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DRUG DISCOVERY

Subtractive genomics approach for identification of drug targets against *Chlamydophila pneumonia J138*

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ABSTRACT

Pneumonia is an inflammatory condition affecting the lung alveoli. Approximately 450 million people around the world were infected with pneumonia with an estimated mortality of 4 million. *Chlamydophila pneumoniae* is an obligate intracellular bacterium that infects humans and is a major cause of pneumonia. The present study aims at prediction and analysis of new possible drug targets for *Chlamydophila pneumoniae J138* using subtractive genomics approach.

Keywords: Pneumonia, *Chlamydophila pneumoniae J138,* Subtractive genomics approach, Drug target.

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1. INTRODUCTION

Pneumonia is an inflammatory condition affecting the lung alveoli and for years it has been recognized as a common and potential lethal condition. Approximately 450 million people around the world were infected with pneumonia with an estimated mortality of 4 million. *Chlamydophila pneumoniae* is known to account for a relatively large number of community-acquired pneumonia cases, pharyngitis, bronchitis, sinusitis, exacerbations of chronic bronchitis and asthma. It participates in co-infection involving other bacterial agents in about 30% of the community-acquired pneumonia patients (Blasi et al. 2009). *Chlamydophila pneumoniae* belongs to the order *Chlamydiales* representing a group of obligate intracellular bacteria that reside in a membrane-bound inclusion. *Chlamydia pneumoniae* has a unique biphasic developmental cycle involving two functionally and morphologically distinct forms; the invasive elementary bodies and the non invasive, metabolically active reticulate bodies. It was first described as a respiratory pathogen in 1986 (Rajalingam et al. 2001). Macrolides, tetracyclines, quinolones and rifamycins are some of the commonly used antibiotics against *C. pneumoniae.* Among them, Macrolides are the most widely used and effective for acute *C. pneumoniae* infections of the upper respiratory tract owing to their anti-inflammatory and antimicrobial properties (Villegas et al. 2008). However, development of resistance against antibiotics is a common in bacterial isolates and hence prediction of new drug targets is an important area of research. Among the several strains of *C. pneumoniae, Chlamydophila pneumoniae J138* is isolated in Japan in 1994 (Shirai et al. 2000). The present study, aims at prediction and analysis of new possible drug targets for *Chlamydophila pneumoniae J138* using subtractive genomics approach.

2. SCOPE OF THE STUDY

The aim of carrying out this research is to predict and analyze new possible drug targets for *Chlamydophila pneumoniae J138* using subtractive genomics approach.

2.1. Materials

2.1.1. Dataset

Complete genome sequence of *Chlamydophila pneumoniae j138* strain was downloaded from NCBI server *ftp://ftp.ncbi.nlm.nih.gov/genomes/.*

2.1.2. Identification of Essential genes in *C. pneumoniae j138*

Genes that are indispensable to support cellular life are called Essential genes. These genes constitute a minimal gene set required for a living cell and the functions encoded by this gene set are essential and could be considered as a foundation of life itself. The essential gene products of microbial cells are promising new targets for antibacterial drugs. Database of Essential Genes (DEG), is a database available at http://tubic.tju.edu.cn/deg/ which contains all the essential genes that are currently available. To predict the essential genes in *C. pneumoniae j138,* sequences were subjected to BLASTX against the DEG database with Expectation value (E-value) of 0.0001.

