BIOINFORMATICS AND BIOMEDICAL RESEARCH JOURNAL OPEN ACCESS Freely available online
VOL. 1, NO. 1, 11 – 16, February 2018 Submitted November 2016; Revised January 2017; Accepted February 2017

Interaction Between Receptor TIR1 and Auxin Plant Hormone in *Arabidopsis thaliana*

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ABSTRACT

Auxins in gene transcription have influence that primarily mediated by TIRI receptor, which can change the conformation of receptors and there by promotes their interaction with auxin proteins. Recent research findings provide an increased understanding of the auxins that usually used in *Arabidopsis thaliana* was IAA and IBA in plant culture. The objectives of this to know the most potential auxin for inducting TIR1 receptor. Ligan (IAA, IBA, 2-4D, IPA, NAA, and indole acetamid) and receptor (T1R1) collected from PDB, structure visualization usung pymol, docking between them using PyRx, and analysis of the interaction using LigPlot+. Each ligand dock with receptor T1R1 in the same banding site. Docking result show IAA and IBA have highest binding affinity than other ligands. Binding analysis result show each ligand binding with different amino acid on receptor T1R1. 2,4D bind with Ser438; IAA with Leu439, Ser438, and Arg403; IBA with Leu439, Ser462, Arg436, and Arg403; indole acetamid with Leu439, Ser438, and Argg403; IPA Leu439, Arg403 and Ser438; also NAA with Leu439.

Keywords: *Auxins, docking, in silico, TIR1*

INTRODUCTION

Growth is the target of first hormone founded in plants one of the compound named auxin. Recently, auxin is perhaps the best understood of plant hormones and the one most synthesized in one place and acting at another part of plant. The auxins hormones was a major regulator of plant growth and development. The influence auxins in gen transcription primarily mediated by binding to TIR1 receptors, that can change the conformation of receptors and thereby promotes their interaction with auxin proteins. Auxins as root-promoting chemicals were most frequently applied to part of plant, its using to helps development of plant, its usually aplied to stem cuttings using a basal quick-dip in a concentrated solution [1].

Auxins are class of hormones that have charactreized originally modulating growth activities. Natural and synthetic auxins hormones have been used extensively in plant cell, tissue and organ culture to elicit spesific morphogenic responses that will happened in plant. There are many types of auxin hormones in plant such as IAA (*Indole Acetic Acid*), NAA (*Napthaleneacetic acid*), and etc. *Arabidopsis thaliana* was a plant easily obtainable information, encodes approximately 25.500 gene , its has a small genome = 125 Mb , has a short generation time : approximately 6 weeks, easy to grow, produce seeds in large quantities, easy to be transfered and easy to studied in moleculer biology [2].

Although there are several different biologically auxins in plant, recent research findings provide an increased understanding of the auxins that usually used in *Arabidopsis thaliana* was IAA and IBA in plant culture. The objectives of this research is to know the potensial of auxin (IAA, NAA, 2-4D, IBA, IPA, and Indole 3-acetamide) in *Arabidopsis thaliana* plant for preface study of plant culture using in silico approach.

MATERIALS AND METHODS

Collecting data of TIR1

TIR1 (protein transport inhibitor response 1) used as macromolecules protein from *Arabidopsis thaliana.* Protein TIR1 (PDB ID: 2PIP) can be download in PDB through the website http://www.rscb.org/pdb/. Macromolecules visualized on PyMol. The ligand that used is

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How to cite:
Sari AN, Nindyawati DL, Aqmarina A, Widhiya EW, Lestari ND (2018) Identification of Potential Auxin Interaction with TIR1 Receptor *Arabidopsis thaliana.* J. Bioinfo. Biomedic. Research. 1 (1): 11-16

IAA (Indole Acetic Acid) (PubChem ID: NAA (Naphalen Acetic Acid) (PubChem ID: 6862), 2-4D (2,4-dicholorophenoxyacetic acid) (Pubchem ID: 1486), IBA (Indole Butyric Acid) (Pubchem ID: 8617), IPA (indole Propionic Acid) (PubChem ID: 3744), and indole 3-acetamide (PubChem ID: 397) who kind of auxin and ligan 3D structure can be download in PubChem through the website http://pubchem.ncbi.nlm.nih.gov/. 3D structure of the ligand have been visualized on PyMOL.

