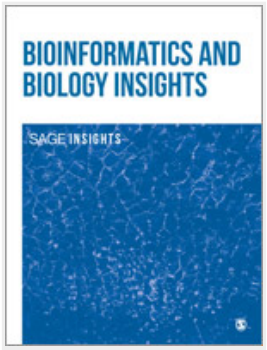
Bioinformatics and Biology Insights

Table of Contents

Volume 11, January-December 2017

Original Research

Methodology



R Script Approach to Infer *Toxoplasma* Infection Mechanisms From Microarrays and Domain-Domain Protein Interactions

Ailan F Arenas, **Gladys E Salcedo**, **Jorge E Gomez-Marin**

First Published December 17, 2017

Abstract
> Preview

Original Research

Bioinformatic Analysis of Circadian Expression of Oncogenes and Tumor Suppressor Genes

Abbas Salavaty, **Niloufar Mohammadi**, **Mozhdeh Shahmoradi**, **Maryam Naderi Soorki**

First Published December 13, 2017

Abstract
> Preview

Computational Model of the Effect of a Surface-Binding Site on the *Saccharomycopsis fibuligera* R64 α-Amylase to the Substrate Adsorption

***Muhammad Yusuf**, ***Umi Baroroh**, **Khomaini Hasan**, **Saadah Diana Rachman**, **Safri Ishmayana**, **Toto Subroto**

First Published November 6, 2017

Abstract
> Preview

A Metagenomic Analysis of Bacterial Microbiota in the Digestive Tract of Triatomines

Nicolas Carels, **Marcial Gumiel**, **Fabio Faria da Mota**, **Carlos José de Carvalho Moreira**, **Patricia Azambuja**

First Published October 4, 2017

Abstract
> Preview

Short Report

Finding the Sources of Missing Heritability within Rare Variants Through Simulation

Baishali Bandyopadhyay, **Veda Chanda**, **Yupeng Wang**

First Published October 4, 2017

Abstract
> Preview

Research Proposal

Bioinformatics Study of m.9053G>A Mutation at the *ATP6* Gene in Relation to Type 2 Diabetes Mellitus and Cataract Diseases

***Iman Permana Maksum**, **Sandy Risfi Saputra**, **Nenden Indrayati**, ***Muhammad Yusuf**, **Toto Subroto**

First Published September 12, 2017

Abstract
> Preview

Original Research

Reverse Nearest Neighbor Search on a Protein-Protein Interaction Network to Infer Protein-Disease Associations

Apichat Suratanee, **Kitiporn Plaimas**

First Published July 13, 2017

Abstract
> Preview

CellTrans: An R Package to Quantify Stochastic Cell State Transitions

Thomas Buder, **Andreas Deutsch**, **Michael Seifert**, **Anja Voss-Böhme**

First Published June 16, 2017

Abstract
> Preview

Methodology

A Computational Methodology to Overcome the Challenges Associated With the Search for Specific

Enzyme Targets to Develop Drugs Against *Leishmania major*

Larissa Catharina, **Carlyle Ribeiro Lima**, **Alexander Franca**, **Ana Carolina Ramos Guimarães**, **Marcelo Alves-Ferreira**, **Pierre Tuffery**, **Philippe Derreumaux**, **Nicolas Carels**

First Published June 12, 2017

Abstract
> Preview

Original Research

Prepartal Energy Intake Alters Blood Polymorphonuclear Leukocyte Transcriptome During the Peripartal Period in Holstein Cows

A Agrawal, **MJ Khan**, **DE Graugnard**, **M Vailati-Riboni**, **SL Rodriguez-Zas**, **JS Osorio**, **JJ Loor**

First Published April 28, 2017

Abstract
> Preview

In Silico Approach for Characterization and Comparison of Repeats in the Genomes of Oil and Date Palms

Jaire Alves Ferreira Filho, **Lucas Soares de Brito**, **André Pereira Leão**, **Alexandre Alonso Alves**, **Eduardo Fernandes Formighieri**, **Manoel Teixeira Souza, Júnior**

