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Amino Acid Composition among Linear B-Cell Epitope of Different Organisms - A Statistical Study

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Abstract

This study hypothesized that, linear B-cell epitopes of different organism possesses different preferential amino acid residues and hence, an organism specific linear B-cell epitope prediction method could be designed, which in turn could enhance the accuracy of the linear B-cell epitope prediction.

Introduction

T-cell and B-cell epitopes are comprehensively studied due to their potential in synthetic vaccine design [1]. B-cell (Linear) Epitopes (LBE), in particular, play major role in immunodiagnostics of specific disease or condition. Beside several computational methods exist for the prediction of LBE, organism specific epitope prediction methods are in lacunae [2-4]. This may be due to the thought that the general prediction methods are good enough to predict the LBE accurately. However, we hypothesize that the LBE of different organism possesses different preferential amino acid residues, which can influence the accuracy of the prediction methods. Hence, in this study, to explore the amino acid preference or differences in LBE of different organisms, experimentally verified LBE of *Leishmania*, *Plasmodium*, *Mycobacterium*, *Mus Musculus*, and *Arachis hypogea* were collected and compared. As hypothesized, statistically significant differences in amino acid composition were observed between the difference organisms.

Materials and Method

Experimentally verified organism specific Linear B-cell Epitopes (LBE) were collected from IEDB database [5]. Duplicate entries and epitopes of length less than 5 were not used for this study; the sequence pre-processing was done using in-house perl scripts. Composition profiler was used to compute the statistical significance (based on two-sample t-test) between the dataset [6].

Results and Discussion

The LBE of each organism were compared with all the SWISS-PROT entries and the statistically significant ($p<0.005$; 99.5% level) residues (enriched and depleted) were listed in Table 1 [7]. It could be observed from the results that the residues I (Isoleucine) and L (Leucine) were depleted in all the organisms LBE. This suggests that residues I and L are not preferred in the LBE. However, there are no residues in common that are preferred by LBE in all organisms. Closely related organism *Leishmania* and *Plasmodium* were enriched with the residues K (Lysin) and S (Serine), while in the other organisms, the same was not preferred. Similarly, the residue P (Proline) was enriched in *Mycobacterium*, *Mus Musculus*, and *Arachis hypogea*, but was not in *Leishmania* and *Plasmodium*. This result indicates that no single residue is commonly enriched in LBE of all organisms (included

Table 1: Statistically significant enriched and depleted residues of linear B-cell epitopes against SWISS-PROT.

Organism	Enriched[a]	Depleted[a]
Leishmania	A,K,S	I,L
Plasmodium	D,E,K,N,S	A,F,G,H,**I**,**L**,M,R,T,V,W
Mycobacterium	A,G,P,W	C,E,F,H,**I**,K,**L**
Mus Musculus	G,H,P,Q,R,W,Y	A,F,**I**,**L**,V
Arachis hypogea	E,P,Q,R	A,**I**,K,**L**,M,T,V

[a]Statistical significance ($p<0.005$; 99.5% level) based on two-sample t-test; Residues common in all organisms were bold faced.

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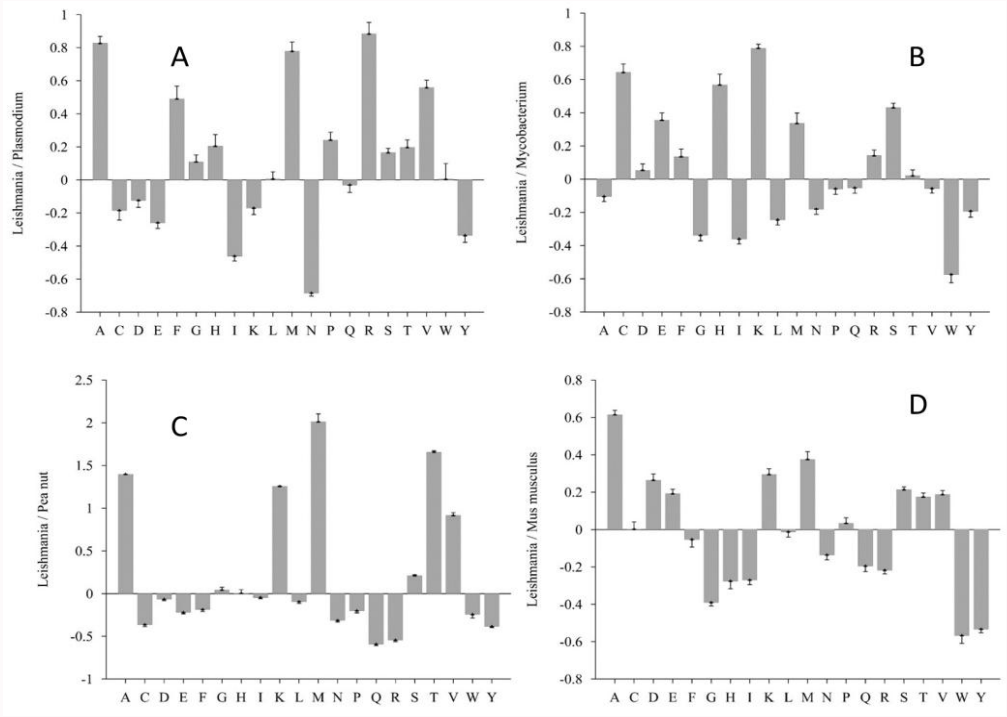

Figure 1: Amino acid composition profiles of LBE of different organisms. A) Comparison of *Leishmania* and *Plasmodium* LBE. B) Comparison of *Leishmania* and *Mycobacterium* LBE. C) Comparison of *Leishmania* and Pea nut LBE. D) Comparison of *Leishmania* and *Mus musculus* LBE.

Table 2: Statistically significant enriched and depleted residues of *Leishmania* linear B-cell epitope against other organism linear B-cell epitopes.

Organism	Enriched[a]	Depleted[a]
Le - *Plasmodium*	A,F,M,P,R,V	E,I,K,N,Y
Le - *Mycobacterium*	C,E,H,K,S	G,I,L,W
Le - *Arachis hypogea*	A,K,M,S,T,V	C,E,N,P,Q,R,Y
Le - *Mus musculus*	A,D,K,S	G,I,R,W,Y

[a]Statistical significance (p<0.005; 99.5% level) based on two-sample t-test; Le - *Leishmania*

in this study). To observe the enriched and depleted residues between the LBE's of different organisms, Leishmania epitopes and each other organisms were subjected to composition profiling. The results of the analysis were plotted in Figure 1 and the corresponding statistically significant (p<0.005; 99.5% level) residues (enriched and depleted) were listed in Table 2. Residues K and S are enriched in *Leishmania* LBE on comparison to other organism LBE. It could also be observed that the amino acid preference of each organism LBE differ significantly with respect to each other. Since the amino acid preferences of LBE differ with each organism, a general LBE prediction method may not be sufficient for the more accurate prediction of LBE. Hence, more specific organism specific LBE prediction methods should be developed, in order to achieve efficient LBE predictions.

Conclusion

Linear B-cell epitopes are of high importance in the field of vaccine development. This study was intended to study the difference in composition of amino acid residues among linear B-cell epitopes of different organisms. Despite several state-of-the-art epitope predictions methods are available for LBE prediction, no tools are available for organism specific LBE prediction. Hence, the results of this study suggest that organism specific LBE predictions methods could improve the prediction accuracy of LBE, in comparison to the general LBE prediction methods.

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