

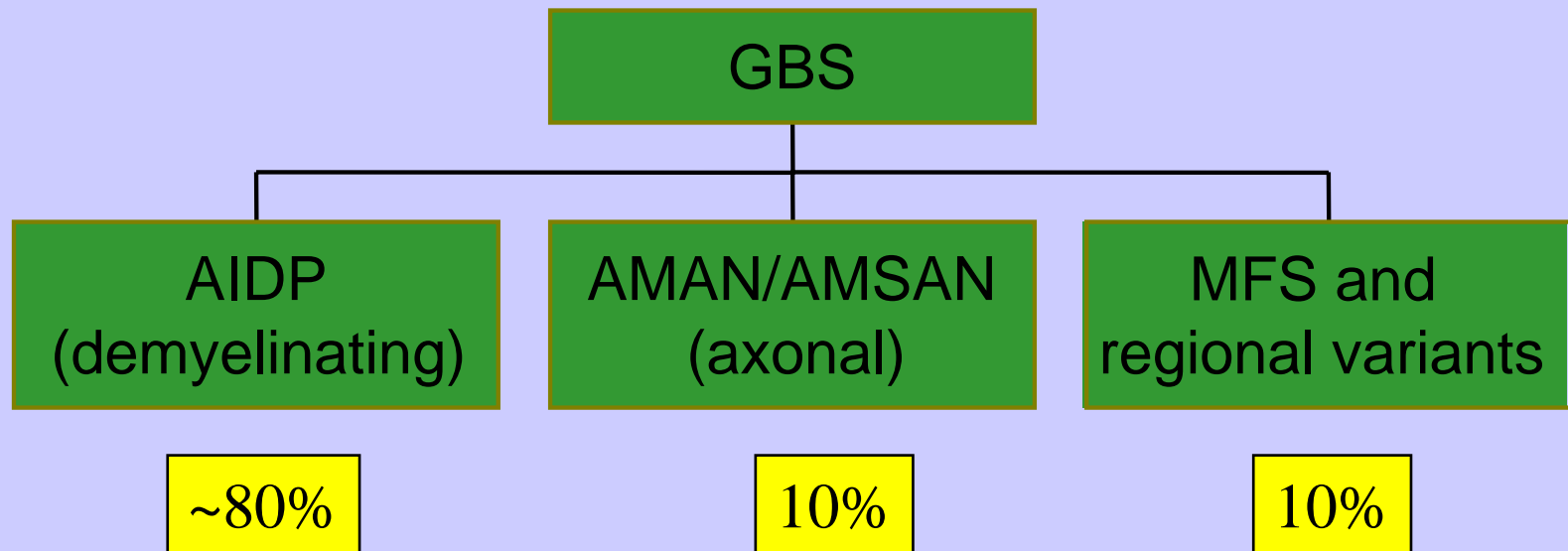


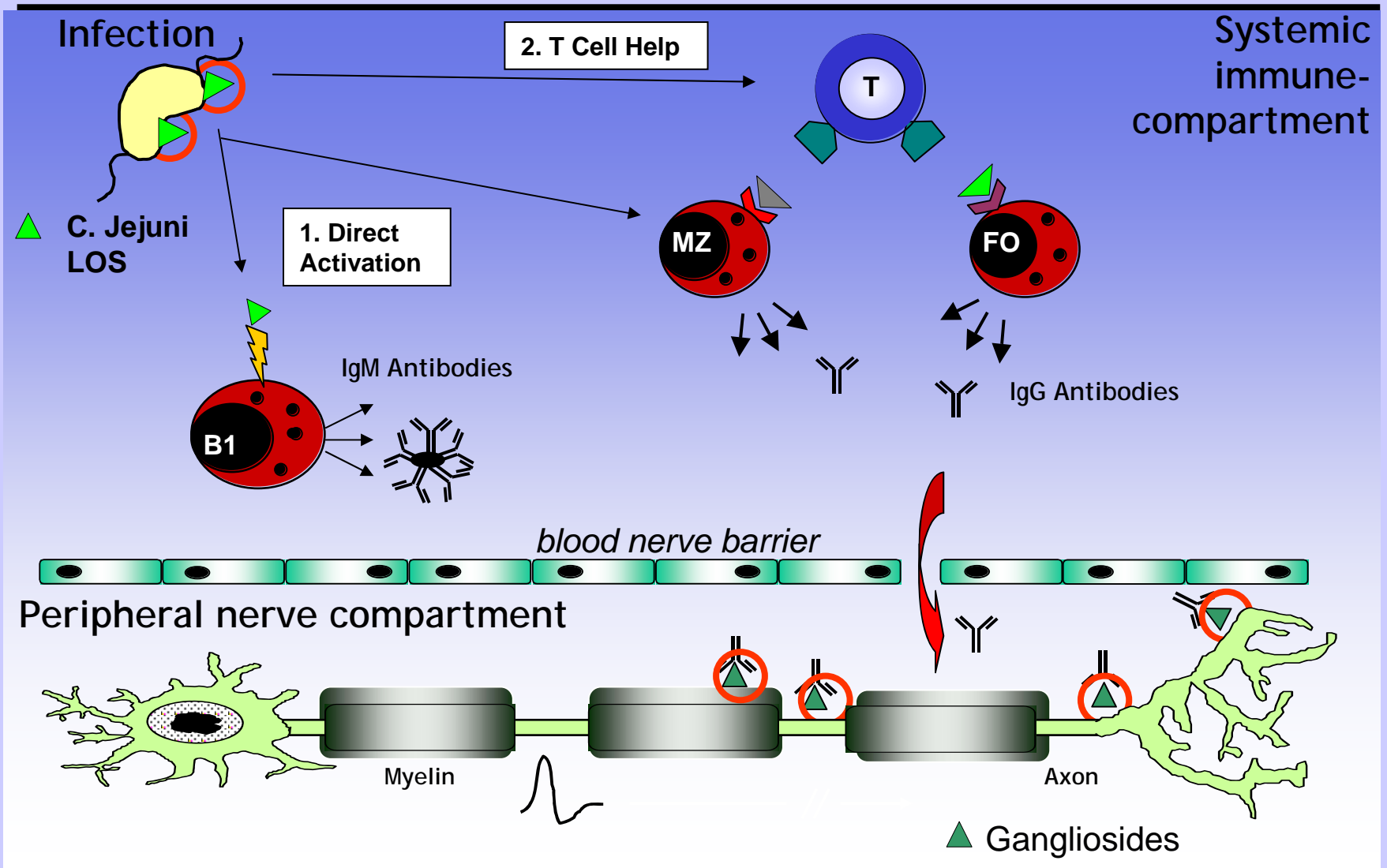
10th Course
Therapeutic Frontiers in Neurology
March 10-13 2010, Bergamo