First Published April 18, 2017

Abstract
> Preview

Methodology

PISMA: A Visual Representation of Motif Distribution in DNA Sequences

Rogelio Alcántara-Silva, **Moisés Alvarado-Hermida**, **Gibrán Díaz-Contreras**, **Martha Sánchez-Barrios**, **Samantha Carrera**, **Silvia Carolina Galván**

First Published March 30, 2017

Abstract
> Preview

Original Research

An Insight Into Structure, Function, and Expression Analysis of 3-Hydroxy-3-Methylglutaryl-CoA Reductase of *Cymbopogon winterianus*

Kamalakshi Devi, **Lochana Patar**, **Mahendra K Modi**, **Priyabrata Sen**

First Published March 30, 2017

Abstract
> Preview

Editorial

Current Developments in Machine Learning Techniques in Biological Data Mining

Gerard G Dumancas, **Indra Adrianto**, **Ghalib Bello**, **Mikhail Dozmorov**

First Published March 22, 2017

Abstract
> Preview

Methodology

Transcriptologs: A Transcriptome-Based Approach to Predict Orthology Relationships

Luca Ambrosino, **Maria Luisa Chiusano**

First Published February 23, 2017

Abstract
> Preview

Original Research

Plasma MicroRNA Levels Following Resection of Metastatic Melanoma

Nicholas Latchana, **Zachary B Abrams**, **J Harrison Howard**, **Kelly Regan**, **Naduparambil Jacob**, **Paolo Fadda**, **Alicia Terando**, **Joseph Markowitz**, **Doreen Agnese**, **Philip Payne**, **William E Carson, III**

First Published February 23, 2017

Abstract
> Preview

SAGE Video
Streaming video collections

SAGE Knowledge
The ultimate social sciences library

SAGE Research Methods
The ultimate methods library

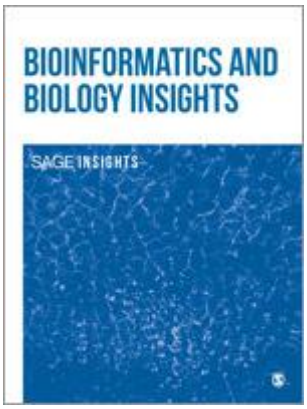
SAGE Stats
Data on Demand

CQ Library
American political resources

Bioinformatics and Biology Insights

ISSN: 1177-9322

Online ISSN: 1177-9322



Bioinformatics and Biology Insights

Editor

Erich Bornberg-Bauer, PhD University of Münster, Germany

Other Titles in:

Computational Biology | Molecular Biology & Genetics

eISSN: 11779322 | ISSN: 11779322 | Current volume: 11 | Current issue: 1

Bioinformatics Study of Mm.9053G>A Mutation at the *ATP6* Gene in Relation to Type 2 Diabetes Mellitus and Cataract Diseases

Bioinformatics and Biology Insights
Volume 11: 1–5

DOI: 10.1177/1177932217728515

*Iman Permana Maksum[1], Sandy Risfi Saputra[1], Nenden Indrayati[1], *Muhammad Yusuf[1,2], and Toto Subroto[1,2]

[1]Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Padjadjaran, Bandung, Indonesia. [2]Research Centre of Molecular Biotechnology and Bioinformatics, Universitas Padjadjaran, Bandung, Indonesia.

