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Studies of the Ligand Binding to Cholera Toxin, I

The Lipophilic Moiety of Sialoglycolipids*

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Summary: The fixation of cholera toxin by ganglioside $G_{Gtet}1$ is dependent on the nature of the carbohydrate as well as the lipid moiety of the glycolipid. The role of the lipid in binding to the toxin was investigated with synthetic ganglioside analogues (gangliosidoides). The interaction between glycolipid and toxin was followed by precipitate formation, by inhibition of toxicity and in polyacrylamide gel electrophoresis. For specific precipitation, an aliphatic hydrocarbon chain at least 14 C-atoms in length is required. Some of the gangliosidoides form high molecular weight complexes with cholera toxin at lower molar ratios of ligand to protein than the natural compound. None of the synthetic gangliosidoides equalled natural ganglioside in its ability to inhibit the effects of the toxin in vivo, but some did show considerable inhibitory activity in the vascular permeability test. Reaction of cholera toxin with monosialo-gangliotetraose or corresponding sialo-glycolipids prevents the easy degradation of the B-protein of cholera toxin into protein subunits by sodium dodecylsulfate.

Untersuchungen zur Bindung von Liganden an Choleratoxin, I: Über den lipophilen Anteil der Sialoglycolipide

Zusammenfassung: Die Bindung von Choleratoxin durch das Gangliosid $G_{Gtet}1$ hängt sowohl von der Natur des Kohlenhydrates wie des Lipidteils des Glykolipids ab. Die Bedeutung des Lipidteils für die Bindung an das Toxin wurde unter Anwendung synthetischer Gangliosid-Analoga (Gangliosidoide) untersucht. Die Wechselwirkung zwischen Glykolipid und dem Toxin wurde verfolgt an Hand der Präzipitation, der Verhinderung der Toxizität sowie in der Polyacrylamidgel-Elektrophorese. Zur spezifischen Präzipitation wird ein Lipid-Teil benötigt, mindestens in der Größe einer aliphatischen Kette von 14 C-Atomen. Mit einigen der Gangliosidoide bildet Choleratoxin hochmo-

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Enzyme:
Galactose oxidase, D-galactose:oxygen 6-oxidoreductase (EC 1.1.3.9).

Abbreviations:
Ganglioside $G_{Gtet}1$ = II^{3}NeuAc-GgOse$_4$-Cer, designation as recommended by IUPAC-IUB Lipid Nomenclature Document, 1976, for the monosialo-gangliotetraosyl-ceramide = Galβ1→3GalNAcβ1→4Gal[3←2αNeuAc]β1→4Glc-Cer. Other abbreviations used for this ganglioside include A_2(Klenk), G_{M1}(Svennerholm), G4 (Korey and Gonatas) and GGnSLC(Mc Cluer).

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