Binding site analysis of TIR1

Determination binding location of auxin on TIR1 from *Arbidopsis thaliana* have been done with looking standard reference using the interaction of one type of auxin is IAA.

Molecular docking between TIR1 and auxin type

Docking was carried out PyRx software. PyRx is a virtual screnning software for use to khow interaction between ligand and receptor molecules. PyRx includes docking wizard with easy-to-user interface which makes it a valuable tool for Computer-Aided Drug Design. PyRx also includes chemical spreadsheet-like functionality and powerfull visualization engine that are essential for Rational Drug Design [3]. Macromoleculer of TIR1 dan six type of auxin includes in PyRx-Autodock-Vina software. Gridbox placed at the location of the receptor protein with coordinates X: 7,1620 Y:-111,72 Z: -25,4779 and dimension X=10,7683 Y=8,2892 Z=8,4404.

The ligand put on fit binding site place, then do running and obtained data information about binding affinity from the ligan interaction (type auxin) and macromolecules (TIR1) as the higher energy.

Molecular interaction

The analysis based on the interaction with the ligandf residue observed with LigPlot+. As well as the magnitude of the value binding energy as result bond molecular docking calculations (binding affinity).

The visualization binding site type of auxin and TIR1

The result docking in PyRx software then visualized on PyMol software. PyMol is software that can be display the interaction between auxin type and TIR1 in view of the 3D structure (http://www.pymol.org/). The visualization have been done to facilitate the interaction between the type of auxin and TIR1.

RESULTS AND DISCUSSION

TIR1 Receptor

TIR1 interaction is part a SCF (SKP1-cullin-F-box) protein ligase complex. May interact with auxin and auxin-responsive proteins. One wat that plants control auxin levels is to store the molecule in an inactive form until it is needed. Auxin is typically attached to an amino acid or a sugar, then it may be quickly clipped off when the auxin is needed. Is a auxin-xonjugate aminohydrolase that clips off alanine amino acids attached to auxin. The active site is found in the deep groove shown at the top [4]. It probably uses two metal ions in the reaction, 3D structure of TIR1 receptor based on X-ray can obtain in PDB format file. Structure visualized in PyMol (Figure 1).



Figure 1. 3D structure of TIR1 receptor

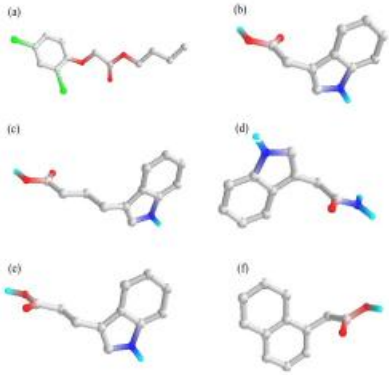


Figure 2. 2D structure of Auxin Type: (a) 2,4D (2,4-dichlorophenoxyacetic acid), (b) IAA (Indole Acetic Acid), (c) IBA (Indole Butyric Acid), (d) indole 3-acetamide, (e) IPA (Indole Propionic Acid), (f) NAA (Napthalen Acetic Acid)

Binding site determination of TIR1 and auxins

Binding site position is important to determine before docking process to get specific location between auxin and TIR1 receptor. So we used binding site TIR1 and natural auxin to get standart conformation of bin ing site. Binding site TIR1 receptor shown in figure 3.

