Department of Biotechnology
Ministry of Science and Technology
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DBT

National Institute of
Advanced Industrial Science
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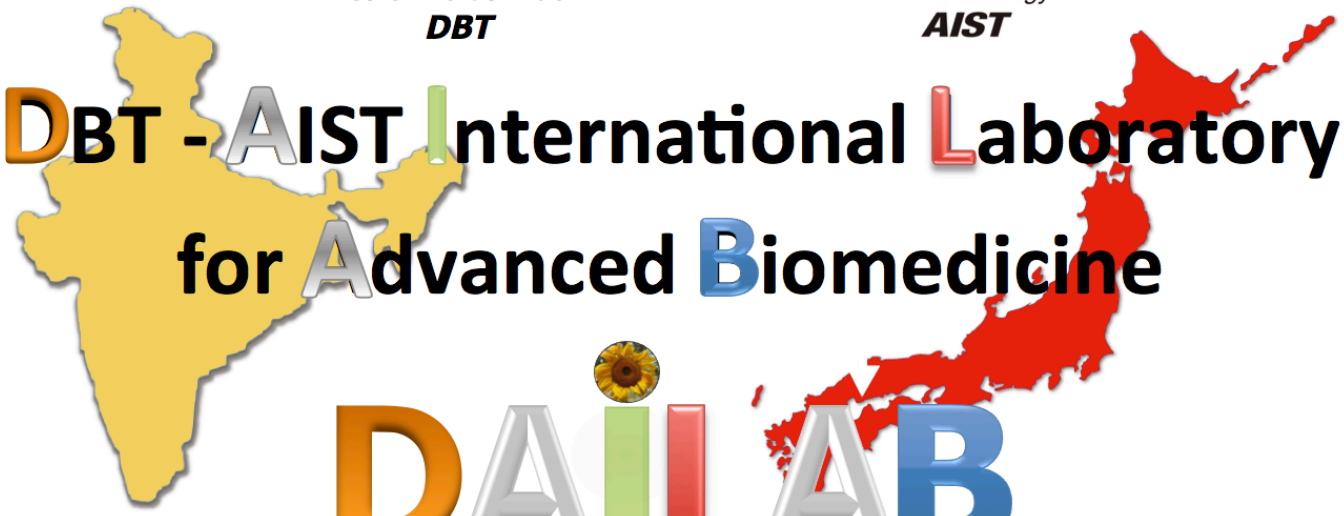

DBT - AIST International Laboratory for Advanced Biomedicine

DAILAB

Classroom for Advanced & Frontier Education

CAFE

CAFE -PLUS

Presentation-Learning for Young Scholars

CAFE -PLUS

Presentation-Learning for Young Scholars

- DAILAB will hold a **CAFÉ-PLUS Series II** on August 27, 2015 (12:30 to 2:00 PM)
- Aim of the CAFÉ-PLUS is to offer chance to Young Scholars to present their work and train them for "Clear/Crisp/Focused/Precise" presentations.
- 4-5 candidates will be selected based on their submitted abstracts from DAILAB-AIST (Japan) and Satellite CAFEs: *IIT-Delhi (India), Hanyang University (Korea); Peking Union Medical College (China) and Brawijaya University* (Indonesia). We will be connected by Skype.
- Each presenter will be given 13 mins (10 min presentation + 3 min QA).
- Experts from team of DAILAB mentors will evaluate the presentations and give comments on how to improve it further from various aspects.
- "**GOLD and SILVER Winners of DAILAB-CAFÉ PLUS**" will be selected and issued a certificate and momentos.

Presenter 1- Didik Huswo Utomo,1,2*

Development of Indonesia Database for Drugs Discovery: Prediction of Accurate Binding Affinity of Novel PKA Inhibitor

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ABSTRACT

Plants are essential component of traditional medicine in Indonesia. Documenting traditional medical knowledge and scientific study of its bioactive compounds, then sharing them, are the priorities on drugs discovery. However, the process to discover and develop a bioactive compounds to be a new drug candidate take a lot of time and cost. To address this issue we present a new database and web service to facilititate the accelerating drug discovery. The database contains comprehensive informations from Indonesia anticancer compounds. Data was performed on PubMed database, pubchem NCBI and others to extract validated information on anticancer compound. Combined informations were put into a MySQL database. For web service construction, we used opensource program like JSME, Openbabel, Autodock Vina and Opal. To validate the utility of ID3 web service (http://id3.chem.itb.ac.id), we evaluated seven flavonoids as PKA inhibitor based on molecular docking and compared the result with IC50 analysis. Result shows that the correlation between free energy binding and IC50 was R2= 0.89. The complex have good stability in molecular dynamics simulation. This computational study confirms clearly that Autodock Vina program in ID3 web service can be used to predict enzyme-inhibitors interactions. In conclusion, we developed successfully a new Indonesia anticancer database and web service that can facilitate drug discovery process.