**Monoclonal antibody to C5 protects motor
nerves in murine autoimmune neuropathy**

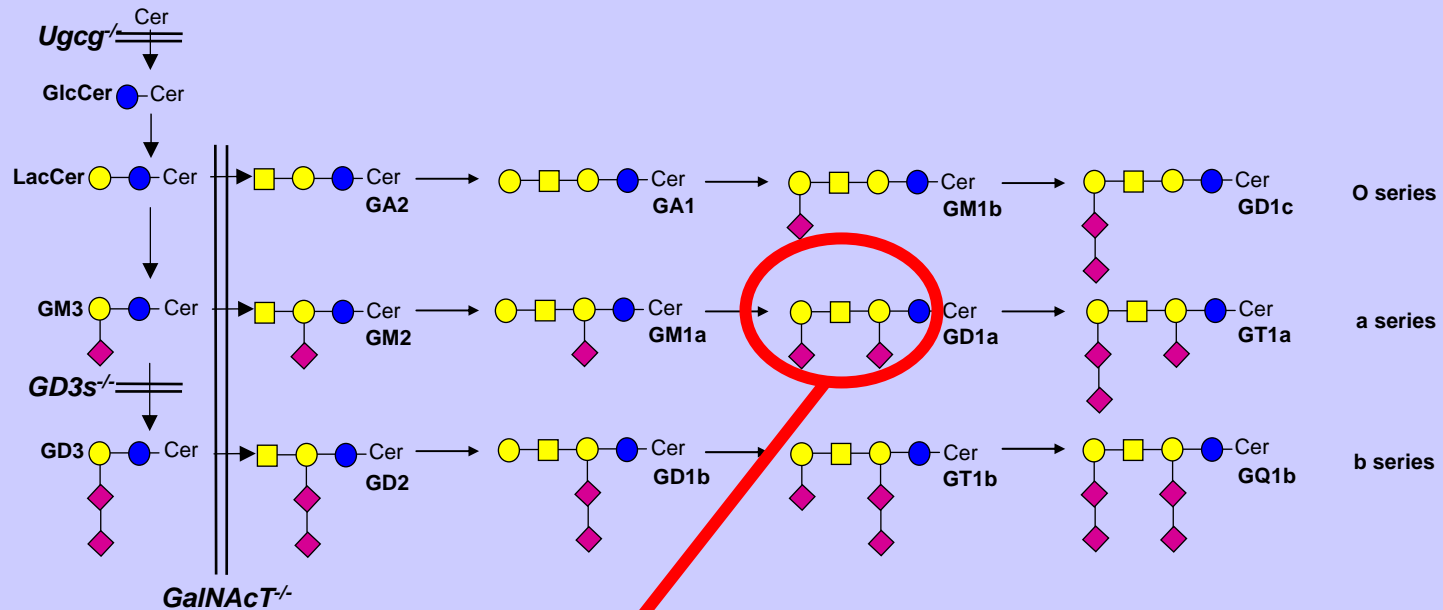
Hugh Willison
University of Glasgow

GBS CAN BE SEPARATED INTO DISTINCT CLINICAL SUBTYPES BY VARIOUS CLINICAL, ELECTROPHYSIOLOGICAL AND LABORATORY FEATURES

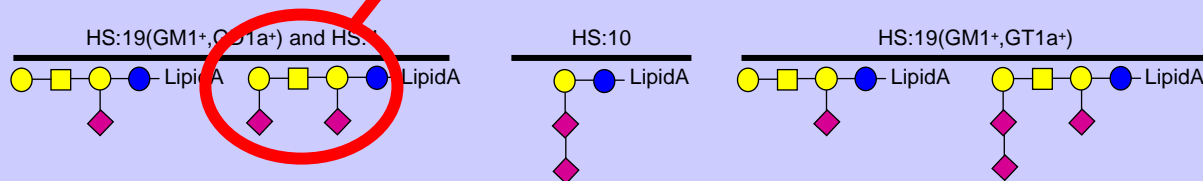




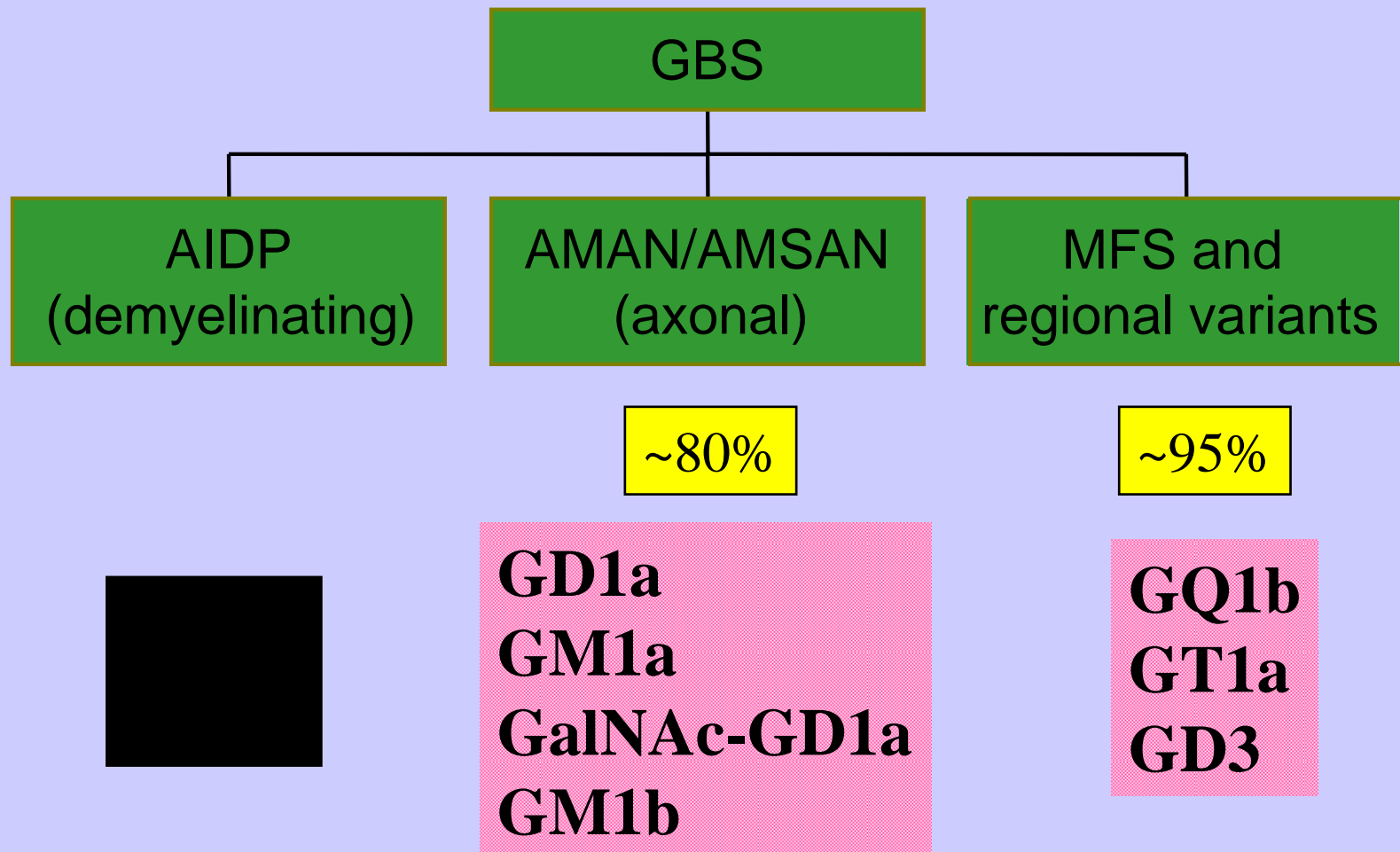
A simplified scheme of the ganglioside biosynthetic pathway



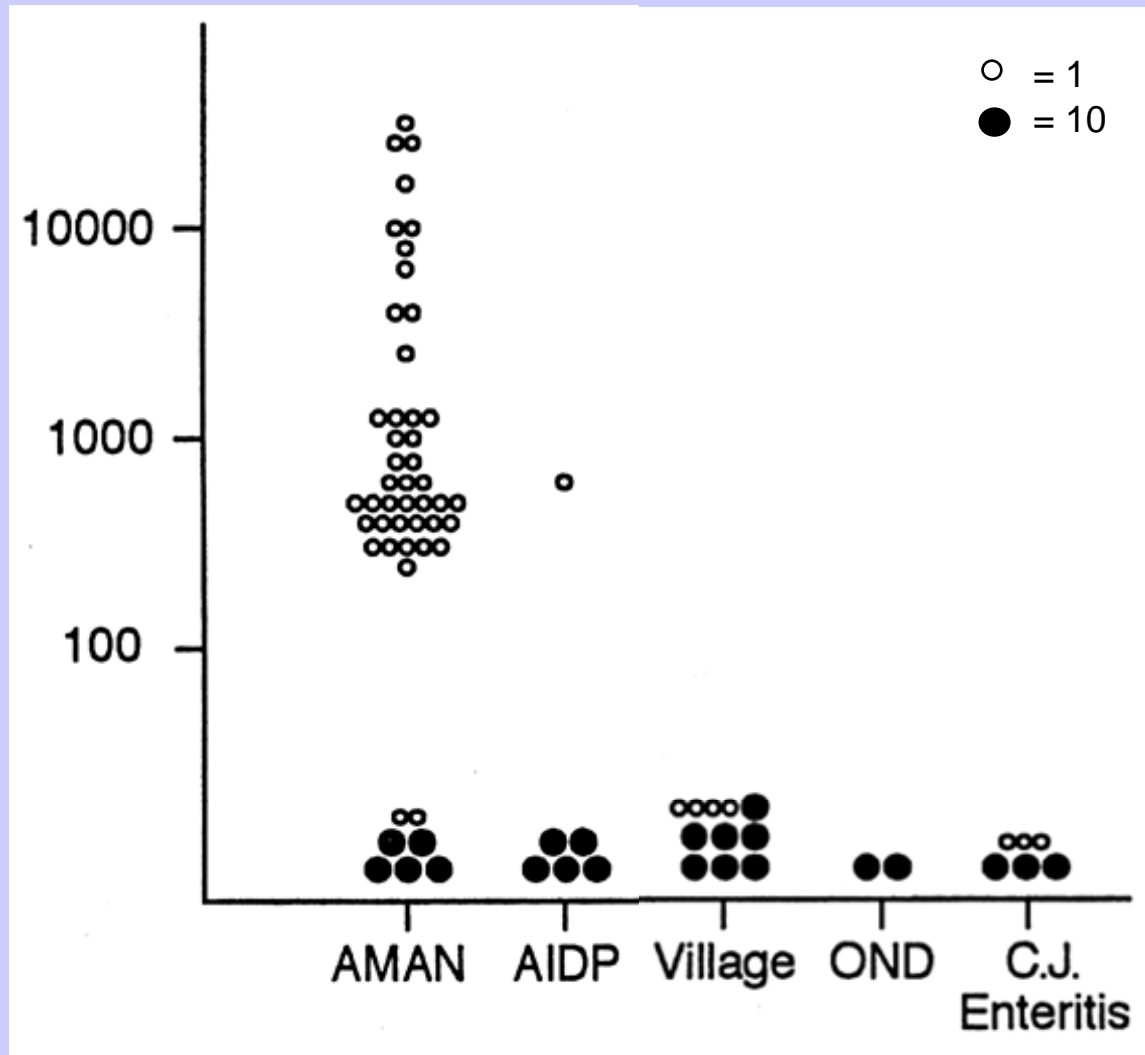
Examples of GBS-associated *C. jejuni* LOS structures