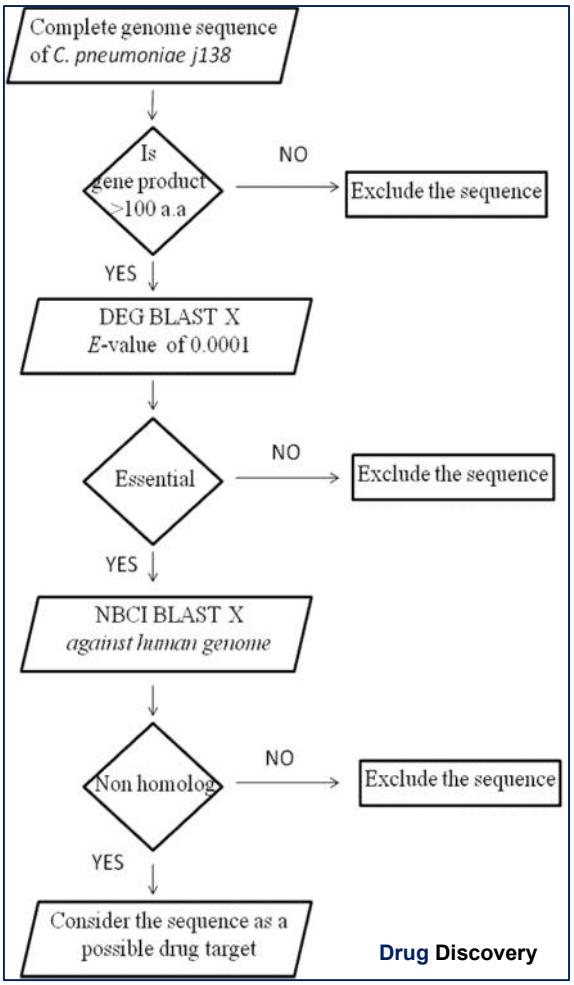

Figure 1

Flowchart of the overall methodology to identify the pathogen specific essential genes using subtractive genomics approach in *C. pneumoniae J138*

Table 1

Classification of genes based on subtractive genomic approach

Total genome sequence of the *Chlamydophila Pneumoniae J138*	1069
Genes whose products are > 100 amino acids	982
Essential genes [cut-off *E*-value of 0.0001]	505
Essential genes that are no human homologs	88

2.1.3. Prediction of non human homologs in *C. pneumoniae j138*

The screened genes, which are possibly the essential genes of *C. pneumoniae j138*, were thus subjected to BLASTX against the human genome in the NCBI server (http://blast.ncbi.nlm.nih.gov/). The homologous sequences were excluded and the lists of non-homologs were compiled.

2.2. Methodology

Flow chart describing the detailed methodology for identification of pathogen specific essential genes using subtractive genomics approach is mentioned in the figure 1.

3. RESULTS AND DISCUSSION

C. pneumoniae j138 strain was found to contain a total of 1069 genome sequences. Among, 1069 genome sequences 982 genes product was found to be greater than 100 amino acids. These 982 genes were subjected to DEG BALSTX to predict the number of essential genes in *C. pneumoniae j138.* Among them, 505 sequences were found to be essential for the survival of *C. pneumoniae j138.* Further, these essential genes were subjected to BLASTX

Table 2

List of genes that are found to be essential and non human homologs in *C. pneumoniae j138*

