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Vibiro vulnificus hemolysin binds to gangliosides.

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Abstract

Abstract Background: Vibrio vulnificus hemolysin (VVH) is a pore-forming toxin secreted by Vibrio vulnificus. Cellular cholesterol was believed to be the receptor for VVH, because cholesterol could bind to VVH and preincubation with cholesterol inhibited cytotoxicity. It has been reported that specific glycans such as N-acetyl-D-galactosamine and N-acetyl-D-lactosamine bind to VVH, however, it has not been known whether these glycans could inhibit the cytotoxicity of VVH without oligomer formation. Thus, to date, binding mechanisms of VVH to cellular membrane, including specific receptors have not been elucidated. Results: We show here that gangliosides are a good candidate cellular receptor for VVH. Binding of VVH was not affected by depletion of cholesterol on ghost membrane. In contrast, ganglioside GM1a, Fucosyl-GM1, GD1a, GT1c, and GD1b bind to VVH directly, and the GD1a inhibited the cytotoxicity of VVH without the formation of oligomers. Conclusion: This is the first report of a molecule able to inhibit the binding of VVH to target cells without oligomerization of VVH.

Full-text

Due to technical limitations, full-text HTML conversion of this manuscript could not be completed. However, the manuscript can be downloaded and accessed as a PDF.

Figures

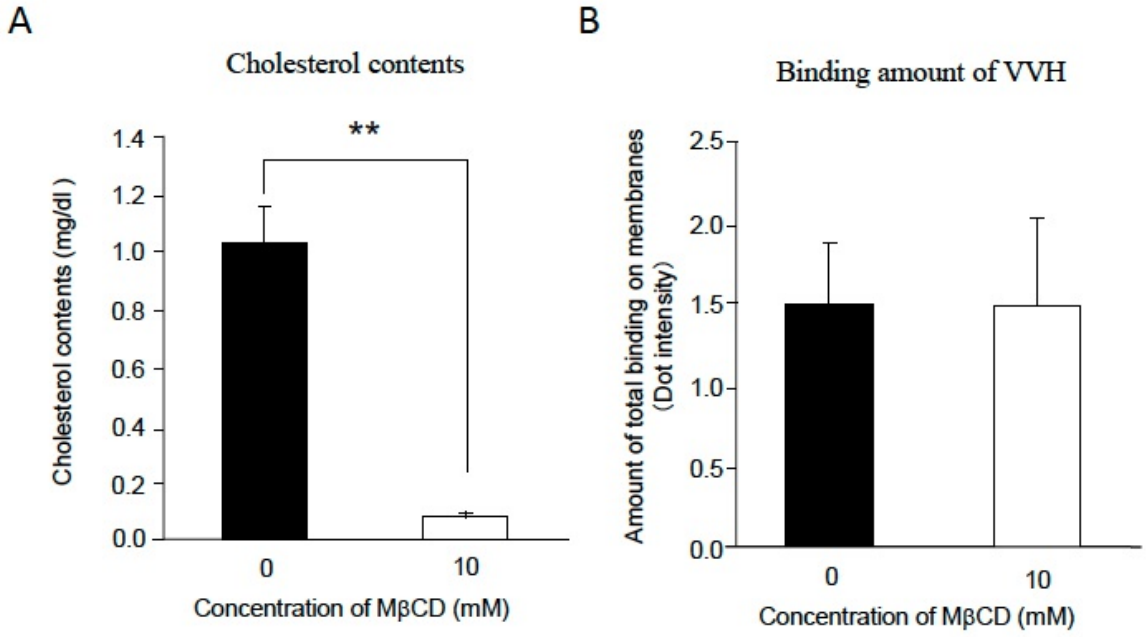
A
Cholesterol contents
**
Cholesterol contents (mg/dl)
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
0
10
Concentration of MβCD (mM)
B
Binding amount of VVH
Amount of total binding on membranes (Dot intensity)
2.5
2.0
1.5
1.0
0.5
0.0
0
10
Concentration of MβCD (mM)