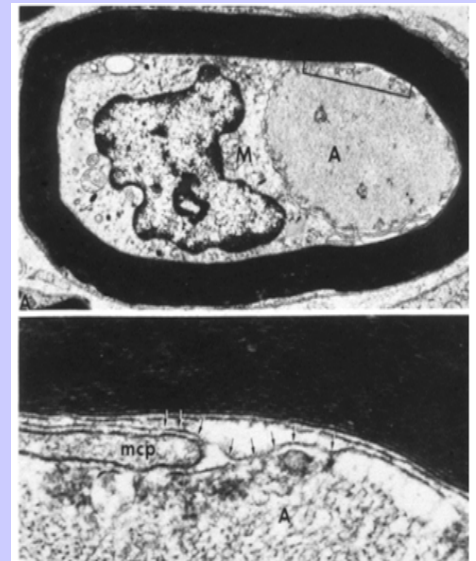
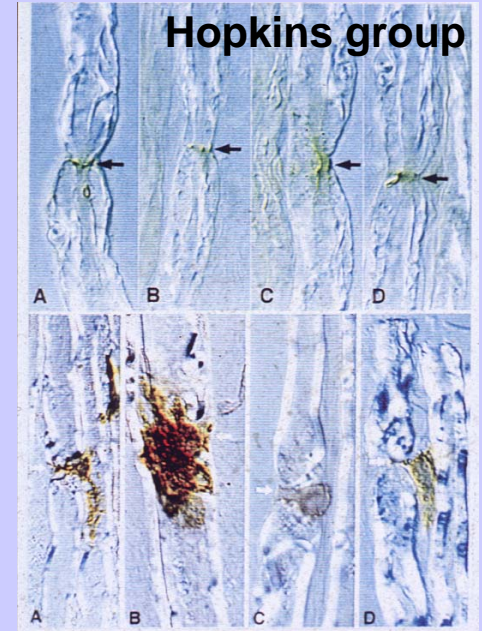
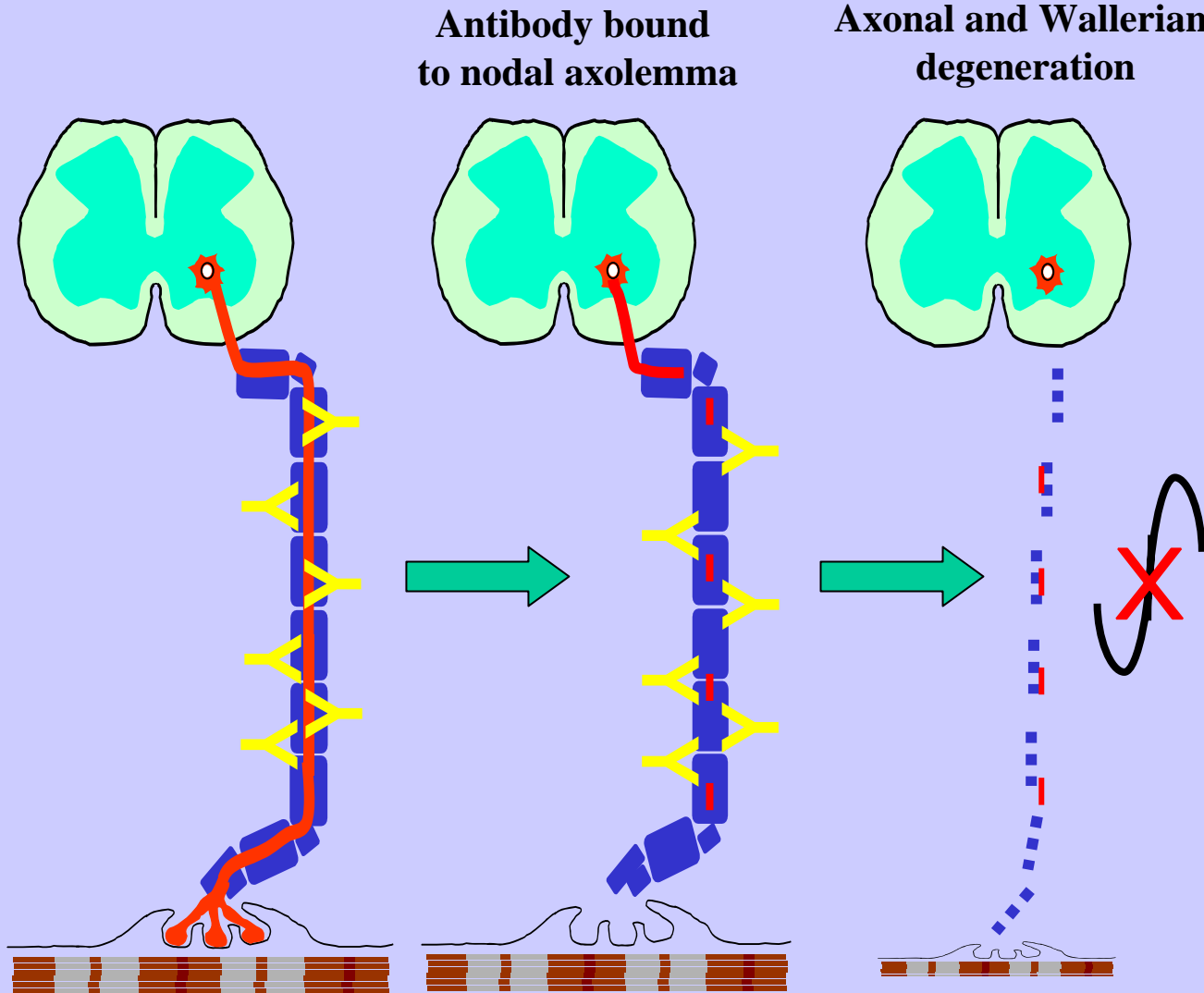
Key
 ● Galactose
 ■ GalNAc
 ● Glucose
 ◆ NeuNAc
 Cer Ceramide



