

**Stony Brook University
The Graduate School**

Doctoral Defense Announcement

Abstract

Hepatocyte-Specific Endocytic Activity Exhibited by the Coxsackie and Adenovirus
Receptor (CAR)

By

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Much of the current knowledge of the coxsackie and adenovirus receptor (CAR) stems from the study of infection of cell cultures by human subgroup B coxsackieviruses and many adenovirus serotypes (Ad), which use CAR for attachment to susceptible cells. Apart from viral infection, knock-out mutations in mice determined that CAR plays a vital role in the development of cardiac tissue during embryogenesis. Many adult tissues also maintain CAR expression at relatively high levels and the importance of sustained CAR expression in these tissues has not been elucidated. A notable limitation of most investigations of CAR cell biology reported to date is that the studies were confined to cell culture models, which may not fully reconstitute the *in vivo* environment. Here, the behavior of CAR expressed in rodent adult liver and prostate tissue was investigated using the Ad-derived knob domain as a monospecific ligand for CAR. The results of these experiments revealed two distinct tissue-specific CAR functions in cell culture as well as *in vivo*. Intravenous injection of knob in male mice stimulated the secretion of two proteins indigenous to the prostate ventral lobe into the mouse urine. The manner by which knob affects this secretion appears to reinforce traditional models established in cell culture, where CAR functions as an epithelial cell adhesion molecule contributing to the maintenance of the paracellular permeability barrier. In strong contrast, CAR on the surface of hepatocytes demonstrated rapid, receptor-mediated endocytosis of knob ligand with subsequent delivery to lysosomes where knob was degraded. This is the first direct evidence of efficient ligand endocytosis mediated by CAR that is recapitulated in an animal model.

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