Journal of Taibah University Medical Sciences (2016) 11(3), 243–249

Taibah University

Journal of Taibah University Medical Sciences

www.sciencedirect.com

Original Article

A comparative analysis of serum albumin from different species to determine a natural source of albumin that might be useful for human therapy

Rizky Nurdiansyah, M.Sc., Muhaimin Rifa'i, PhD and Widodo, PhD *

Biology Department, Faculty of Mathematics and Natural Sciences, Brawijaya University, Malang, Indonesia

Received 27 February 2016; revised 29 March 2016; accepted 4 April 2016; Available online 27 April 2016

الملخص

أهداف البحث: يعتبر زلال الدم أحد أكثر البروتينات انتشارا في البلازما البشرية، ويقوم بوظائف في نقل البروتين، والتخلص من الشوارد الحرة، وتنظيم الضغط الأسموزي. أُستخدم زلال الدم في العلاج البشري في حالات عديدة منها نقص الدم، ونقص الزلال في الدم وأمراض الكبد المزمنة. إلا أن التطبيقات الطبية للزلال تبقى غير واضحة، خاصة في ما يتعلق بالإصابات الفيروسية واختيار المتبرع المناسب. ويُعتبر بديل زلال الدم البشري من مصدر طبيعي آخر بديلا قابلا للاستخدام. لذا درسنا صفات التشابه، والعلاقات البنيوية والتطويرية لزلال الدم لسبع فصائل مختلفة.

طرق البحث: قمنا بمقارنة ترتيب وبنية وخصائص زلال الدم من عدة أنواع من المخلوقات باستخدام أسلوب "إن - سيليكو" التحليلي فقط.

النتائج: تشير المعلومات إلى أن لزلال الدم مجموعات تسلسل متعددة الأشكال ومرتبة، مبنية على الأنواع المتشابهة. إلا أن تعدد الأشكال لا يغير البنية ثلاثية الأبعاد المسئولة عن وظيفتها كناقل. ويمتلك زلال "دجاج الأدغال الأحمر" العدد الأقل من المواصفات الجزيئية التي تشبه إلى حد كبير جزيء زلال الدم البشري.

الاستنتاجات: تُعتبر هذه الدراسة محورية في توفير معلومات واضحة عن زلال أنواع أخرى من الكائنات المشابه في بنيته مع زلال الدم البشري. قد يتم استخدام هذه الأنواع الأخرى من الزلال كمصدر أساسي طبيعي لعلاج البشر.

الكلمات المفتاحية: شجرة تطور السلالات؛ الوظيفة البروتينية؛ البنية البروتينية؛ العلاج البروتيني؛ زلال الدم

Abstract

Objectives: Serum albumin (SA) is one of the most abundant proteins in human plasma and performs functions for protein transport, scavenges for free radicals, and regulates osmotic pressure. SA has been used for therapy in humans with several diseases including hypovolemia, hypoalbuminemia, and chronic liver disease. However, the most appropriate source of albumin for medical applications remains unclear, especially in the case of viral infections, which complicates finding viable donors. Substitution of human serum albumin (HSA) with albumin from other natural sources is a viable alternative. Therefore, we elucidated the similarity in character, structure and evolutionary relationship among serum albumin isolated from seven different species.

Methods: We compared the sequence, structure, and properties of SA from different species using an *in-silico* approach.

Results: These data suggested that SA has sequence polymorphism that clusters based on closely related-species. However, these polymorphisms do not change the three-dimensional structure of the protein; this may serve to maintain its function as a transporter. The *Gallus gallus* albumin has the lowest number of the epitopes that closely resemble HSA.

Conclusion: This study is crucial in providing explicit information about the structural similarity of albumin isolated from other species compared to HSA. The *Gallus gallus* SA might be used as a primary natural source of albumin where warranted for human therapy.

* Corresponding address: Biology Department, Faculty of Mathematics and Natural Sciences, Brawijaya University, Jl. Veteran, Malang 65145, Indonesia.
E-mail: widodo@ub.ac.id (Widodo)

Peer review under responsibility of Taibah University.