Figure 1

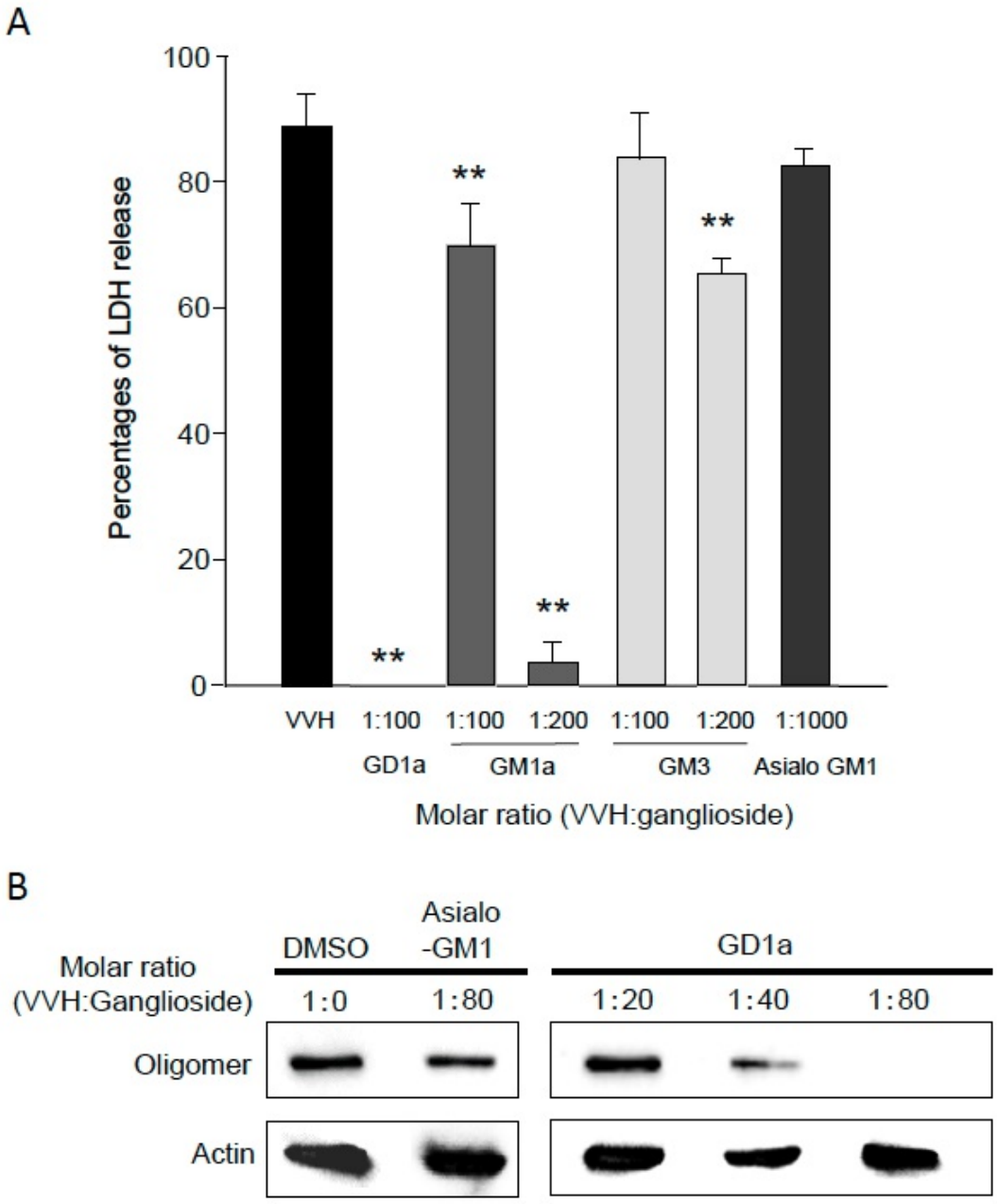
A
100
80
60
40
20
0
Percentages of LDH release
**
**
**
VVH
1:100
1:100
1:200
1:100
1:200
1:1000
GD1a
GM1a
GM3
Asialo GM1
Molar ratio (VVH:ganglioside)
B
Molar ratio
(VVH:Ganglioside)
DMSO
Asialo
-GM1
GD1a
1:0
1:80
1:20
1:40
1:80
Oligomer
Actin

