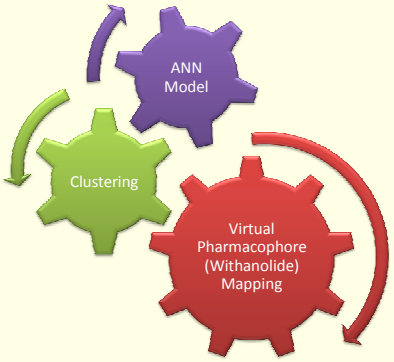
ANN Based Virtual Classification Model for Discriminating Active and Inactive Withanolide E Analogs against Human Breast Cancer Cell Line MCF-7

Om Prakash, Feroz Khan* and R.S. Sangwan
CSIR-Central Institute of Medicinal & Aromatic Plants, Lucknow-226015, India
* Correspondence: f.khan@cimap.res.in

SBC@CIMAP
80th Annual Meeting of the Society of Biological Chemists
Metabolic Pathway Modulations-Applications in Health and Agriculture
(India), 12-15 November, 2011, Lucknow

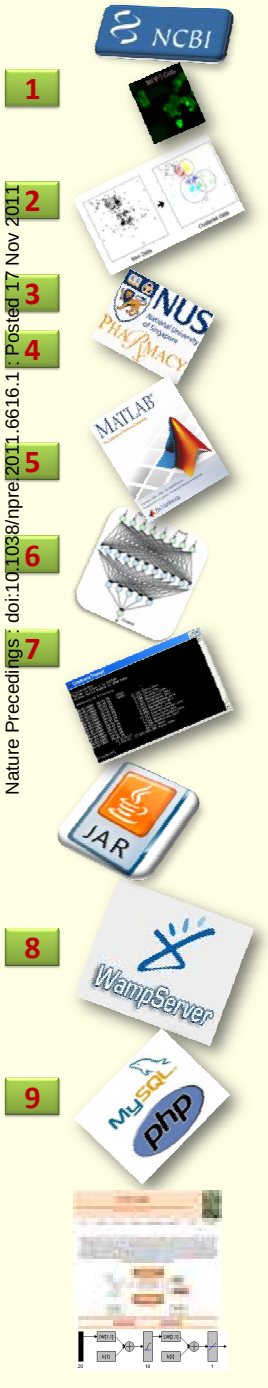
INTRODUCTION

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

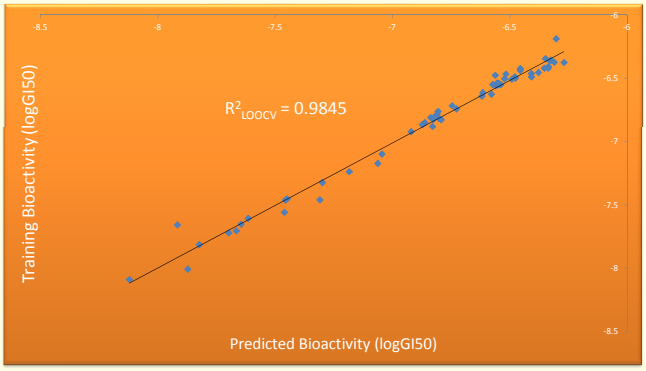
Establishing relationship between '**Virtual Pharmacophore Consensus**' and '**bioactivity**' at cell line level



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.

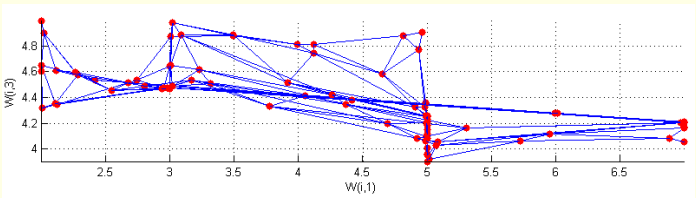


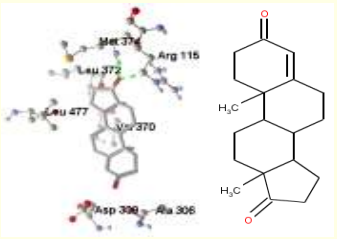
METHODOLOGY

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]

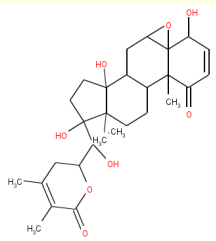
S.No.	NCBI CID	logGI50_M	Target cell line
1.	276293	-9.119	MCF-7
2.	401678	-8.75	MCF-7
3.	24202596	-8.112	MCF-7
4.	388300	-8.02	MCF-7
5.	122736	-8	MCF-7
6.	407582	-7.886	MCF-7
7.	282304	-7.785	MCF-7
8.	314799	-7.823	MCF-7
9.	4605	-7.788	MCF-7
10.	390666	-7.725	MCF-7
11.	286106	-7.624	MCF-7
12.	222156	-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)

Acknowledgement: Presenter (Om Prakash) acknowledges the Council of Scientific & Industrial Research (CSIR) - New Delhi for financial support as Senior Research Fellowship (Trans Disciplinary Area Code TDR/81) at CIMAP, Lucknow, India

References:
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