Production and hosting by Elsevier

 http://dx.doi.org/10.1016/j.jtumed.2016.04.003

Keywords: Phylogenetic tree; Protein function; Protein structure; Protein therapy; Serum albumin

Abbreviations: HSA, Human Serum Albumin; SA, Serum Albumin

Introduction

Serum albumin (SA) is one of the most abundant proteins in blood plasma, which is easily found in the animal system. Their functions are transport protein, scavenge free radicals, and regulate osmotic pressure.[1–3] SA molecular weighs approximately 67 kDa and is composed of three identical globular domains. The crystal structure of SA from various mammals shows similarities with human serum albumin.[4]

Many medical procedures require SA, such as a therapeutic agent in hypovolemia, hypoalbuminemia, and chronic liver disease.[5] The United States Food and Drug Administration (FDA) approves the use of human SA, which is extracted from human plasma or produced recombinantly.[6] However, the use of SA medically remains problematic, especially due to issues with viral infection, finding viable donors, and the high production cost, all factors that result in a high cost to the consumer. Substituting SA from another source of albumin is one alternative solution that may solve the problem.

Therefore, we elucidated the similarity in character, structure and evolutionary relationship among serum albumin of several species. This study provides critical information on the similarity of albumin from other species compared to human SA and demonstrates which may be most similar. These similar forms of albumin might be used as a primary natural source of albumin where warranted for human therapy.

Materials and Methods

Sequence data mining

The SA amino acid (aa) sequence from seven animal species: human (*Homo sapiens;* P02768) and orangutan (*Pongo abelli;* Q5NVH5) for mammal; chicken (*Gallus gallus;* P19121) for birds; cobra snake (*Naja naja*; Q91134) for reptiles; African frog (*Xenopus laevis;* P08759) for amphibians; and Atlantic salmon (*Salmo salar;* P21848) for fish, as representative proteins from each class, were retrieved from the Uniprot (www.uniprot.org) database in FASTA format. Sea lamprey (*Petromyzon marinus*; Q91274) SA was added as the outgroup for this study. The selection was based on the "reviewed" tag from the Uniprot database.

Alignment and phylogenetic tree reconstruction

To reconstruct a phylogenetic tree, multiple sequence alignment (MSA) was employed to every aa sequence based on protocol.[7] MEGA 6.0[8] was used to apply the MSA using multiple sequence comparison by the log-expectation (MUSCLE) algorithm.[9] MSA results were further validated with the GUIDANCE webserver (http://guidance.tau.ac.il/). Pairwise alignments by Bioedit[10] were used to determine the identity and similarity between each class' representative sequences. The phylogenetic tree was reconstructed using MEGA 6.0. A maximum-likelihood algorithm with a Whelan and Goldman and gamma distribution (WAG + G) model were used to rebuild the tree.[11] The model was chosen based on the MEGA 6.0 prediction for the best evolutionary model. Each gap and missing data in the MSA were deleted.

Molecular modeling

The structure of each of the representatives was predicted. The PSIPRED webserver (http://bioinf.cs.ucl.ac.uk/psipred/) was used to predict the two-dimensional structure, as well as the function.[12] The PHYRE2 webserver (http://www.sbg.bio.ic.ac.uk/phyre2/html/page.cgi?id=index) was used to predict each representative three-dimensional structure with the intensive mode modeling method.[13] The three-dimensional models for *Homo sapiens* were retrieved as a PDB (www.pdb.org) (accession number: 1N5U) and visualized using PyMOL 1.3 (The PyMOL Molecular Graphics System, Version 1.3 Schrödinger, LLC).

Protein surface analysis

Webserver 3D-surfer (http://dragon.bio.purdue.edu/3d-surfer/) with its VisGrid algorithm[14] was used to perform local surface geometry analysis of the models for each SA representative. The results obtained included regions of the cavity, protrusion, and the flat geometry for each model. The surface analysis was visualized using PyMOL 1.3 (The PyMOL Molecular Graphics System, Version 1.3 Schrödinger, LLC).

Antigenicity analysis

Antigenicity analysis was employed using webserver hosted by the Immunomedicine Group, Universidad Complutense Madrid (http://imed.med.ucm.es/Tools/antigenic.pl). The models were assessed for antigenicity to B Cells based on the Kolaskar and Tangaonkar method.[15] The antigenic region was then visualized using PyMOL 1.3 (The PyMOL Molecular Graphics System, Version 1.3 Schrödinger, LLC).

Results

Sequence alignment and phylogenetic tree

The phylogenetic tree suggests that SA can classify the animal species based on the respective class (mammal, bird, amphibians, fish, and reptile) with high bootstrap value (Figure 1). These data suggested that SA might be used to distinguish species and is separated according to evolutionary status. SA was initially used as the molecular clock and as the immunological marker to determine relationships in some animal groups. Cross reactivity between two species anti-sera may indicate the closeness in the phylogenetic relationship