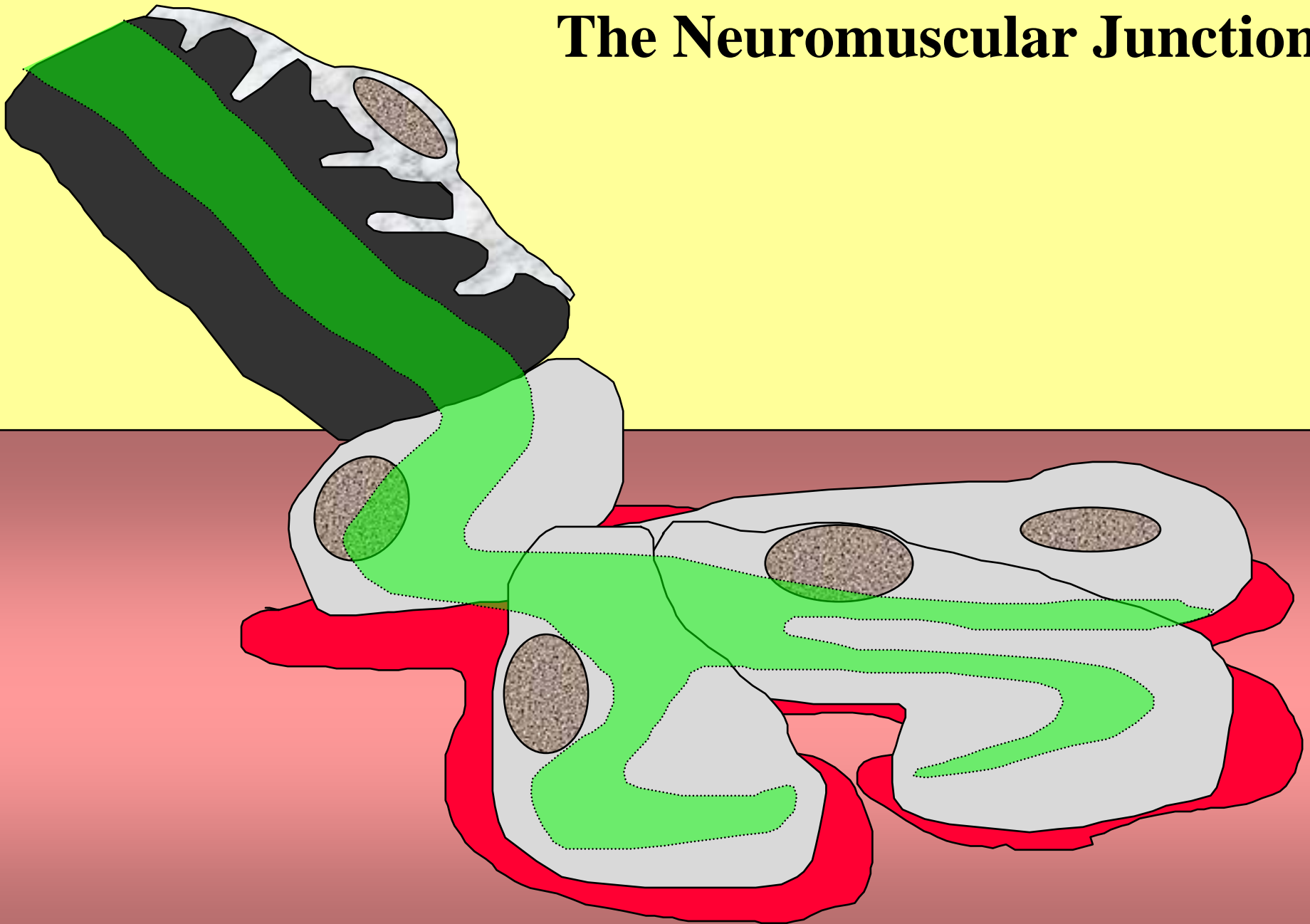
Anti-GD1a IgG antibodies are highly associated with the axonal form of post-Campylobacter GBS (AMAN) in rural China



IMMUNOPATHOGENESIS OF AMAN



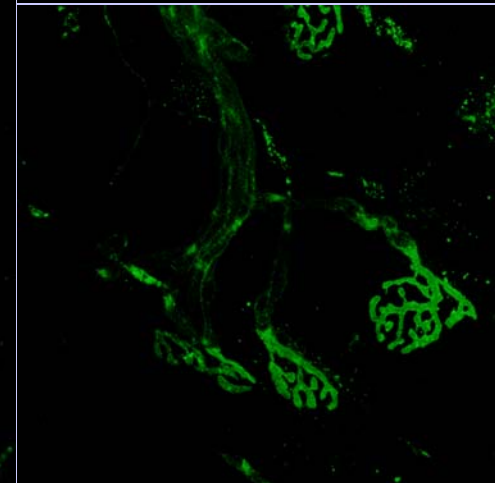
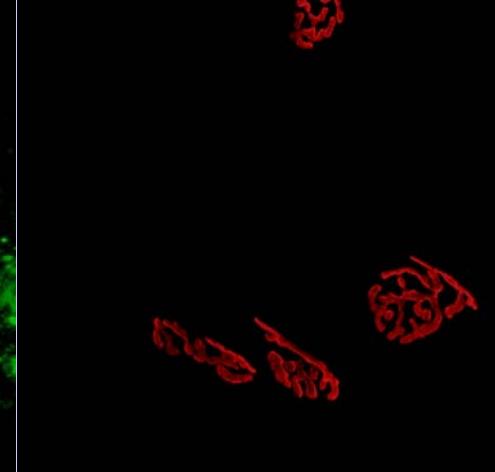
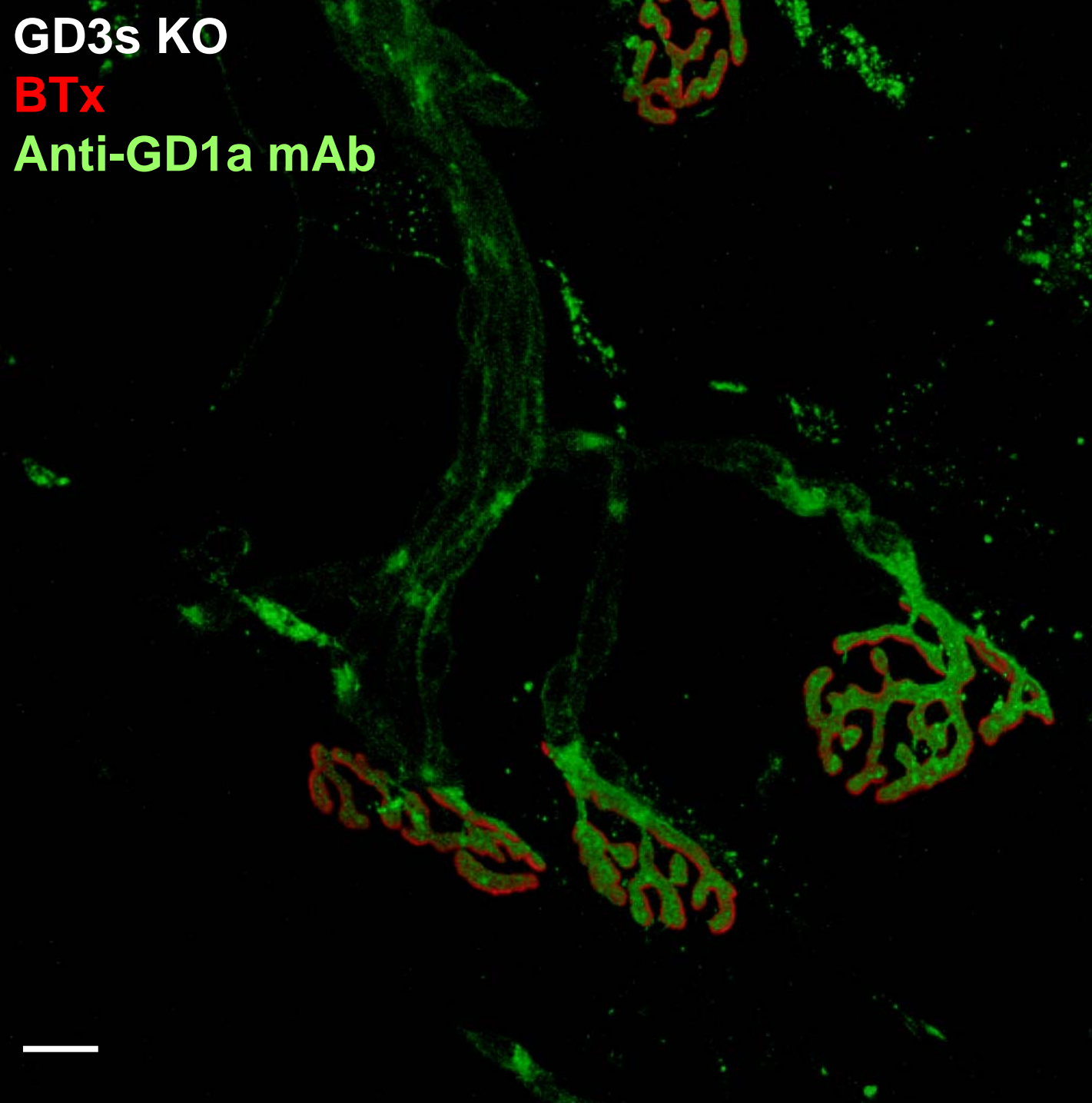
The Neuromuscular Junction