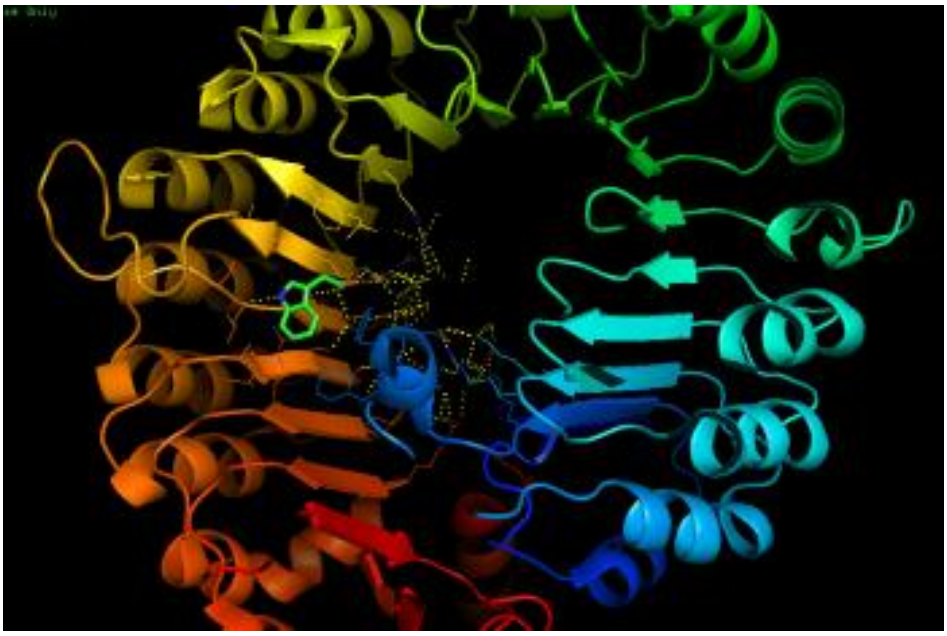


Figure 3. Binding site of receptor (The cartoon shape is TIR1 receptor and 2D structure is a natural auxin)

Molecular docking between TIR1 and auxin type

Docking between TIR1 receptor and ligands protein was done using PyRx program in current binding site of receptor. Result shown with table cotain of information about binding affinity, RSMD/ub, and RSMD/lb of each ligand (table 1). Interaction analysis between receptor protein and ligand receptor (figure 4) been done using LigPlot+ program. Each interaction shown binding between amino acid in receptor protein and ligand protein. The binding affinity classified the auxin.

Table 1. Binding affinity value of TIR1 and type of auxin (kcal/mo)

Type of Auxins	Binding Affinity Value (kcal/mol)
IAA	-6,6
IBA	-6,6
Indole 3-acetamide	-6,5
IPA	-6,3
NAA	-6,3
2-4D	-5,6

