

## Overexpression of Coxsackie-Adenovirus Receptor, Interferon $\beta$ , Peroxisome Proliferator-Activated Receptor $\gamma$ , and Heat Shock Protein 72 in Transgenic HIV-1-Positive Fischer Rat Hearts Following Chronic Alcohol Administration.

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### Background and hypothesis

To date, possible pathogenic interactions between alcohol and HIV-1 in the heart have not been well investigated. We hypothesized that pathogenic cooperation between HIV-1 and alcohol exposure might lead to myocardial injury. To identify possible genetic mechanisms of action linking these pathogenic factors, the aim of this study was to determine mRNA expression levels for the Coxsackie virus and adenovirus receptor (*Cxadr*), interferon  $\beta$ 1 (*Ifnb1*), peroxisome proliferator-activated receptor  $\gamma$  (*Pparg*), and myocardial heat shock protein 72 (*Hsp72i*) following chronic alcohol exposure in a transgenic HIV-1+ rat model.

### Methods

We determined mRNA expression levels for *Cxadr*, *Ifnb1*, *Pparg*, and *Hsp72i* using RT-PCR with subsequent delta-delta Ct analysis in 4 groups of laboratory animals: group 1 consisted of normal control Fischer rats unexposed to alcohol; group 2, of rats fed alcohol for 12 weeks; group 3, of transgenic HIV-1+ rats unexposed to alcohol; and group 4, of transgenic HIV-1+ transgenic rats fed alcohol for 12 weeks (n=6 in each group). Morphological analyses of 6 micron sections of heart stained with Tri-Chrome were performed as well.

### Results

Table I shows RT-PCR analysis of mRNA expression levels in the experimental animals as fold increases in comparison with controls. \* - statistically significant differences (p<0.05)

Morphological changes in the myocardium of rats fed alcohol for 12 weeks were characterized by slight cellular and nuclear hypertrophy. As expected, the HIV-1+ group that remained unexposed to alcohol had mild fibrosis. This fibrosis was more severe, specifically around the perivascular areas, in the HIV-1+ group exposed to alcohol. Additionally, myofilament disruption, as assessed by light microscopy, was present in the myocardium of the latter group.

### Conclusions

To our knowledge, this is the first study of *Cxadr* and *Pparg* overexpression in an alcohol-induced heart injury model and in HIV-1+ transgenic animals. In addition, we found increased expression of *Ifnb1* and *Hsp72i* in the HIV-1+ group exposed to alcohol. *Cxadr* and *Ifnb1* overexpression may provide a link between chronic alcohol intake and the first steps of alcohol-induced cardiac damage in promoting heart muscle damage. Severe myocardial damage positively correlated with the highest levels of *Cxadr*, *Ifnb1*, *Pparg*, and *Hsp 72i* expression in alcohol-fed HIV-1 transgenic animals, providing additional evidence suggesting pathogenic cooperation between HIV-1 and alcohol exposure leading to myocardial injury.

mRNA expression evaluation	Control	Alcohol, folds and 95 % CI	HIV, folds and 95 % CI	HIV+Alcohol, folds and 95 % CI
<i>Cxadr</i>	1(0.8-1.2)	<b>3.6(2.4-5.4)*</b>	<b>4.3(2.2-8.2)*</b>	<b>8.5(6.8-10.5)*</b>
<i>Ifnb1</i>	1(0.3-3.0)	3.2(1-9.9)	0.6(0.2-1.5)	<b>11.8(7.8-17.7)*</b>
<i>Hsp72i</i>	1 (0.6-1.6)	2.6 (1.5-4.5)	1.1(0.48-2.9)	<b>4.5(2.9-7.2)*</b>
<i>Pparg</i>	1 (0.9-1.1)	<b>2.7 (1.5-4.6) *</b>	<b>5.5 (4.2-7.1)*</b>	<b>7.6 (5.8-10)*</b>