CD38 and Ceramide-Enriched Membrane Platforms in Bovine Coronary Myocytes

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Background

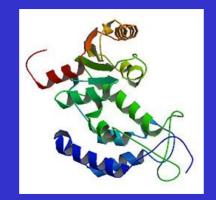
Ceramide-enriched microdomains





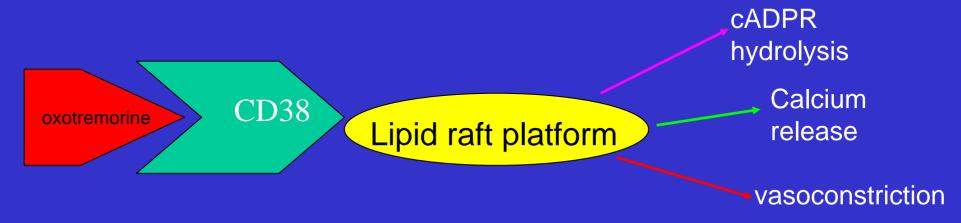
Oxotremorine

- CD38
- 45 kDa



Hypothesis

 Lipid raft membrane microdomains are involved in oxotremorine-induced CD38 activation in bovine coronary myocytes.



Methods

- •DMT Myograph: tension recording studies of fresh bovine myocardial vasculature
- •Vasoconstrictor: Oxotremorine (20 uM, 40 uM, 60 uM, 80 uM)
- •Drugs: Methyl-ß-cyclodextrin (1mM), desipramine (0.1 mM), filipin (1µg/mL), nicotinamide (6mM), treated for 15 minutes

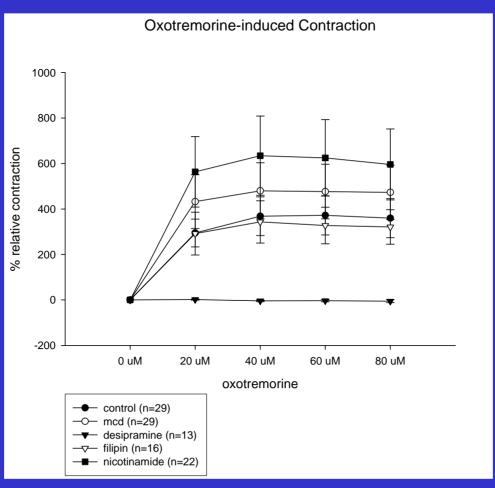
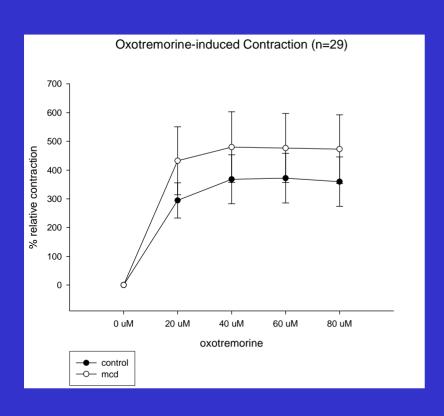
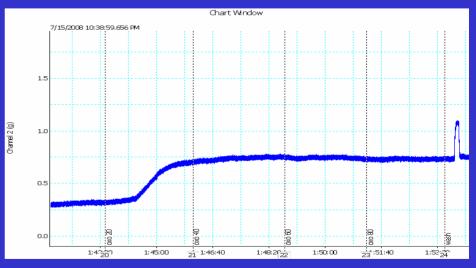
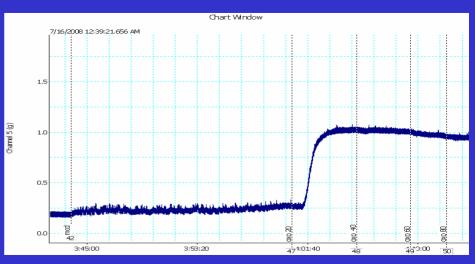


