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Original Article

Reverse vaccinology: An approach to search vaccine leads of *Shigella sonnei*

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ABSTRACT

Aim: To develop vaccine leads by reverse vaccinology approach for *Shigella sonnei*.
Materials and methods: Study screened the coding proteins of *S. sonnei* as vaccine targets collected from NCBI website and filtered as cell surface proteins using programs such as SignalP 4.1, TMHMM, LipoP 1.0, PsortB and BLASTP.
Observation and results: In recent years due to rapid development in genome sequencing technology vaccine development program has achieved defined specificity and success. In our study, in total 63 cell surface proteins as vaccine leads were searched which are highly conserved among genus Shigella.
Conclusion: Study successfully used reverse vaccinology in search of vaccine leads in *S. sonnei*.

1. Introduction

Shigella sonnei is a non-motile, non spore-forming, facultative anaerobic Gram-negative intracellular pathogenic bacterium causing dysentery in human.[1] It is normally transmitted by uncooked food or contaminated water. In the US, 70% cases of shigellosis are caused by *S. sonnei*.[2] Occasional food borne outbreaks by antimicrobial drug-resistant *S. sonnei* have been reported from the United States, Japan, and European countries, mostly among children.[3–6] Several reports confirmed the outbreak of *S. sonnei* in Indian states such as Kerala and Maharashtra reported the extension of *S. sonnei* in India.[7] It was found to be remarkably immunogenic in doses ranging from 10^3 to 10^6 CFU.[8] In a present study, we tried to find out the best scored cell surface antigens by reverse vaccinology approach.[9]

2. Materials and methods

2.1. Data collection

The protein sequence information of *S. sonnei* was gathered from the website: http://www.genome.jp/kegg-bin/show_organism.[10]

2.2. SignalP 4.1

SignalP 4.1 was used to predict membrane based signal peptide and its cleavage sites in protein using Gram negative prokaryotes as default setting. The method involves prediction of cleavage sites and a signal peptide/non-signal peptide prediction by artificial neural networks matrix. The website address is: www.cbs.dtu.dk/services/SignalP.[11]

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2.3. TMHMM

The TMHMM server involved to predict transmembrane helices in *S. sonnei* coded proteins with maximum two transmembrane helices, as more than two helices containing protein is not showing prominent expression *in vitro*. The web address is: www.cbs.dtu.dk/services/TMHMM/.[12]

2.4. LipoP

The lipoP used to record positive signals as SpI for signal peptidase I and SpII for signal peptidase II and recorded negative signals of transmembrane helices and cytoplasmic proteins. The web address is: www.cbs.dtu.dk/services/LipoP.[13]

2.5. PSORTb

A protein sub cellular localization was influenced by several features present within the protein's primary structure, such as the presence of a signal peptide or membrane-spanning alpha-helices. The server used to predict the membrane spanning probability. The web address is: http://www.psort.org/psortb/.[14]

2.6. BLASTP

Those proteins selected from aforementioned programs were screened and filtered further for conserved nature among the genus Shigella sp. In view, protein databases of *S. boydii* (Sbd), *S. flexneri* (Sfx), *S. dysenteriae* (Sdt), *S. pseudotuberculosis* (Spt), and *S. rettegeri* (Srt) were used in analysis. Finally, those proteins shown homology in all four Yersinia sp. were considered as vaccine leads. The web address is: http://www.ncbi.nlm.nih.gov/.[15,16]

3. Results

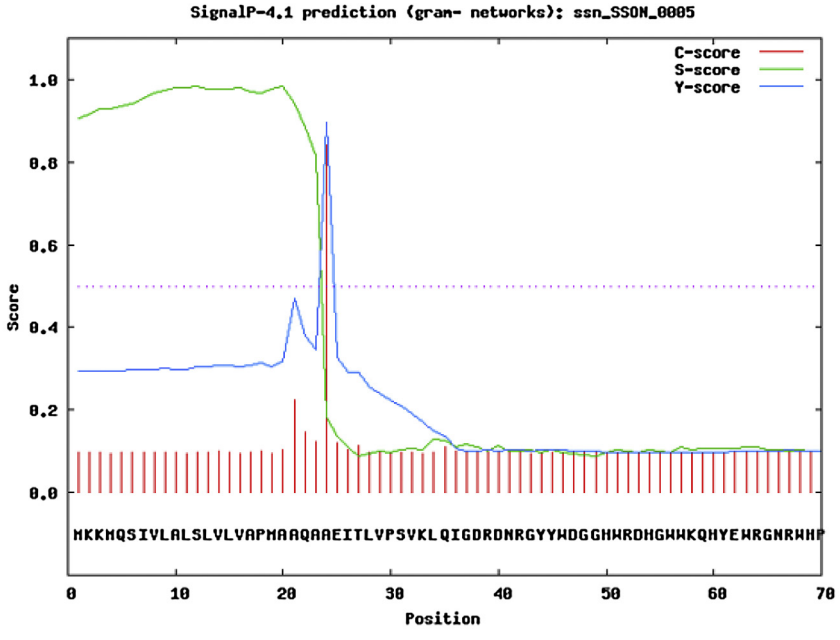
3.1. SignalP 4.1

In total 4470 proteins of *S. sonnei*, signalP sorted 333 proteins harboring signal sequence. The selection of each surface antigen was based on positive peptide signals for all five values measured as: max. C, max. Y, max. S, mean S, and mean D as shown in Fig. 1(A and B).

3.2. TMHMM

By screening 4470 proteins of *S. sonnei*, algorithm predicted presence of transmembrane helices in the 326 proteins, which were further screened for number of transmembrane helices spanned by each protein in the membrane. Hence in decision, leads having more than two transmembrane helices were not considered as leads as in Fig. 2.

A



B

# Measure	Position	Value	Cutoff	signal peptide?
max. C	24	0.841		
max. Y	24	0.895		
max. S	12	0.984		
mean S	1-23	0.950		
D	1-23	0.921	0.570	YES

Name=ssn_SSON_0005 SP='YES' Cleavage site between pos. 23 and 24

Fig. 1 – (A): SignalP – Graphical view by neural network method for C, S and Y scores. (B): SignalP – Tabular data by neural network method for C, S and Y scores.