-7 |
| 20. | 272581 | -7.258 | MCF-7 |

| S.No. | NCBI CID | logGI50_M | Target cell line |
|---|---|---|---|
| 21. | 3879 | -7.292 | MCF-7 |
| 22. | 222159 | -7.263 | MCF-7 |
| 23. | 317839 | -7.112 | MCF-7 |
| 24. | 401955 | -6.953 | MCF-7 |
| 25. | 289842 | -6.796 | MCF-7 |
| 26. | 385532 | -6.726 | MCF-7 |
| 27. | 73621 | -6.73 | MCF-7 |
| 28. | 433361 | -6.632 | MCF-7 |
| 29. | 388098 | -6.566 | MCF-7 |
| 30. | 407583 | -6.284 | MCF-7 |
| 31. | 267360 | -6.337 | MCF-7 |
| 32. | 222155 | -6.334 | MCF-7 |
| 33. | 401302 | -6.231 | MCF-7 |
| 34. | 392623 | -6.183 | MCF-7 |
| 35. | 385534 | -6.161 | MCF-7 |
| 36. | 398800 | -6.062 | MCF-7 |
| 37. | 397889 | -6.111 | MCF-7 |
| 38. | 382983 | -6.125 | MCF-7 |
| 39. | 378635 | -6.139 | MCF-7 |
| 40. | 318696 | -6.027 | MCF-7 |




Mapped Aromatase bonded ligand (Androstenedione) PDBID: 3EQM



4beta-Hydroxywithanolide E (Mother compound)

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References:
1. D. W. Salt, N. Yildiz, D. J. Livingstone and C. J. Tinsley. "The Use of Artificial Neural Networks in QSAR". Pesticide Science, 36: 161–170 (1992). doi: 10.1002/ps.2780360212
2. R. W. Brueggemeier, J. A. Richards and T. A. Petrel. "Aromatase and cyclooxygenases: enzymes in breast cancer". Journal of Steroid Biochemistry & Molecular Biology 86, 501-507 (2003).
3. K. Jaiswal and P. K. Naik. "Distinguishing compounds with anticancer activity by ANN using inductive QSAR descriptors". Bioinformation 2(10): 441-451 (2008).