Molecular interaction

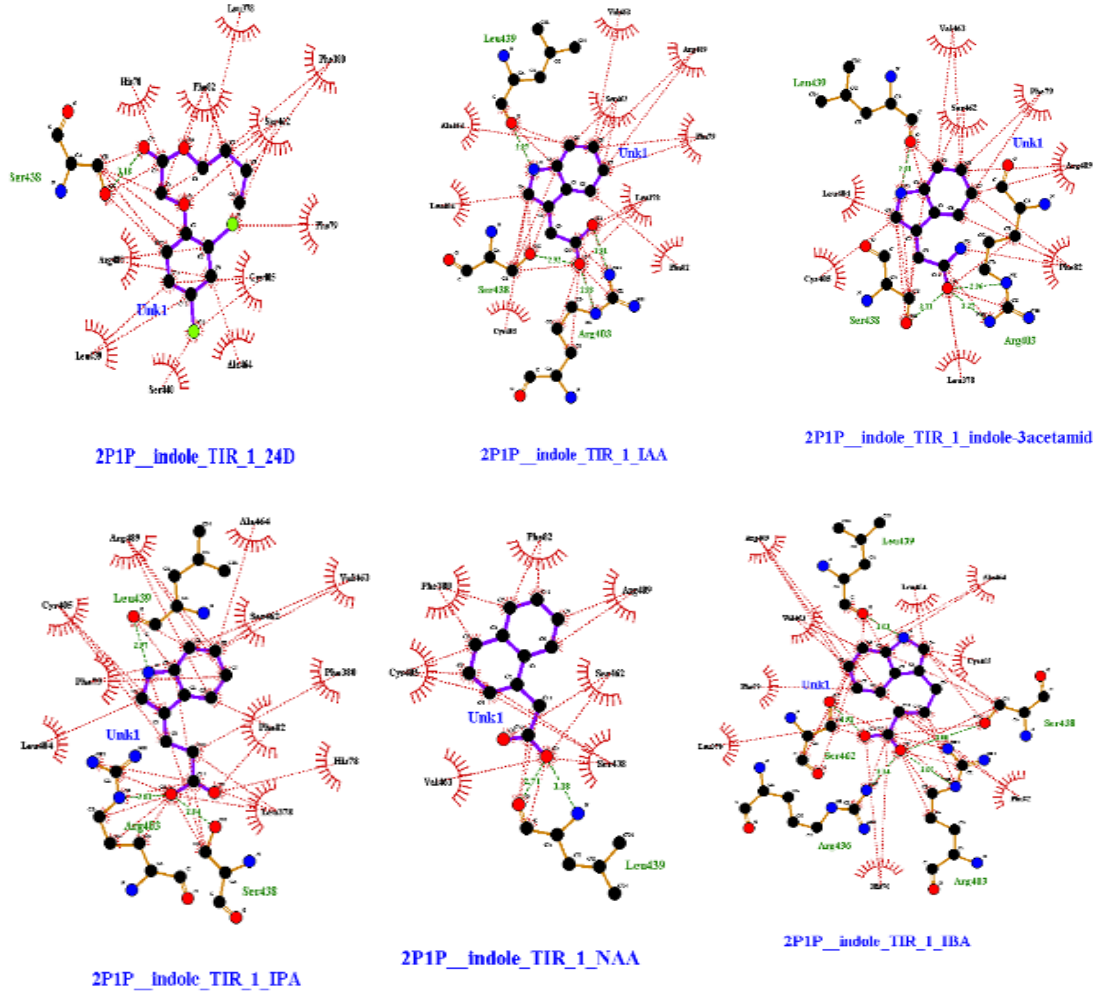


Figure 4: Interaction analysis result of binding between TIR1 and each auxins

Tabel 2. The specific binding site in types of auxin to TIR1 receptor

Natural Auxin	TIR1-IAA	TIR1-IBA	TIR1- IPA	TIR1-NAA	TIR1-2-4D	TIR1-Indole Acetamic acid
Leucine (439)	+	+	+	+	-	+
Serine (438)	+	+	+	-	+	+
Arginine (403)	+	+	+	-	-	+
Cystein (403)	+	+	+	+	+	+
Leucine (378)	+	+	+	-	-	+
Arginine (489)	+	+	+	+	+	+
Phenylalanine (82)	+	+	+	+	+	+
Serine (462)	+	-	+	+	+	+
Valine (463)	+	+	+	+	-	+
Alanine (464)	+	+	+	-	+	

The visualization binding site type of auxin and TIR1

The result docking in PyRx software then visualization visualized on PyMol software. Result shown in figure. 5