Fig. 1. Effect of LR inhibitors on oxotremorine-induced constriction

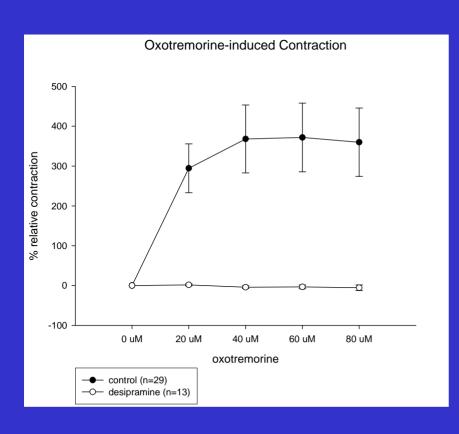
Methyl-ß-cyclodextrin vs. Control

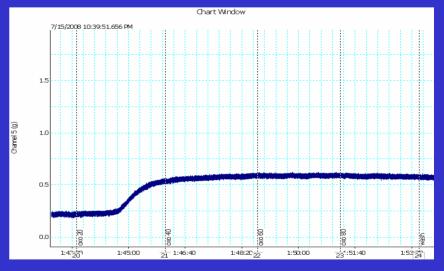


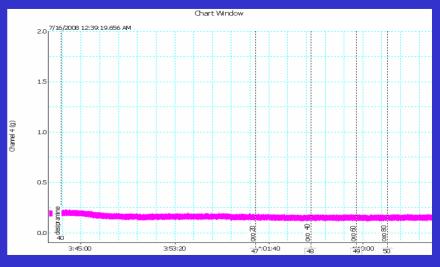




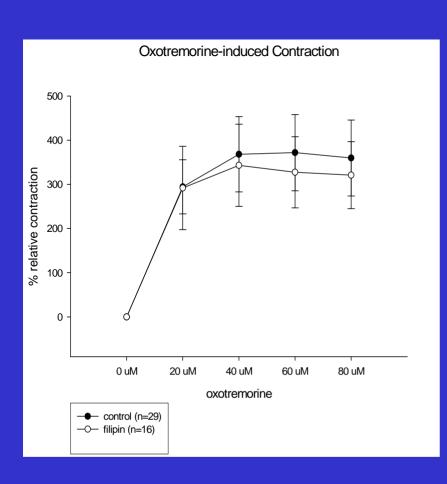
Desipramine vs. Control

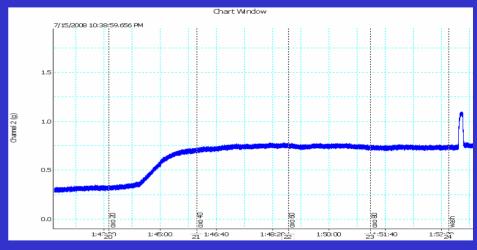


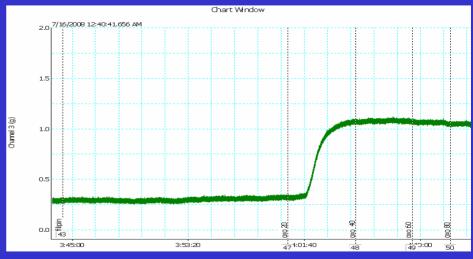




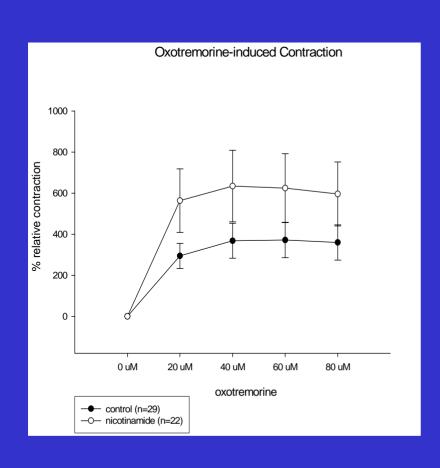
Filipin vs. Control

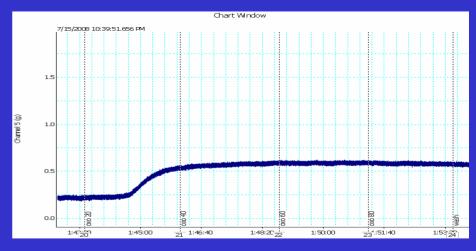


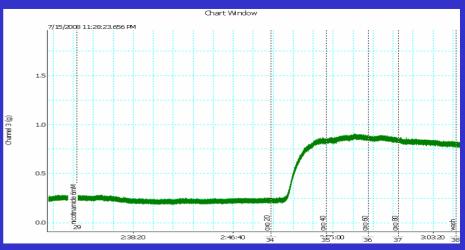


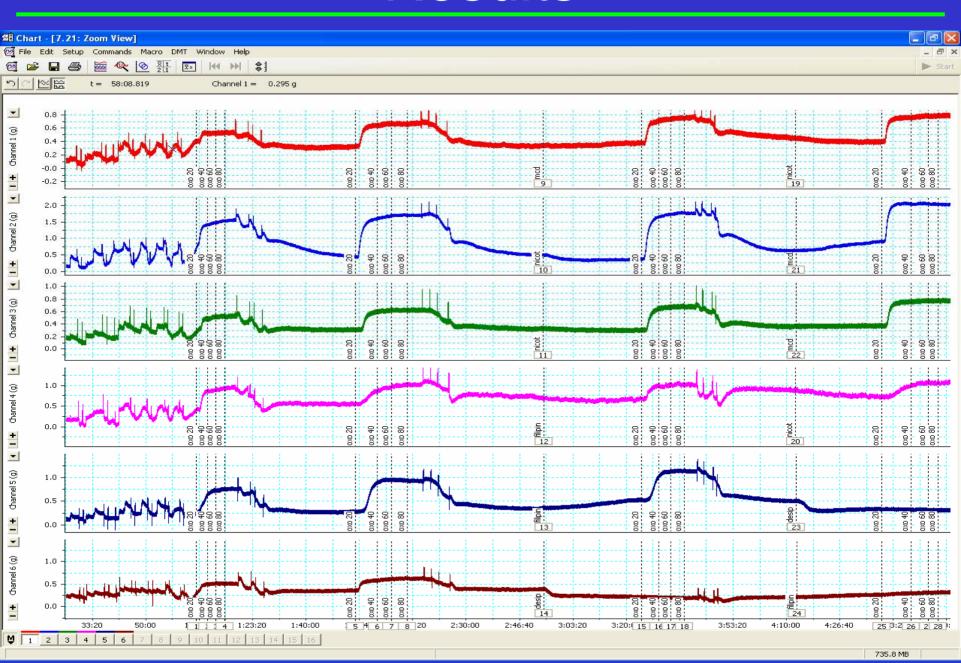


Nicotinamide vs. Control









Discussion

- CD38 as receptor and enzyme
- ASM inhibition
- Role of ceramide in CD38 activation?
- Raft aggregation and oxotremorine stimulation

Questions and Future Directions

- Inhibitor concentrations
- Oxotremorine dosage levels
- Myograph-specific conditions?

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VCU Pharmacology & Toxicology