>gi|15835535|ref|NC_002491.1|:573-878
>gi|15835535|ref|NC_002491.1|:c37267-36329
>gi|15835535|ref|NC_002491.1|:c39296-38430
>gi|15835535|ref|NC_002491.1|:75210-75887
>gi|15835535|ref|NC_002491.1|:92135-92833
>gi|15835535|ref|NC_002491.1|:129834-131180
>gi|15835535|ref|NC_002491.1|:131191-132225
>gi|15835535|ref|NC_002491.1|:144478-144807
>gi|15835535|ref|NC_002491.1|:c171112-169277
>gi|15835535|ref|NC_002491.1|:197603-198916
>gi|15835535|ref|NC_002491.1|:c221398-220841
>gi|15835535|ref|NC_002491.1|:c232249-231596
>gi|15835535|ref|NC_002491.1|:237193-238500
>gi|15835535|ref|NC_002491.1|:238784-240364
>gi|15835535|ref|NC_002491.1|:240657-241601
>gi|15835535|ref|NC_002491.1|:241632-242486
>gi|15835535|ref|NC_002491.1|:248568-250220
>gi|15835535|ref|NC_002491.1|:c265732-265031
>gi|15835535|ref|NC_002491.1|:273384-273839
>gi|15835535|ref|NC_002491.1|:295871-296761
>gi|15835535|ref|NC_002491.1|:295871-296761
>gi|15835535|ref|NC_002491.1|:c354060-353194
>gi|15835535|ref|NC_002491.1|:354612-354980
>gi|15835535|ref|NC_002491.1|:370770-372350
>gi|15835535|ref|NC_002491.1|:372863-374617
>gi|15835535|ref|NC_002491.1|:380272-381216
>gi|15835535|ref|NC_002491.1|:c381649-381194
>gi|15835535|ref|NC_002491.1|:383036-383659
>gi|15835535|ref|NC_002491.1|:c389298-388324
>gi|15835535|ref|NC_002491.1|:c390644-389298
>gi|15835535|ref|NC_002491.1|:c392393-391410
>gi|15835535|ref|NC_002491.1|:c407534-406761
>gi|15835535|ref|NC_002491.1|:418089-419930
>gi|15835535|ref|NC_002491.1|:c407534-406761
>gi|15835535|ref|NC_002491.1|:418089-419930
>gi|15835535|ref|NC_002491.1|:c447593-447201
>gi|15835535|ref|NC_002491.1|:c461565-461263
>gi|15835535|ref|NC_002491.1|:c466544-464583
>gi|15835535|ref|NC_002491.1|:471917-473428
>gi|15835535|ref|NC_002491.1|:474391-475032
>gi|15835535|ref|NC_002491.1|:c480612-479182
>gi|15835535|ref|NC_002491.1|:499885-502671
>gi|15835535|ref|NC_002491.1|:c561056-560277
>gi|15835535|ref|NC_002491.1|:589655-590131
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>gi|15835535|ref|NC_002491.1|:c608016-607027
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>gi|15835535|ref|NC_002491.1|:c696028-695468
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>gi|15835535|ref|NC_002491.1|:c713460-712837
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>gi|15835535|ref|NC_002491.1|:c732822-731983
>gi|15835535|ref|NC_002491.1|:c733296-732835
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>gi|15835535|ref|NC_002491.1|:c800428-799409
>gi|15835535|ref|NC_002491.1|:807004-807813
>gi|15835535|ref|NC_002491.1|:c820924-819281
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>gi|15835535|ref|NC_002491.1|:854431-855783
>gi|15835535|ref|NC_002491.1|:c879094-878516
>gi|15835535|ref|NC_002491.1|:990554-991018
>gi|15835535|ref|NC_002491.1|:c1026087-1025206
>gi|15835535|ref|NC_002491.1|:1031556-1032605
>gi|15835535|ref|NC_002491.1|:1034584-1035741
>gi|15835535|ref|NC_002491.1|:1035647-1036720
>gi|15835535|ref|NC_002491.1|:c1043364-1042303
>gi|15835535|ref|NC_002491.1|:1075334-1077106
>gi|15835535|ref|NC_002491.1|:c1082135-1079091
>gi|15835535|ref|NC_002491.1|:1112402-1113118
>gi|15835535|ref|NC_002491.1|:c1128405-1127608
>gi|15835535|ref|NC_002491.1|:1133129-1133803
>gi|15835535|ref|NC_002491.1|:c1135900-1135418
>gi|15835535|ref|NC_002491.1|:1136289-1136849
>gi|15835535|ref|NC_002491.1|:1162040-1163302
>gi|15835535|ref|NC_002491.1|:1165412-1166344
>gi|15835535|ref|NC_002491.1|:c1173642-1172737
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>gi|15835535|ref|NC_002491.1|:c1190402-1189065
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against human genome and only 88 sequences were found to be non homologs to human genome. The results that were obtained by the subtractive genomic approach were summarized in the Table 1 given below. List of genes that are predicted to be essential and non homologous to human genome is shown in the Table 2 given below. The objective of the work was to find and locate those essential genes of *C. pneumoniae j138* that are important in the normal functioning of the bacterium within the host. Further, subsequent screening of the functionality of the protein encoded by these genes is likely to lead to development of drugs that specifically interact with the pathogen. The non-human homologs among the above mentioned 88 sequences encoding the surface proteins would represent ideal vaccine targets.

4. CONCLUSION

Completion of human genome project and large scale genome sequencing projects has increased the availability of completely sequenced genomic data in public domain. The computational approach used in the present study is more efficient than conventional methods for identification of essential genes and facilitates the exploratory identification of the most relevant drug targets in the pathogen. Further, investigation of protein products of the genes predicted in the study might be useful in the future discovery of novel therapeutic targets in *C. pneumoniae j138.*

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