Figure 2

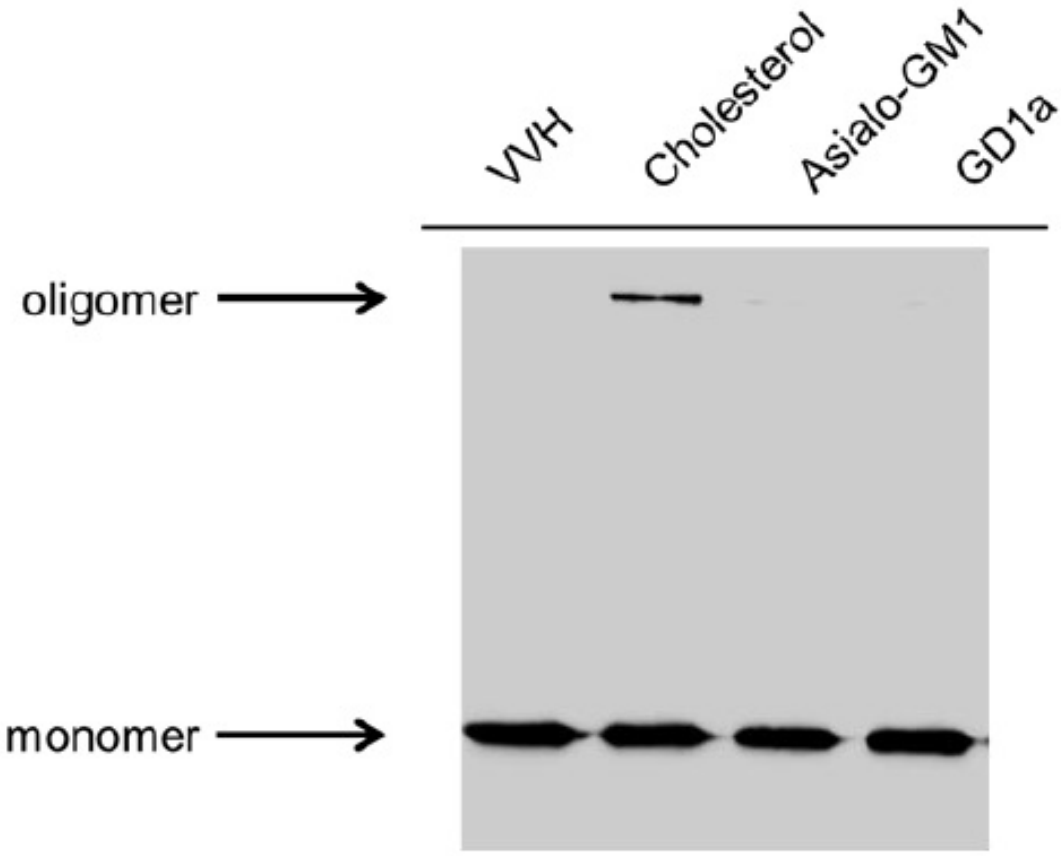

Figure 3

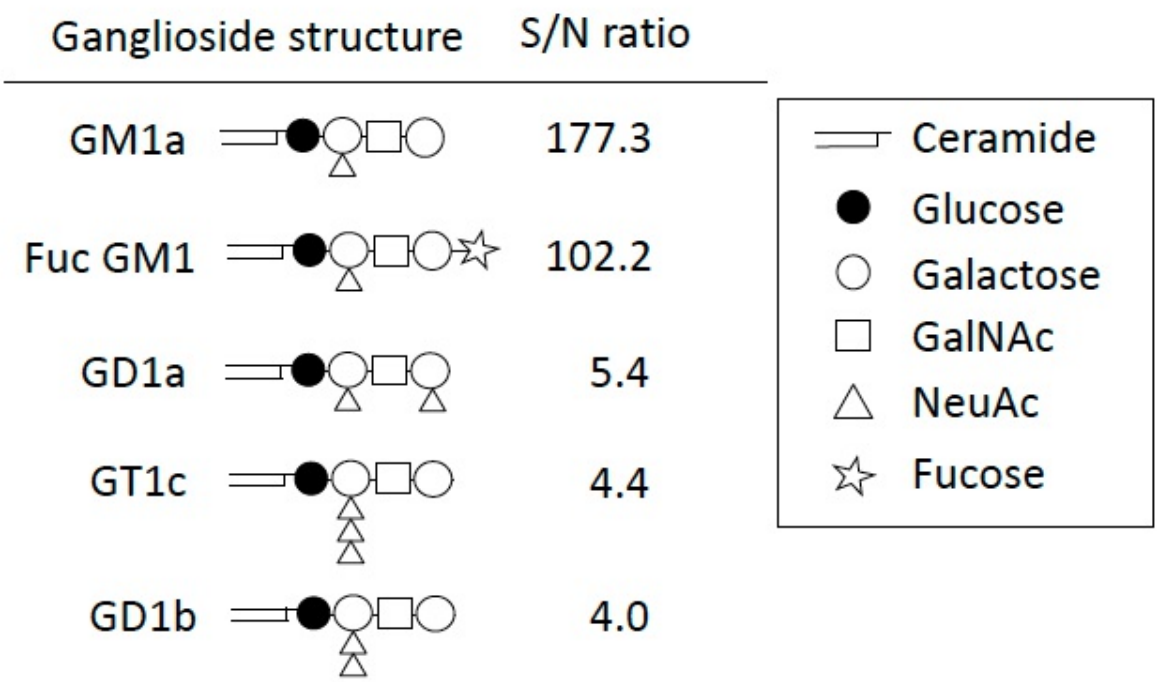
Ganglioside structure
S/N ratio
GM1a
177.3
Fuc GM1
102.2
GD1a
5.4
GT1c
4.4
GD1b
4.0
Ceramide
Glucose
Galactose
GalNAc
NeuAc
Fucose

Figure 4