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MERS-Cov and Immunobioinformatics

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Editorial

MERS (Middle East Respiratory Syndrome) is an emerging infectious disease threat, caused by the single-stranded, positive sense (+) RNA MERS-Cov, a highly virulent coronavirus [1,2]. In this editorial report, the immunobioinformatic techniques previously applied to influenza A, described elsewhere in this issue of the Journal of Medical Microbiology and Diagnosis [3] are applied to the spike protein (S) of human MERS-Cov. The S protein is precursor of the S1 and S2 proteins. S1 protein contains a receptor binding domain (RBD; amino acid positions 367–606) which binds to CD26 on the target lymphocyte membrane [4,5]. S2 protein probably facilitates membrane fusion and entry of bound MERS-Cov into the target cell.

The dataset of 13 complete MERS-Cov S human protein sequences was downloaded from GenBank [6] on July 4, 2014. Hamming distance (**D**; [7,8]) and **Bepipred Score** [9] were determined for each of the 1353 S protein amino acid positions (Figure 1). There were 14 amino acid positions with D>0.0 (Figure 1, top). Three of these 14 amino acid positions were within the RBD in the S1 region of the S protein (positions 400, 506, 520). Amino acid 520 possessed a Bepipred Score of 0.437, which is above the recommended cutoff of 0.350. These results suggest that an A520S mutation at an S1 protein epitope within the RBD domain influences the evolutionary trajectory of MERS-Cov by mechanisms involving host immunological responses. Such a mutation may be a component of a suitable epitope target for a preventive vaccine [10].

The maximum observed value of D was at amino acid position 1020, within the the S2 region of the S protein. The Bepipred Score at this position was only 0.302, below the recommended threshold of 0.350, however position 1020 is located between two epitopic regions beginning at position 1010 and ending at amino acid position 1031. It remains to be determined whether the relatively high D value at position 1020 reflects non-immunological forces or whether amino acid 1020 is a component of one of the closely neighboring epitope regions. The mutations observed at S protein position 1020 were H1020R and H1020Q. Histidine is an essential amino acid, which suggests that host dietary factors may be involved in the mutations at position 1020. All three of the amino acids occurring at position 1020 possess nitrogen-containing side-chains. Thus, these results suggest viral structural influences and constraints on the viral mutational process at S protein position 1020.

Contiguous positions 1158 and 1159 each had a positive **D** value and significant **Bepipred Score** in a densely epitopic section of the S2 region of the S protein. These results suggest antigenic activity of the S protein in a non-RBD region. Such an epitope may serve as a vaccine antigen target to ameliorate, but not prevent, MERS.

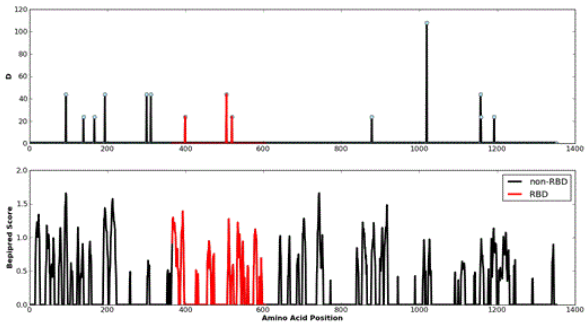

Figure 1: Immunobioinformatic Analysis of MERS-Cov Spike (S) Protein (top) Hamming Distance (**D**); (bottom) Predicted B-cell epitope score (**Bepipred Score**). Results for the Receptor Binding Domain (RBD) are in red; results for the other regions of the S protein are in black. Light blue circles are displayed at the local maxima of the D plot so that the discrete D values at contiguous amino acid positions 1158, 1159 would be discernible. **Bepipred Scores** are shown only for values above the recommended cutoff (0.350).

It is proposed, and hoped, that the results presented in this editorial demonstrate the potential usefulness of immunobioinformatic analysis of MERS-Cov as a tool to increase our understanding of the pathophysiology of MERS on a level that assists our ability to design protective strategies, treatments and vaccines.

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