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# Bioinformatics analysis of the structure and linear B-cell epitopes of aquaporin-3 from *Schistosoma japonicum*

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ABSTRACT

**Objective:** To analyze the structure of aquaporins-3(AQP-3) from *Schistosoma japonicum*(SJAQP-3) using bioinformatical methods, and to provid of references for vaccine targets research. **Methods:** Protparam, BepiPred, TMHMM Server, MLRC, Geno3d, DNA star software packages were used to predict the physical and chemical properties, hydrophilicity plot, flexibility regions, antigenic index, surface probability plot, secondary structure, and tertiary structure of amino acid sequence of SJAQP-3. **Results:** SJAQP-3 had six transmembrane regions and two half-spanning helices that form a central channel. The half-spanning helices fold into the centre of the channel. Either of the half-spanning helix had a conserved motif of NPA common to all aquaporins. Predicted linear B-Cell epitopes were most likely at the *N*-terminal amino acid residues of 5aa-7aa, 59aa- 62aa, 225aa-230aa, 282aa -288aa, 294aa -298aa and 305aa -307aa area. 59aa- 62aa, 225aa-230aa located outside the membrane, the others located inside the cell. **Conclusions:** SJAQP-3 is a integral membrane protein in *Schistosoma japonicum* tegument. There are six potential epitopes in SJAQP-3. It might be a potential molecular target for the development of vaccines.

## 1. Introduction

*Schistosomiasis japonica* is a chronic and morbid disease that affects hundreds of millions of the poorest individuals in the endemic areas of China, Philippines and Indonesia. Control measures of praziquantel chemotherapy, health education, improved sanitation, environmental modification and snail control are not good way to control the prevalence of *Schistosomiasis japonica*. So the deployment of anti-schistosome vaccines is urgently needed to meet the prevailing challenges.

The set of integral membrane proteins at the host-parasite interface is very important for the parasitic organism. They are concerned with immune evasion, osmoregulation, absorption of nutrients, excretion waste and metabolic end-products, and so on. The aquaporins(AQPs) are small integral membrane proteins. They selectively transport water and some small solutes cross plasma membranes in mammals, plants, and lower organisms[1]. According to their transport function the aquaporin family is divided into two subfamilies. One subfamily conducts pure water, the other, aquaglyceroporins conducts glycerol well at close to diffusion rates for glycerol or urea and have low conductance of water[2]. Interference with aquaporin function may substantially harm basic parasite systems, such as osmotic protection, lipid synthesis and glycolysis[3]. Aquaporins-3(AQP-3) are aquaglyceroporins that transport water and some small solutes[4]. AQP-3 is found in *Schistosoma japonicum* tegument belonged to integral membrane proteins at the host-parasite interface, the schistosome tegumentis generally accepted to present an ideal target for the development of vaccines[5]. At present studies on AQP-3 of *Schistosoma japonicum*(SJAQP-3) are still scanty. This study aims to analyze the structure of AQP-3 from *Schistosoma japonicum*, and to predict its potential vaccine target by bioinformatics methods.

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## 2. Materials and methods

The amino acids sequences of SJAQP-3 were obtained from http://lifecenter.sgst.cn/schistosoma/cn/schdownload.do. The physiological and biochemical characters were predicted based on http://web.expasy.org/protparam/, The secondary and 3D structure were predicted according to http://npsa-pbil.ibcp.fr/cgi-bin/npsa_automat.pl?page=/NPSA/npsa_seccons.html, http://geno3d-pbil.ibcp.fr/cgi-bin/geno3d_automat.pl?page=/GENO3D/geno3d_home.html, respectively. The water pore was predicted based on Caver2_1_2_pymol_plugin. Transmembrane helices and linear B-cell epitopes were predicted based on http://www.cbs.dtu.dk/services, hydrophilicity plot, flexibility regions, antigenic index, surface probability plot were predicted based on DNA star software package.

## 3. Results

### 3.1. Analysis of amino acids sequences

The accession number of amino acid of SJAQP-3 was CPRT0000005211.

### 3.2. Physiological and biochemical characters of SJ AQP-3

The predicted isoelectric point of SJAQP-3 was 8.05 and the molecular weight was 32 957.3 Da. The estimated half-life of protein predicted in mammals, yeast and *Escherichia coli* were 30 h, > 20 h, > 10 h, respectively, and its instability coefficient was 26.28. Thus SJAQP-3 was predicted as a stable protein. The total average hydrophobicity was 0.459.

### 3.3. Structure of SJAQP-3

SJAQP-3 was a membrane protein that contained six membrane-spanning helices, with 1aa- 32aa, 93aa-111aa, 190aa-201aa, 274aa-310aa locating inside the cell and 56aa-69aa, 135aa-169aa, 225aa-250aa locating outside the membrane. The secondary structure of SJAQP-3 included α -helix (46.77%), β - strands (19.35%), random coil (33.87%)（Figure 1）.

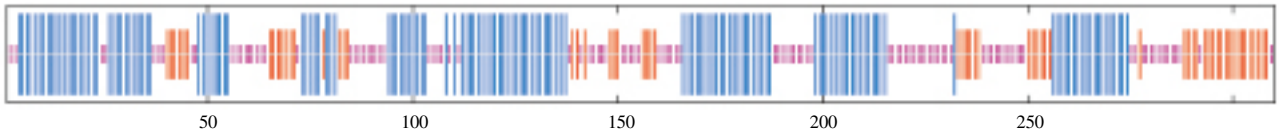


**Figure 1.** The secondary structure of SJAQP-3.
The vertical lines from long to short as follows: α -helix, β - strands and random coil.