ABSTRACT: The mitochondrial disease often associated with various illnesses in relation to the activity of cells metabolites and the synthesis of adenosine triphosphate (ATP), including alteration in the mitochondrial DNA. The mutation of m.9053G>A at the *ATP6* gene was found in patients with type 2 diabetes mellitus (DM type 2) and cataract. Therefore, this mutation is predicted to be clinical features of the 2 diseases. *ATP6* gene encodes protein subunit of ATPase6, a part of ATP synthase, which is important in the electron transfer and proton translocation in intracellular respiration system. This study aims to investigate the mutation effect of m.9053G>A at the *ATP6* gene (S167N) to the structure and function of ATPase6 using bioinformatics method. The structure of ATPase6 was constructed using homology modeling method. The crystal structure of bovine's ATP synthase (Protein Data Bank ID 5FIL) was used as a template because of high sequence similarity (77%) and coverage (96%) of the input sequence. The effect of mutation was investigated at the proton translocation channel of ATPase6. It is predicted that the channel was disrupted due to changes in electrostatic potential from serine to asparagine. Furthermore, molecular docking suggests that water binding on the proton translocation channel in the S167N mutant was different from the wild type. The result of this study is hoped to be useful in the development of a new genetic marker for DM type 2 and cataract.

KEYWORDS: ATP6, diabetes mellitus, cataract, bioinformatics, proton translocation

RECEIVED: May 18, 2017. **ACCEPTED:** August 2, 2017.

PEER REVIEW: Three peer reviewers contributed to the peer review report. Reviewers' reports totaled 297 words, excluding any confidential comments to the academic editor.

TYPE: Research Proposal

FUNDING: The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This study was supported by Academic Leadership Grant (ALG) from Universitas Padjadjaran, which has been used to purchase computer and software for the computational experiment.

DECLARATION OF CONFLICTING INTERESTS: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

CORRESPONDING AUTHOR: Toto Subroto, Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Padjadjaran, Jalan Raya Bandung - Sumedang Km. 21, Jatinangor 45363, Jawa Barat, Indonesia.
Email: t.subroto@unpad.ac.id

Introduction

Mitochondria are organelles of eukaryotic cells which play an important role in producing energy in the form of adenosine triphosphate (ATP) by ATP synthase complex.[1] The complex of ATP synthase in mammals is composed of 2 parts, which are F_1 that has a catalytic site for ATP synthesis and hydrolysis and F_0 that has proton channel to translocate proton across the mitochondrial membrane.[2] Two subunits of F_0, ie, ATPase6 (subunit a) and ATPase8 (A6L), are coded by mitochondrial DNA (mtDNA), whereas the rest of subunits are coded by nuclear DNA.[3] Therefore, mutations in mtDNA, especially that of subunits a and A6L, would affect the cell metabolism in producing energy that is crucial for all organs in human body.[4] There are 2 mutations of mtDNA which are related to type 2 diabetes mellitus (DM type 2) that complicated with cataract disease, ie., A3243G and C12258A.[5] Thus, mitochondrial disorder–related diseases are interesting to be studied. In 2014, World Health Organization reported that Indonesia is the fifth and the second largest country regarding a number of diabetes and cataract cases, respectively.

In 2010, Maksum reported 6 mutations in mtDNA which specifically occurred in patients having type 2 DM and cataract. Among the mutations, m.9053G>A was located at respiration complex protein, ATPase6, and was found to be unrelated to neuromuscular diseases, eg, myopathy and deafness.[6] ATPase6 plays a role as proton translocation channel in the mitochondrial matrix through the rotation of F_0 ring and hence triggers the change of catalytic site of F_1 for ATP synthesis.[7] Maassen et al[8] suggested that mitochondrial disorder was related to diabetes due to the decreasing of insulin secretion as a result of the low concentration of ATP.

This study aims to investigate the changes of structural properties of ATPase6 due to m.9053G>A mutation (S167N) using bioinformatics methods. The structure of ATPase6 was built using homology modeling technique. Furthermore, the electrostatic properties of protein were calculated using Adaptive Poisson-Boltzmann Solver (APBS) program. The water affinity on the proton translocation channel was predicted using molecular docking by AutoDock Vina.

Methods

Homology modeling of human ATPase6

A structure of bovine mitochondrial ATP synthase, resolved by electron microscopy, was used a template for homology modeling (Protein Data Bank [PDB] ID 5FIL).[9] The sequence of the human *ATP6* gene was retrieved from