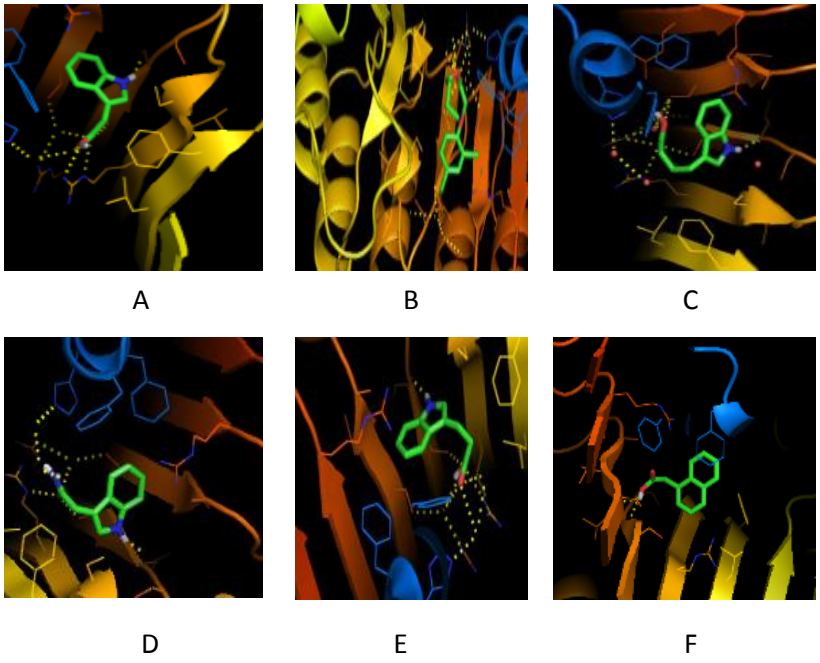


Figure 5. (a-f) Visualization docking position of type of auxin and receptor TIR1. (a) TIR1 and IAA interaction (standart) (b) TIR1 and 2-4D interaction (c) TIR1 and IBA interaction (d) TIR1 and IBA interaction (d) TIR1 and indole 3-acetamine interaction (e) TIR1 and IPA interaction (f) TIR1 and NAA interaction.

Based on docking of the type of auxin and TIR1 receptor used PyRx application, the result is auxin-type of IAA and IBA have the best binding affinity as compared to the other type of auxin (Table 1). This indicates that IAA and IBA have binding activity of the receptor TIR1 so can trigger the growth of a plant is better compared to the other type of auxin. According to Patricks- more negative values are generated, then the better the affinity of the ligand-protein complex, so expect any activity the better.

Based on visualization in Pymol, binding site auxin and TIR1 receptor, the auxin analogues are all shown as green stick models. Variations of binding position cause by differences conformation to local residue of auxin structure. The variation caused differences affinity binding site of each auxin because of different hydrophobic bonds by each auxin. The conformation determine of the bond between auxin and TIR1 receptors that will affect plant growth responds.

Binding site conformation of each auxin will determine the bonds of amino acids needed on the growth process of the plant. The higher activity of auxin as the regulator of plants growth determined by the bond with a compound exact amino acids and much-needed to promote plant growth.

Based on identification bonds in binding site of types of auxin, IAA is the best auxin to bonds with some amino acids in plant growth. IAA formed bonds with Cystein (405), Leucine (378), Phenylalanine (79), Phenylalanine (79), Leucine (404), Arginine (489), Phenylalanine (82), Serine (462), Valine (463), Alanine (464) that needs in plant growth. IAA also has the best binding affinity to binds in TIR1 receptor to promote auxin activity. In *Arabidhopsis thaliana,* IAA and IBA have molucule interaction with amino acids needed in plant growth. In laboratium practice of tissue culture [5] shows that IAA is natural auxin and usually spread to other parts of plants. IAA is potential auxin to promote *Arabidhopsis thaliana* because have nuclear localisation sequences in addition to four conserve regions for protein interaction and protein stabilization. The Aux/IAA proteins have nuclear - localisation sequences in addition to four conserved regions (domains I, 11, I11

and IV) which are important for protein/protein interactions and protein stabilization. The ARFs contain homologous region to domains I1I and IV of the Aux/IAA proteins, and also a DNA binding domain. Domains I11 and IV of the Aux/IAA and ARF proteins can mediate homo- or hetero- dimerization between these proteins, leading to activation or repression of specific genes. Arabidopsis has 25 genes encoding Aux/IAA proteins and 23 genes encoding ARFs, so the number of possible interactions is quite large. The AuxlZAA genes show tissue-specific expression, and several mutations in AuxlZAA and ARF genes have been found that give rise to auxin-related phenotypes [6, 7].

CONCLUSION

Based on in silico analysis IAA is the most suitable with receptor TIR1 in *Arabidopsis thaliana* with binding affinity -6,6 kcal/mol and formed with amino acid to promote plant growth such as Cycstein (405), Leucine (378), Phenylalanine (79), Leucine (404), Arginine (489), Phenylalanine (82), Serine (462), Valine (463), and Alanine (464). Molecular interaction of auxin and TIR1 receptors determine of carbon atoms, nitrogen atoms, oxygen atoms, non ligand bonds, ligand bonds, hydrophobic bonds with amino acid, hydrogen bonds, non-ligand residue, hydrophobic residue the specific binding site important to bonds with acid that needs in plant growth.

ACKNOWLEDGMENT

The writers are gratefull for invaluable help from Bioinformation lecture in Brawijaya University, Prof Fatciyah, Prof, Estri Laras Aruminingtyas, Widodo, PhD, Med., Sc.

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