CD38 and Ceramide-Enriched Membrane Platforms in Bovine Coronary Myocytes

July 31, 2008
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Summer Program for Undergraduate Research 2008
Background

- Ceramide-enriched microdomains
  - Sphingomyelin
  - ASM
  - Ceramide
  - Lipid rafts
  - De novo
- 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-β-cyclodextrin (1mM), desipramine (0.1 mM), filipin (1µg/mL), nicotinamide (6mM), treated for 15 minutes
Results

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

Oxotremorine-induced Contraction

- oxotremorine
- % relative contraction
- control (n=29)
- mcd (n=29)
- desipramine (n=13)
- filipin (n=16)
- nicotinamide (n=22)

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

Methyl-ß-cyclodextrin vs. Control

Oxotremorine-induced Contraction (n=29)
Results

Desipramine vs. Control

Oxotremorine-induced Contraction

- Desipramine (n=13)
- Control (n=29)
Results
Filipin vs. Control

Oxotremorine-induced Contraction

- Control (n=29)
- Filipin (n=16)
Results
Nicotinamide vs. Control

Oxotremorine-induced Contraction

% relative contraction

oxotremorine

- control (n=29)
- nicotinamide (n=22)
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?
Acknowledgements

• Dr. Li and Dr. Zou
  - special thanks for making this summer possible

• VCU Pharmacology & Toxicology