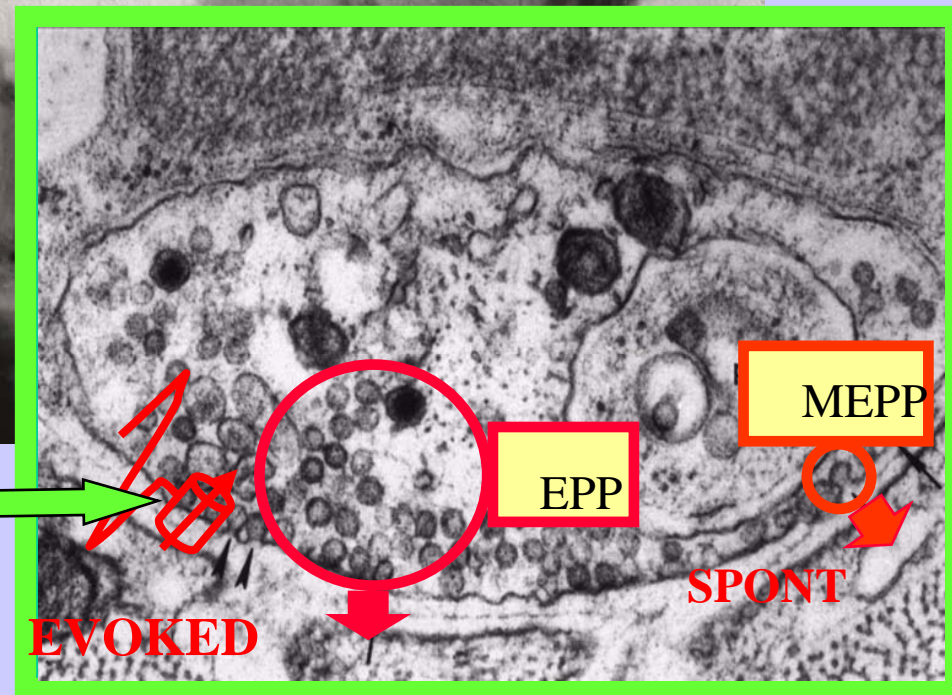
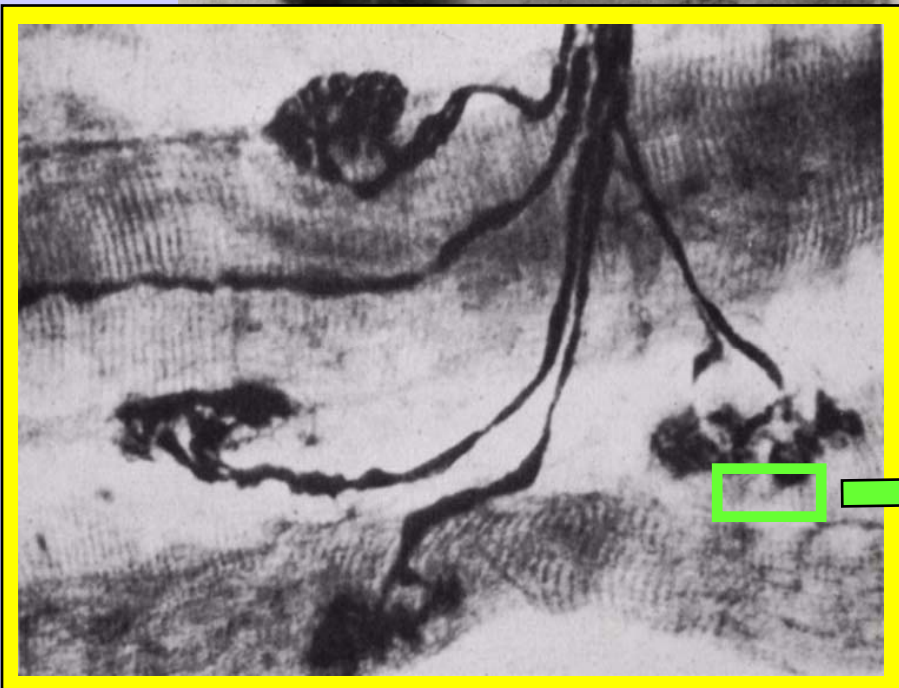
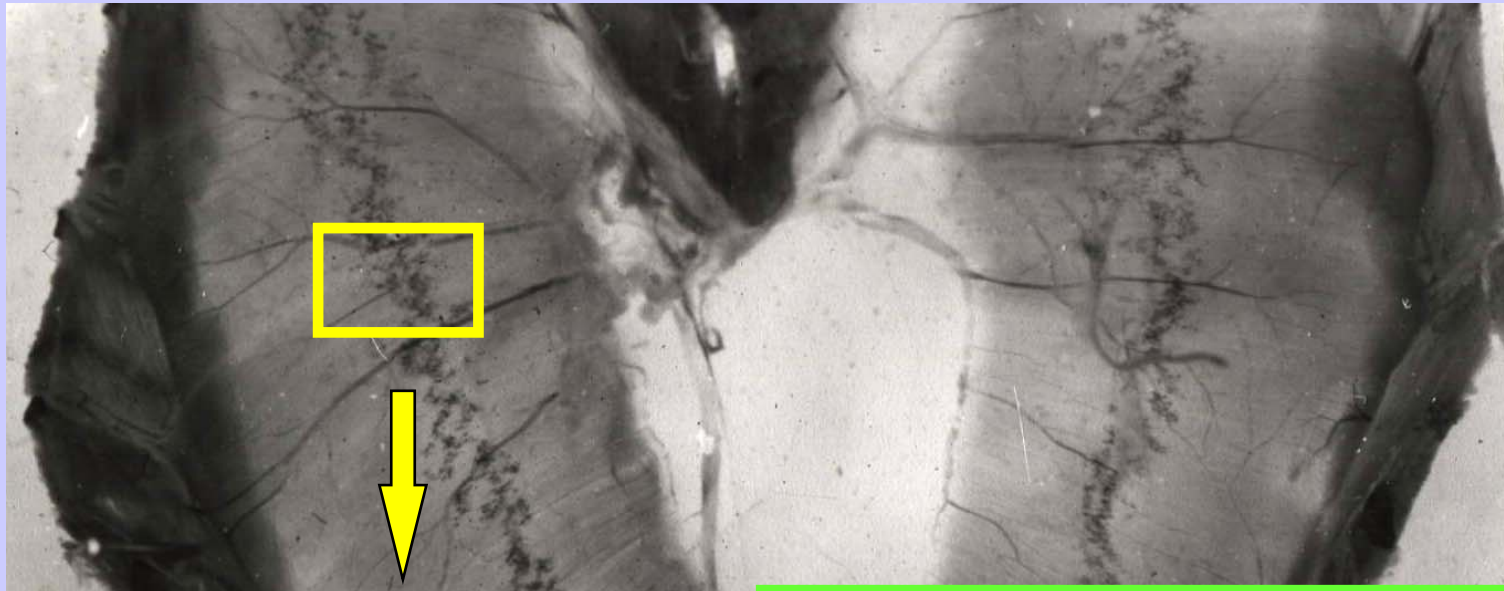
GD3s KO