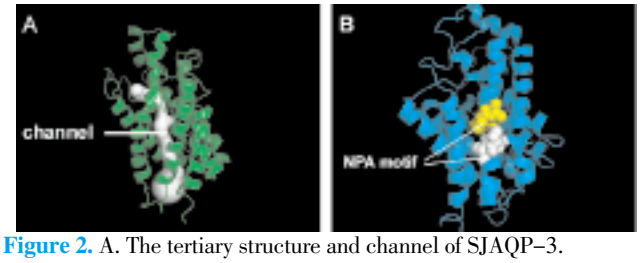


**Figure 2.** A. The tertiary structure and channel of SJAQP-3.
B. The tertiary structure and NPA motif of SJAQP-3.

The tertiary structure of SJAQP-3 showed that it had six transmembrane regions and two half-spanning helices that form a central channel (Figure 2A). The half-spanning helices fold into the centre of the channel. Either of the half-spanning helix had a conserved motif of NPA (asparagine-proline-alanine) common to all AQPs(Figure 2B).

### 3.4. LSinear B-Cell epitope

BepiPred Server results showed that SJAQP-3 1aa-8aa, 58aa-63aa, 88aa-94aa, 159aa-166aa, 188aa-189aa, 191aa-195aa, 223aa-230aa, 243aa-247aa, 282aa-310aa all were the preponderant B-cell epitopes.

Hydrophilicity plot, flexibility regions, antigenic index, surface probability plot were predicted by DNAStar software package. The results showed that SJAQP-3 5aa-7aa, 10aa-14aa, 59aa-62aa, 225aa-230aa, 280aa-288aa, 294aa-298aa, 305aa-307aa were the preponderant B-cell epitopes(Figure 3).

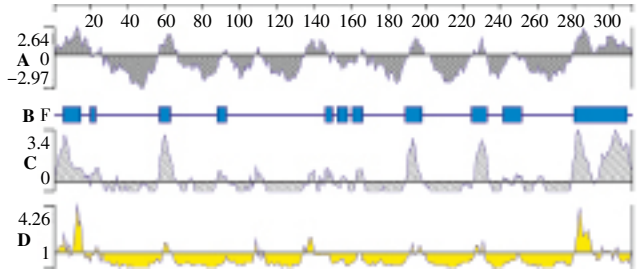


**Figure 3.** The hydrophobic regions, flexible regions, antigen regions and surface possible regions of SJAQP-3.
A:hydrophilicity plot Kyte-Doolittle; B:Flexible regions Karplus-Schulz; C:antigenic index -Jameson-Wolf; D: Surface probability plot- Emini.

According to the hydrophilicity plot, flexibility regions, antigenic index, surface probability plot, BepiPred Server

results and binding to secondary structure of SJAQP-3, predicted preponderant B-cell epitopes were most likely at the *N*-terminal amino acid residues of 5aa-7aa, 59aa-62aa, 225aa-230aa, 282aa -288aa, 294aa -298aa and 305aa-307aa area. 59aa-62aa, 225aa-230aa located outside the membrane, the others located inside the cell.

## 4. Discussion

A B-cell epitope is defined as that part of antigen recognized by either a particular antibody molecule or a particular B-cell receptor of the immune system. Epitopes have been classified as linear (continuous) or conformational (discontinuous). The linear epitopes can be directly used for vaccine design and immune diagnosis[6]. Though B-cell epitopes can be directly identified using many biochemical or physical experiments, such as X-ray crystallography of antibody-antigen complexes, these experiments are usually costly, time-consuming and are not always successful[7]. Computational methods to predict B-cell epitope are much more efficient and cost-effective[8].The commonly used methods for the prediction are hydrophilicity, flexibility, accessibility and turns. BepiPred 1.0 server predicts the location of linear B-cell epitopes using a combination of a hidden Markov model and a propensity scale method[9-11]. It is also a commonly used method. The percentage of correct prediction used single method was not high[12]. Multi parameters prediction can overcome limitations of single parameter prediction and reduce the difference. We combined hydrophilicity, flexibility, accessibility, turns, BepiPred and found that SJAQP-3 5aa-7aa, 59aa-62aa, 225aa-230aa, 282aa -288aa, 294aa -298aa and 305aa-307aa area would be used as the preponderant linear B-cell epitopes.

The predicted tertiary structure of SJAQP-3 showed that it contains a central channel and linear B-cell epitopes all located on the surface, some B-cell epitopes located inside the cell. At present the character of the channel is still unclear, but in *Schistosoma mansoni* there is a aquaglyceroporins located in tegument that it can allow praziquantel to pass through the channel into the cell[13]. The vaccine might be pass through the channel into the cell. So the B-cell epitopes located into the cell might also be used as vaccine targets.

The surface layer of *Schistosoma japonicum* tegument is covered externally by the dual membrane - membranocalyx complex. The tegument has SJAQP-3. AQP-3 can be involved in the transport of water, ion transport, on the body has an important role, inhibition of SJAQP-3 may seriously affect the body's physiological function, so SJAQP-3 has very good vaccine target application prospect.

## Conflict of interest statement

We declare that we have no conflict of interest.

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