

**Apoptosis in HCV and HCV/HIV
Coinfected Patients:
Evaluation Using M30 Serum
Caspase Assay**

**Philippe J. Zamor, Susan D. Rouster,
and Kenneth E. Sherman**

University of Cincinnati College of Medicine
Cincinnati, OH

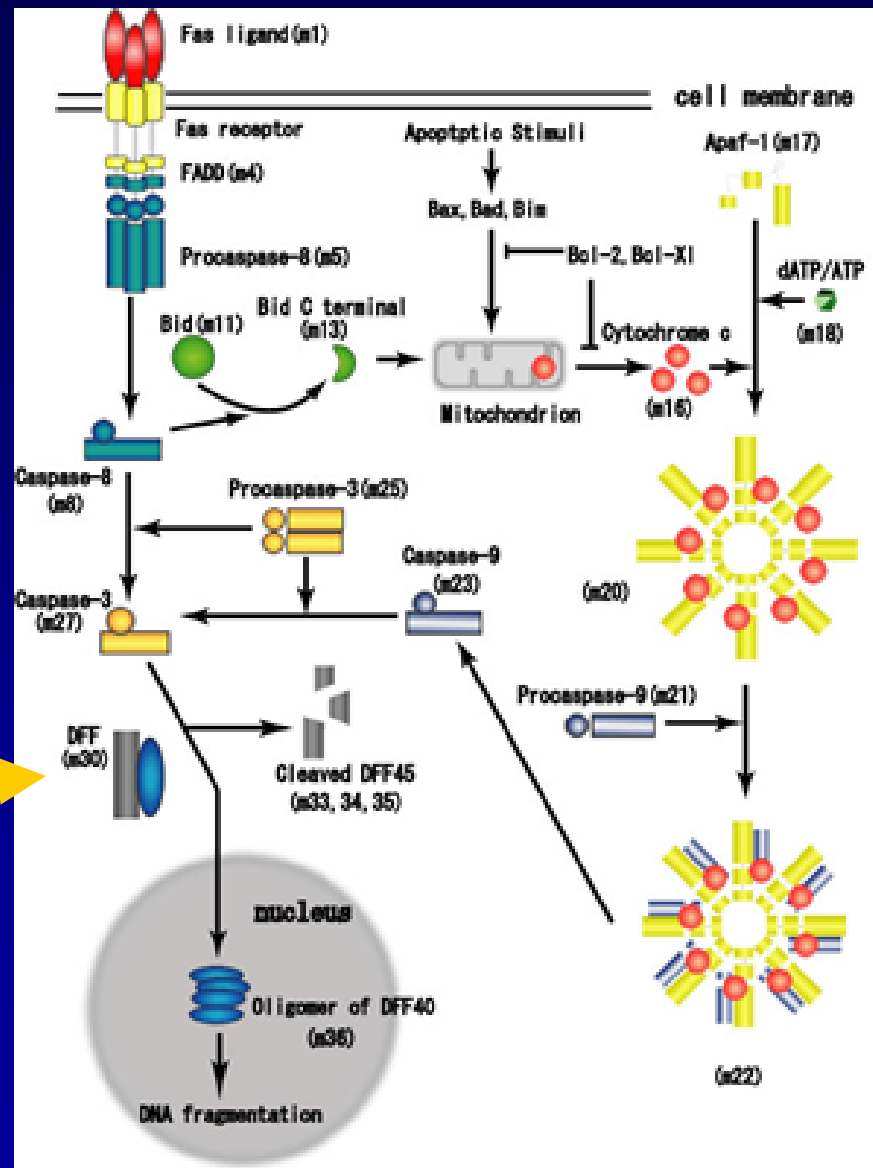
Background

- Apoptosis, or programmed cell death may represent the primary mechanism of hepatocyte loss in the setting of chronic Hepatitis C infection
- Caspases are a family of intracellular cysteine proteases that mediate the complex events leading to apoptosis, initiated by death receptor ligands or apoptotic stimuli
- Serum caspase activity is upregulated in HCV-infected liver and has been shown to correlate with the grade of inflammatory disease activity and early stages of fibrosis

Background

- HIV coinfection has been shown to accelerate hepatic fibrosis in those infected with HCV-liver injury
- Immunocytological staining of liver biopsy sections suggests greater degree of apoptosis in HCV/HIV coinfecting patients
- Cytokeratin-18(CK-18) is a caspase generated neoepitope, found abundantly in hepatocytes which can be detected by the M30 monoclonal antibody on cells and in serum