BTx

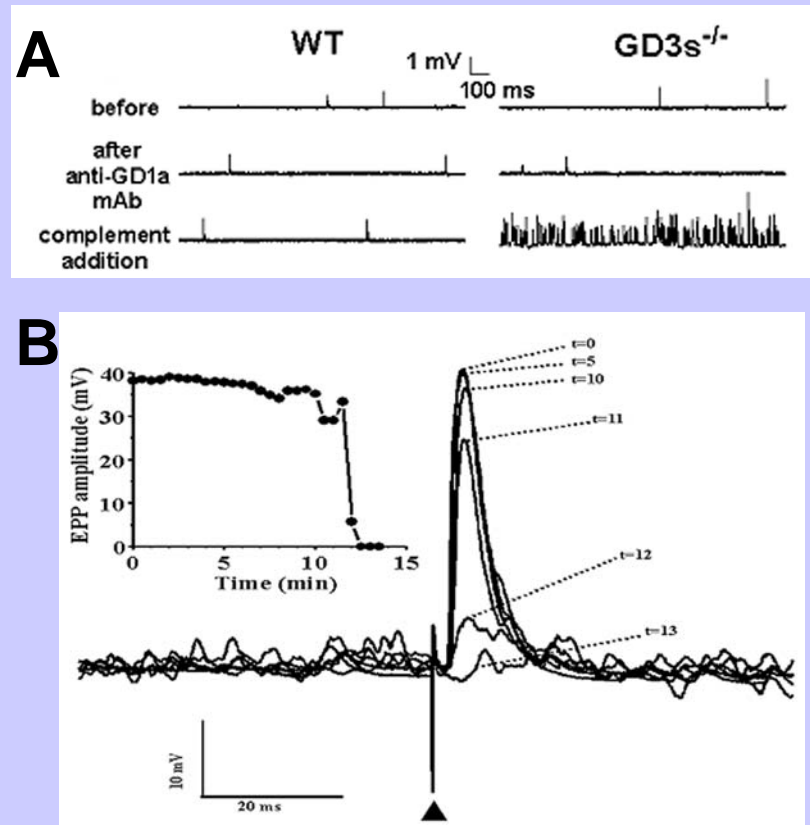
Anti-GD1a mAb



The mouse hemi-diaphragm electrophysiology preparation

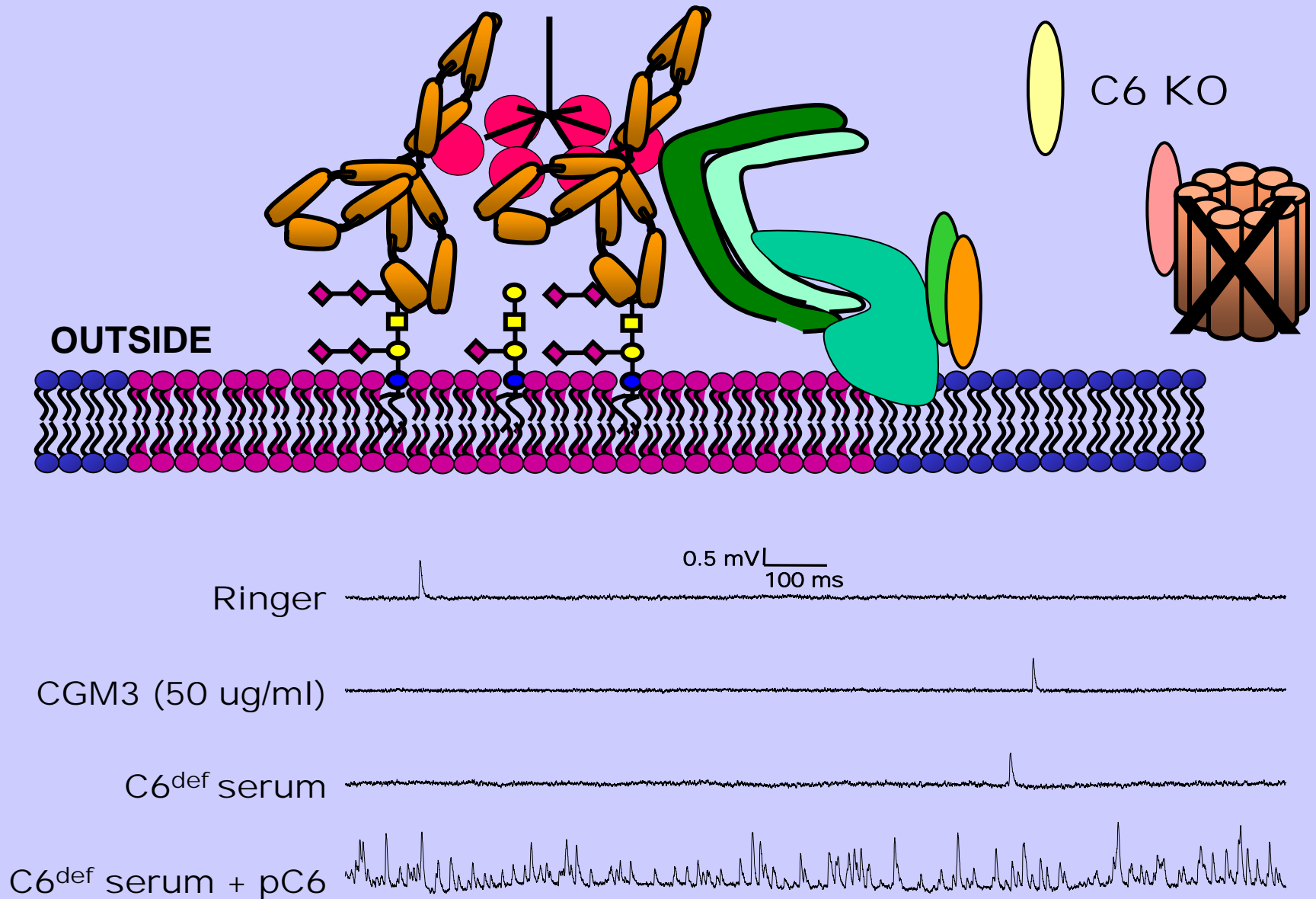


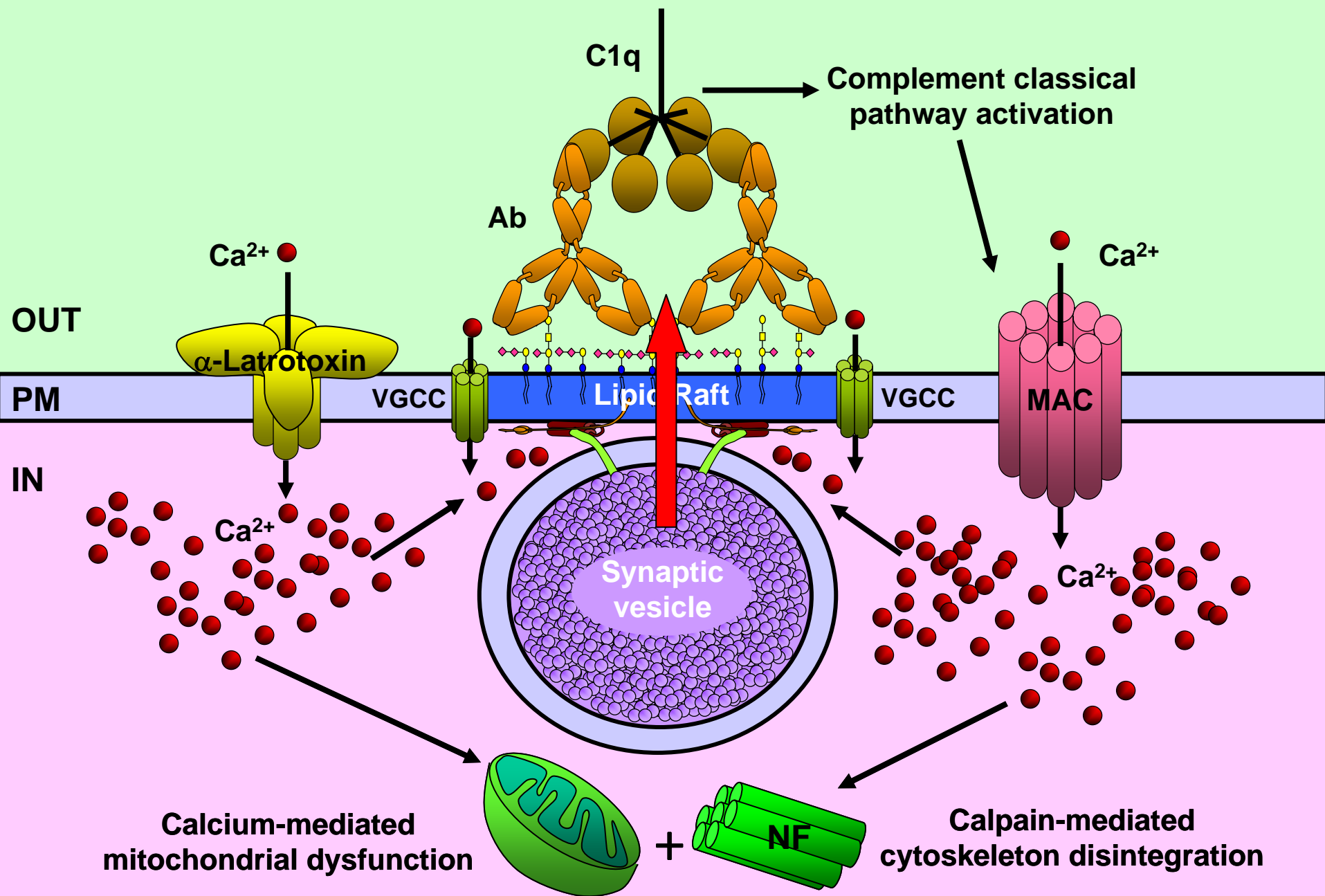
MEPP FREQUENCIES RISE AT GD3s^{-/-} (HIGH GD1a) ENDPLATES