Keywords: Anticancer, database, drug discovery, free energy binding, PKA inhibitor

Presenter 2- Kejuan LI

In vitro and *in vivo* Anticancer Activity of aqueous extract of *Helicteres angustifolia* L. Root and Its Anticancer Mechanisms

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ABSTRACT

Helicteres angustifolia L. (*H. angustifolia*) is a medical plant that forms a common ingredient of health supplements, tonics, and home remedies for cancer prevention and anticancer treatment in many oriental countries. Although many benefits have been gained from this medical plant, still, scientific evidence about the anticancer activity of *H. angustifolia* root is limited, and the mechanism involved is unclear as well. In order to provide more evidence on the anticancer activity of *H. angustifolia* root, aqueous and ethanolic extract (HAR_{aq} and HAR_{et}) were obtained from *H. angustifolia* root and used for the evaluation of potential anticancer activities *in vitro* by evaluating their cytotoxic effect against three human cancer cell lines (including DLD-1, A549, and HepG2 cell lines) and one normal cell line TIG3. Results indicated that HARaq possessed stronger anticancer activities than HARet, while showed less cytotoxicity on normal cells TIG3. BALB/c nude mice model was used to evaluate the anticancer potential of HARaq *in vivo*. Results indicated that orally administration of HAR_{aq} could significantly inhibit the tumor growth and tumor angiogenesis *in vivo*, moreover, no evidence of toxicity was identified in the HAR_{aq} treated mice. In order to verify its anticancer mechanisms underlying, HAR_{aq} was subjected to test the growth inhibition, DNA damage induction, cell cycle distribution and apoptotic induction effects in both human osteosarcoma (U2OS) cells and normal fibroblast (TIG3) cells. Related protein expression levels were further explored by western blotting analysis and immunocytochemistry staining. Results indicated that HAR_{aq} effectively inhibited the growth of U2OS cells, meanwhile comet assay revealed DNA damage, flow cytometry analysis revealed cell cycle (G2/M) arrest and apoptosis induction in HAR_{aq} treated U2OS cells but not TIG3. Accordingly, molecular analysis revealed the up - regulating of p53, p21 and down - regulating of

cyclin B1 and pRb in HAR_{aq} treated U2OS cells. With the regulation of bcl-2 family proteins, HAR_{aq} induced the cleavage of PARP and activated caspases. Taken together, this work provides important information for the validation of the clinical application of aqueous extract of *H. angustifolia* root and development of novel anticancer therapeutics

Presenter 3- Shayoni Dutta

Reprogramming DNA-binding specificity in zinc finger proteins for targeting unique address in a genome

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ABSTRACT

INTRODUCTION: The Cys_2His_2 Zinc finger protein binds guanine/cytosine-rich DNA via a specific DNA- recognition code, governed by cardinal amino acid residues at positions -1, 3 and 6 on the α-helix of the ZFP. Fusion of these ZFPs with different functional domains forms chimeric proteins that can effectively manipulate or modify any genome.

AIM: The need to effectively aid genome therapy can be achieved partly by devising a method that analyses the physico-chemical properties of ZFP-DNA complexes and selects the most optimum zinc finger protein candidate for our target DNA by exploiting the relative strengths based on hydrogen bonding, Van der Waals forces as well as DNA dewetting, bending and desolvation penalties.

METHOD: The parent template for the ZFP was that of Zif-268 and its consensus sequence (PDB ID: 1AAY) which was used to generate all possible DNA-protein PDBs by mutating the key α-helix residues of the individual finger of the ZFP, from a specific pool of residues determined upon confluence of data. The ΔG was quantified at the interface of all these possibilities to generate top 3 optimum ZFP candidates from all predictions based on a scoring function derived from all the above parameters that define affinity and specificity between ZFPs and their respective DNA.

RESULTS: Interfacial Hydrogen bond energy was calculated for both approaches i.e. modular and synergistic and the predictions were in sync with experimental data. The simulation studies further, ascertain the stability of the predictions although highlighting the effect of DNA bending and dewetting on a chosen sample set. During the binding process, the formation of hydrophobic contact surfaces revealed from the above analysis is accompanied by a nanoscale dewetting transition, where the interface water molecules are expelled into the bulk fluid and the interfacial region dewets (desolvates). To further validate the free energy dynamics of DNA bending and desolvation , free energy perturbation was performed as well as deformation based on helical twist and major groove width was evaluated on the same sample set.

This method strongly enables design of unbiased Zinc fingers with desired specificity and affinity for therapeutic purposes like genome targeting backed by experimental datasets.