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Poster presentation

Computational identification of tumour suppressor protein p53 target genes

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Background

The tumour suppressor protein p53 plays a major role in modulating cellular functions such as DNA repair, cell cycle arrest and apoptosis. Mutation in the p53 gene is known to be one of the most frequently observed genetic alterations during tumorigenesis. Under normal cellular condition, the p53 protein is kept at very low levels in a 'stand-by' mode. In response to cellular stresses like hypoxia or nucleotide depletion, p53 is activated and binds to promoter elements (p53 response elements) within its downstream target genes, and regulates their transcriptions initiating the cellular activities that account for most of its tumour suppressor function. The p53 response element (p53 RE) consists of two repeated copies of 5'-PuPuPuC(A/T)(A/T)GPyPyPy-3' with a spacer of up to 13 bp in between. By identifying genes regulated by p53, we hope to achieve a better understanding of their interactions with p53 in maintaining cellular integrity.

Many studies have been carried out on p53 binding sites and in developing different algorithms to identify p53 RE in human genomes. However, the prediction of p53 target genes based on only p53 RE alone might be insufficient. Thus, we have further investigated if additional elements adjacent to the p53 binding site may also have a role in modulating p53 binding in these target genes.

Results

The performance of the program was tested using the sequences of a group of p53 downstream target genes gathered from the literature as positive control genes. It was capable of detecting the p53 response elements in all the control genes. In addition, the consensus motifs adjacent to the p53 response elements were also detected in majority of them. As for the negative control genes, only one gene was predicted to be a weak p53 target gene.

Conclusion

The program is capable of identifying the p53 response elements in the potential p53 target genes, by having selectivity of 76% to pick up the real p53 target genes and sensitivity of 97% to reject the non p53 target genes. It has also proven that the consensus motifs adjacent to the p53 RE are presence in these p53 target genes. Hence, we believe that these additional elements adjacent to p53 RE may play a role in facilitating the p53 binding to its response element.

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