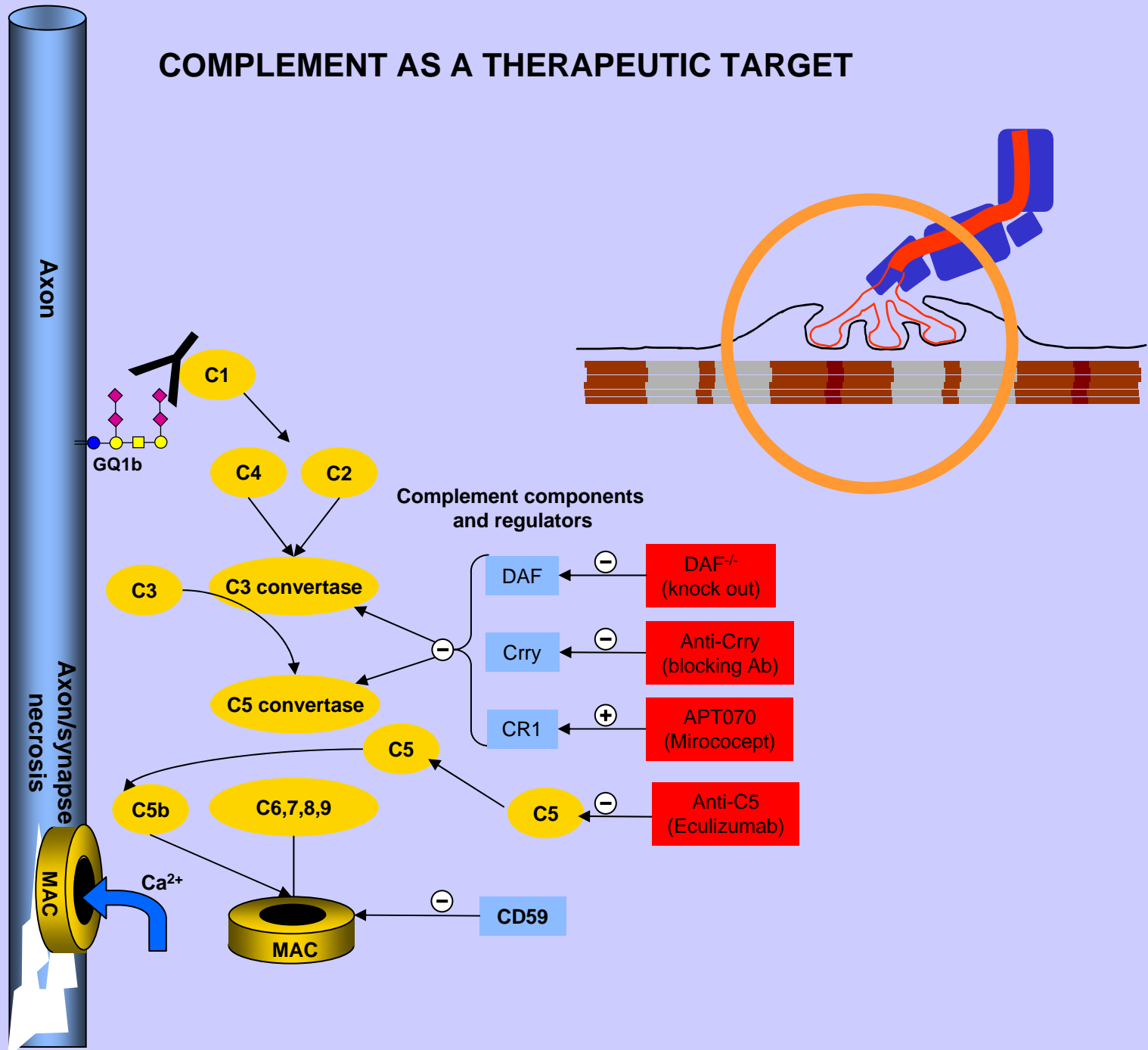
EPP AMPLITUDES DROP
THEN DISAPPEAR AT GD3s^{-/-}
(HIGH GD1a) ENDPLATES

