Characterisation of two meningococcal group C isolates from a case and the contact of a case during the 1997 outbreak at Southampton University

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INTRODUCTION

During an outbreak of meningococcal disease at Southampton University in 1997, two Neisseria meningitidis group C isolates were isolated from a person who died (Case) and a person who performed mouth-to-mouth resuscitation on the case (Carrier). Isolates were shown to have identical serological (PorA and PorB), MLST and PFGE profiles (1, 2). In a later study whole genome comparison (3) demonstrated significant sequence homology with differences found in eight genes, four of which were adjacent to each other. However no further studies were undertaken at the time to investigate if the genetic differences resulted in phenotypic changes.

Here, we further interrogate differences in these isolates using comparative TMT®-proteomic and Serum Bacterial Antibody assay (SBA) using mouse sera raised against Bexsero®. These differences could lead to a better understanding of why the outcomes of the carrier and case were so different.

RESULTS

Case and Carrier isolates in use are shown in this study in Table 1.

Table 1. Carrier and Case isolates in use are shown in this study in Table 1.

<table>
<thead>
<tr>
<th>Isolate</th>
<th>PasteurMLST ID</th>
<th>Isolate country year</th>
<th>species</th>
<th>serogroup ST</th>
<th>Site of collection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carrier</td>
<td>11463235</td>
<td>UK 1997</td>
<td>N. meningitidis C</td>
<td>11</td>
<td>nasopharyngeal fluid</td>
</tr>
<tr>
<td>Case</td>
<td>14728393</td>
<td></td>
<td>N. meningitidis C</td>
<td>11</td>
<td>cerebrospinal fluid</td>
</tr>
</tbody>
</table>

Table 2. Comparative proteomic analysis between Case and Carrier isolates.

Comparative TMT®-proteomic and RT-qPCR

Comparative TMT®-proteomic was performed revealing that factor H binding protein (Fbp, NEIS3049), citrate synthase (prpC, NEIS1732), hypothetical integral membrane protein (Imp, NEIS1147), fructose-1,6-bisphosphate aldolase (Fba, NEIS0350) and aldehyde dehydrogenase A (AldA, NEIS1942) are up-regulated in the Case isolate with fold changes (Case/Carrier) of 32.46, 2.99, 2.21, 1.81 and 1.50 respectively (Figure 1). Type IV plus-associated protein pilC2 (NEIS0033) is instead downregulated in the Case isolate with fold change of 0.05.

Table 2. Comparative proteomic analysis between Case and Carrier isolates.

RT-qPCR confirmed up-regulated expression levels of prpC, imp, fba and aldA in the Case isolate showing relative transcript levels of 1.5, 1.7, 1.2 and 1.3 respectively (Figure 1).

CONCLUSIONS

Comparative proteomic revealed that four proteins (prpC, imp, fba, aldA) are up-regulated in the Case isolate, while one protein (pilC2) is down-regulated; RT-qPCR confirmed expression levels of up-regulated proteins in the Case isolate.

Factor H binding protein (Fbp) resulted as major difference between Case and Carrier isolate.

Due to one base deletion (t366), Fbp is not expressed in the Carrier isolate.

Bexsero® MenB vaccine is effective against both serogroup C Case and Carrier isolates; Bexsero® efficacy

Efficacy of Bexsero® against both serogroup C Case and Carrier isolates was also evaluated. Use of Bexsero® mouse sera in a Serum Bacterial Antibody Assay (SBA) demonstrated killing against both serogroup C isolates and has shown similar killing as a MenB control. Increased titres were observed for the Case isolate compared to Carrier (p=0.005, Figure 3).

REFERENCES and ACKNOWLEDGEMENTS

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