**Anti-GQ1b/LOS antibody has no LTx-like effect
under C6 deficiency conditions (i.e. no MAC)**





COMPLEMENT AS A THERAPEUTIC TARGET

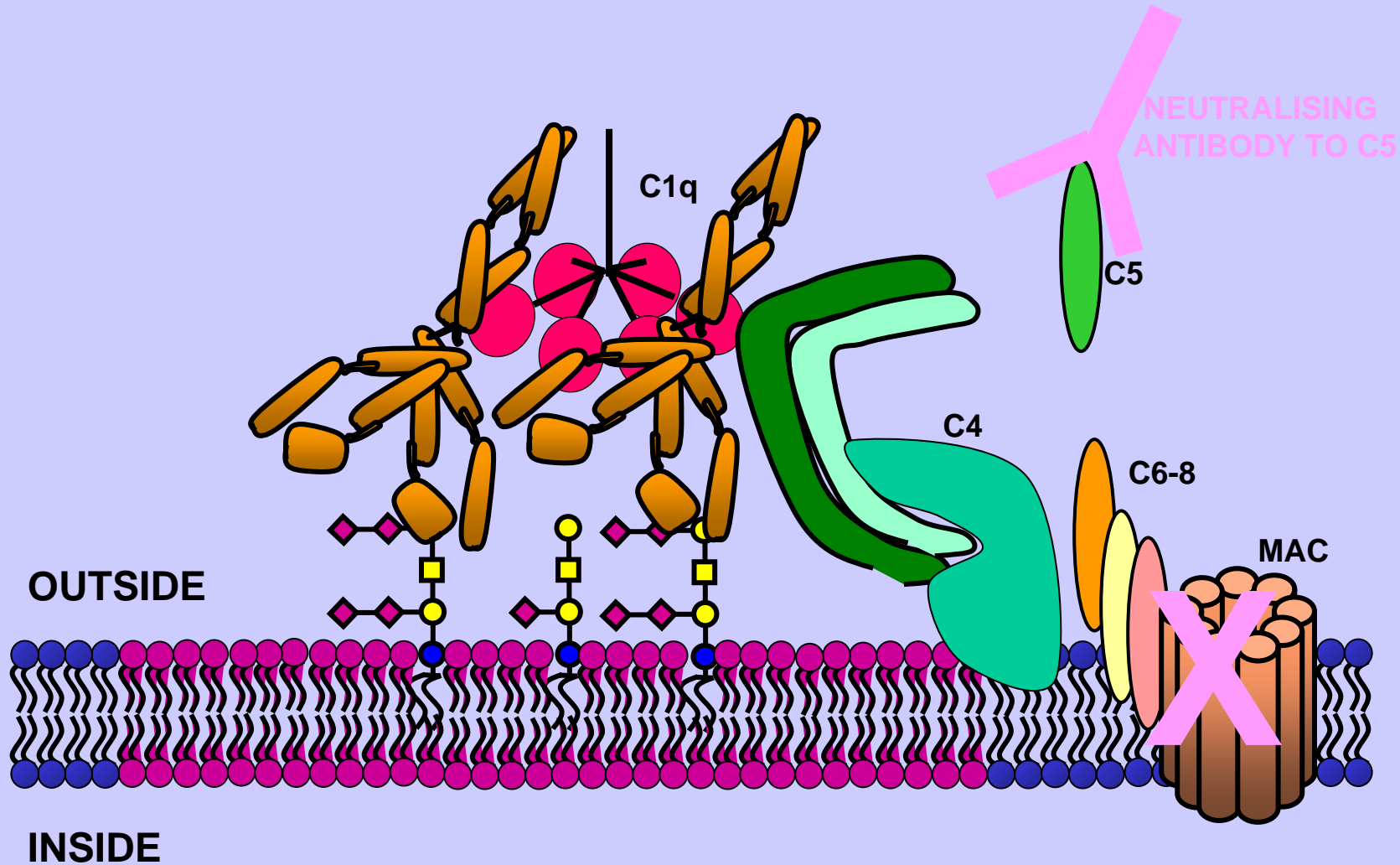


ORIGINAL ARTICLE

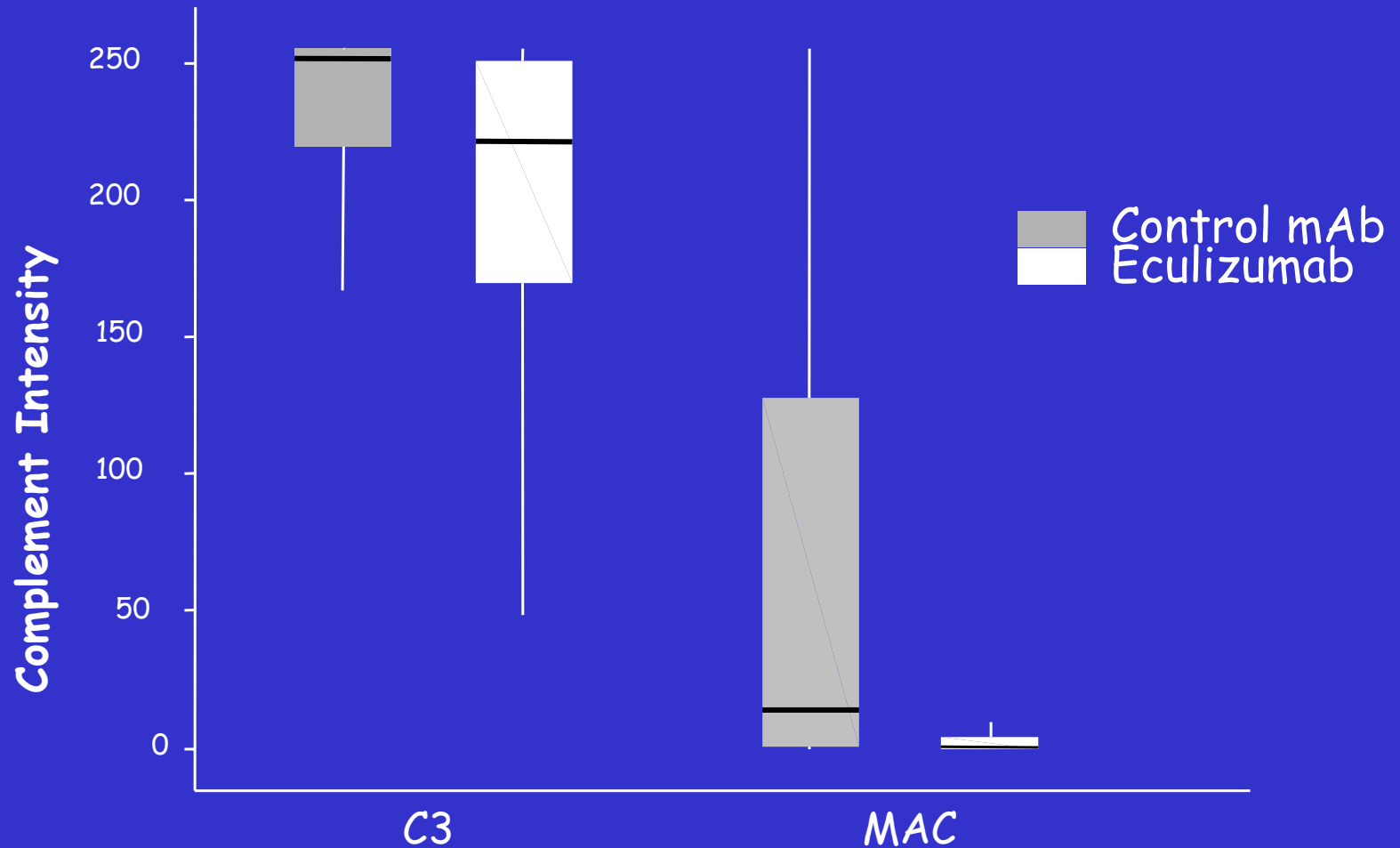
The Complement Inhibitor Eculizumab in Paroxysmal Nocturnal Hemoglobinuria

Peter Hillmen, M.B., Ch.B., Ph.D., Neal S. Young, M.D., Jörg Schubert, M.D.,
Robert A. Brodsky, M.D., Gerard Socié, M.D., Ph.D., Petra Muus, M.D., Ph.D.,
Alexander Röth, M.D., Jeffrey Szer, M.B., B.S., Modupe O. Elebute, M.D.,
Ryotaro Nakamura, M.D., Paul Browne, M.B., Antonio M. Risitano, M.D., Ph.D.,
Anita Hill, M.B., Ch.B., Hubert Schrezenmeier, M.D., Chieh-Lin Fu, M.D.,
Jaroslaw Maciejewski, M.D., Ph.D., Scott A. Rollins, Ph.D.,
Christopher F. Mojcik, M.D., Ph.D., Russell P. Rother, Ph.D., and Lucio Luzzatto, M.D.

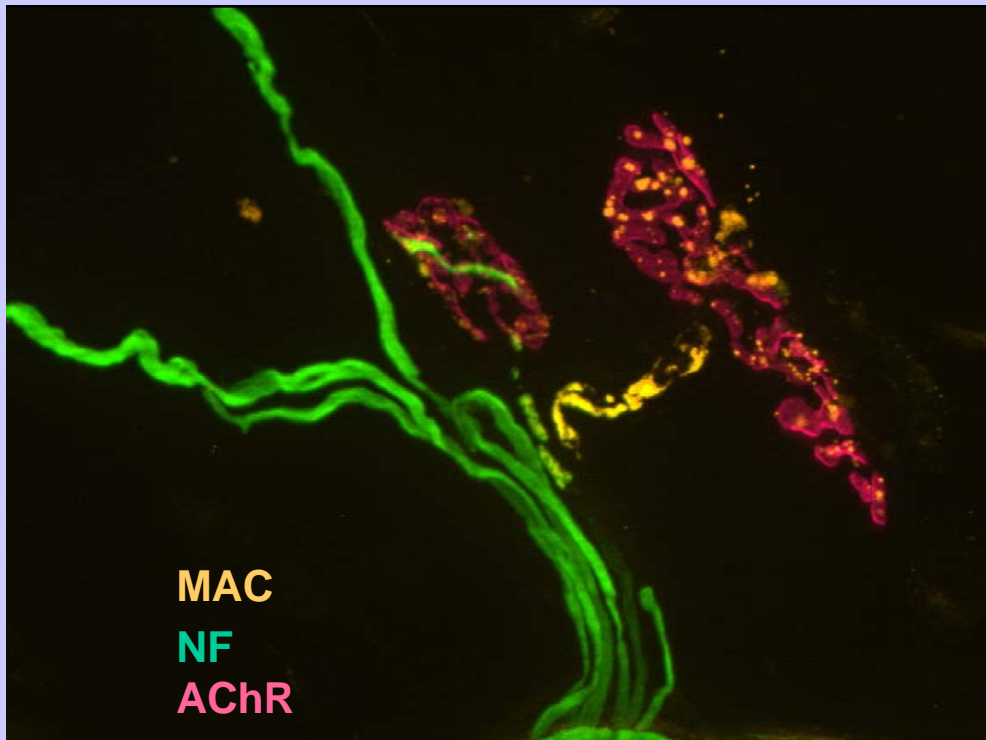
Prevention of MAC pore formation through inhibition of C5



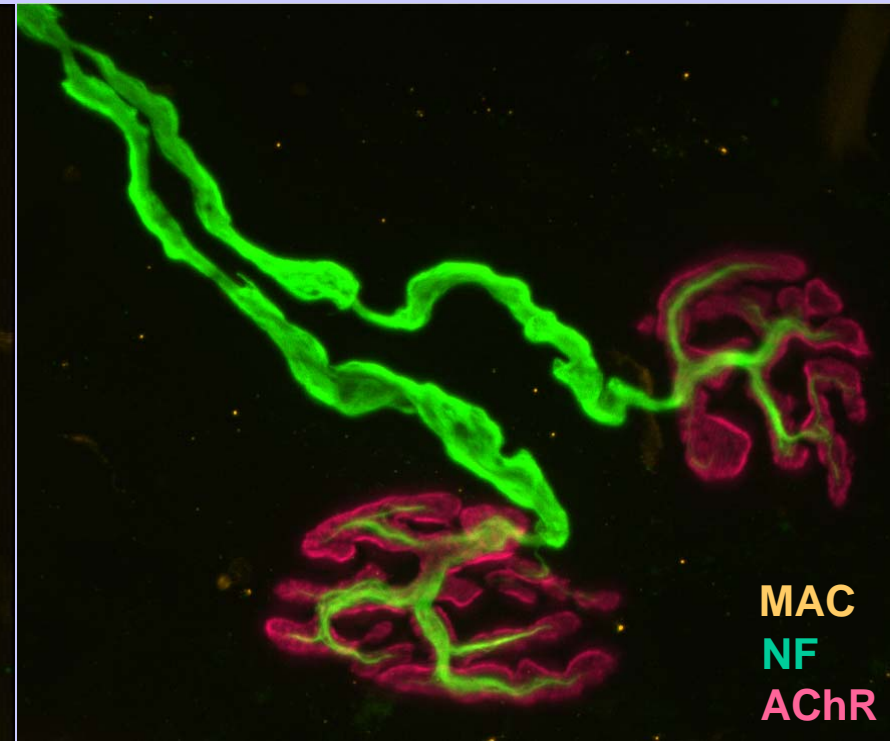
In vivo complement deposits



**NEUROPROTECTION BY ECULIZUMAB ALSO OCCURS IN MICE
EXPOSED TO ANTI-GQ1b ANTIBODY AND COMPLEMENT *IN VIVO***



Control mAb



Anti-C5, eculizumab

GBS pathogenesis: a current model based on ganglioside/LOS mimicry