M30



Goals

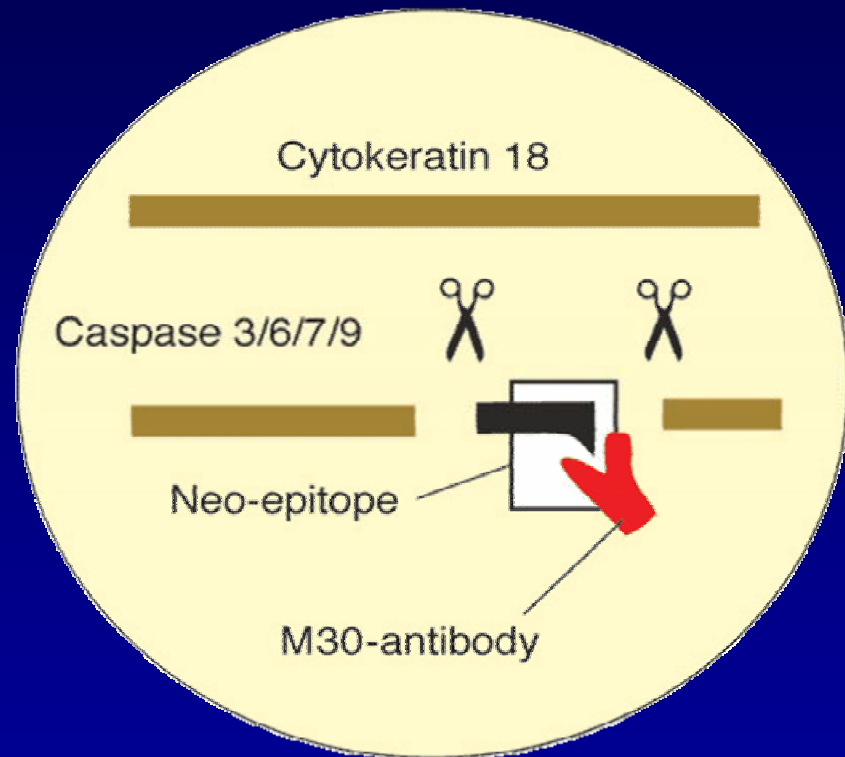
- To determine caspase activity, a marker of apoptosis in subjects with HCV and HCV/HIV co-infection with the M30 antibody ELISA
- To evaluate relationship between M30 neoepitope levels and markers of liver injury, fibrosis and demographic characteristics of a sample population

Methods

- Sera from 29 subjects that were coinfecting with HIV/HCV or HCV alone were analyzed: 23 of those sera samples from The Hemophilia HCV Study Group, and additional 6 randomly selected African-American coinfecting subjects were included
- All subjects were naïve to HCV treatment

Methods

- Samples were analyzed for M30 neo-epitope using M30-Apoptosense® ELISA assay (Peviva, Bromma, Sweden)
- All samples were run in duplicate
- Positive and negative controls, and standards were provided by the manufacturer

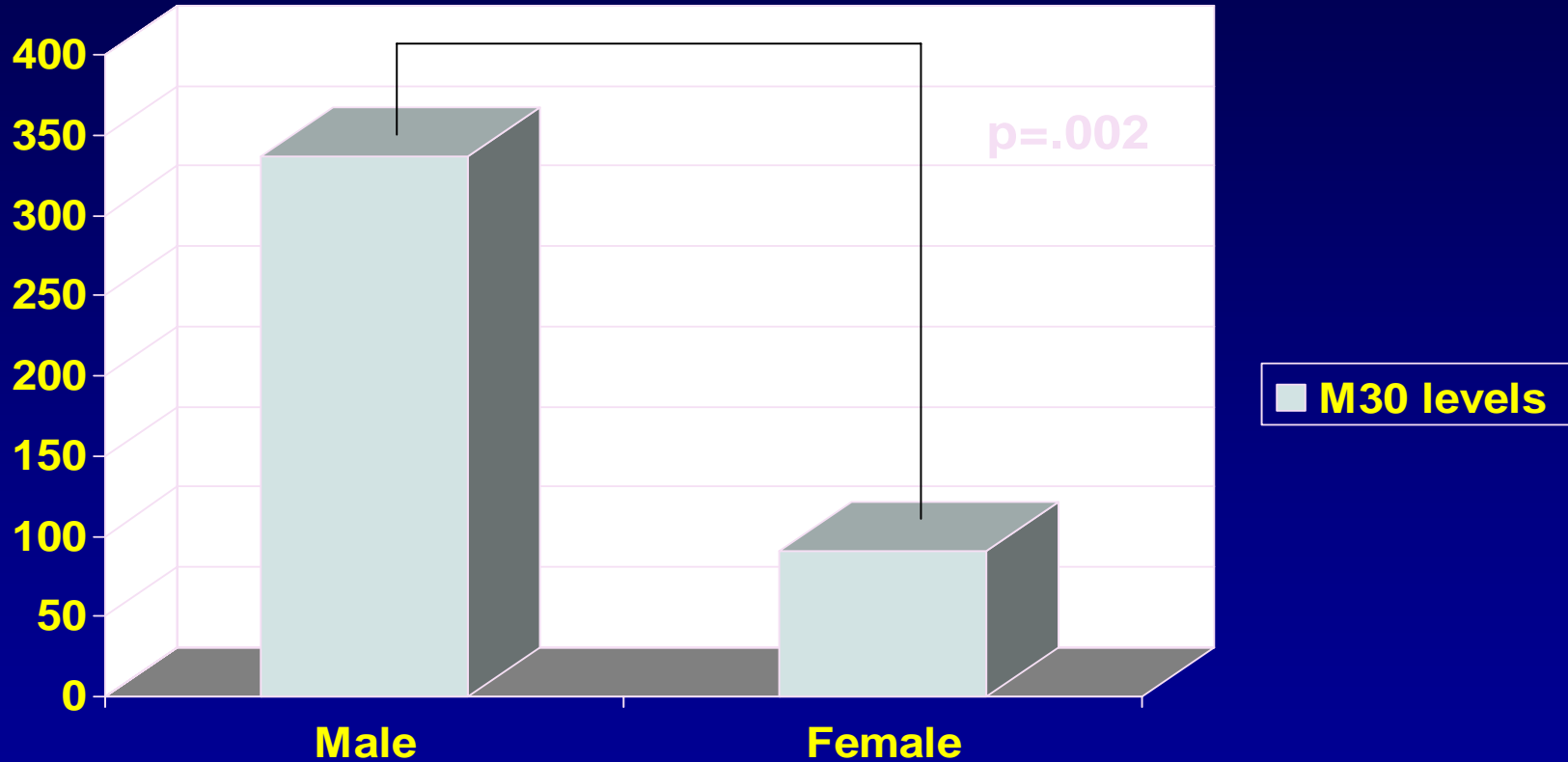


Demographics

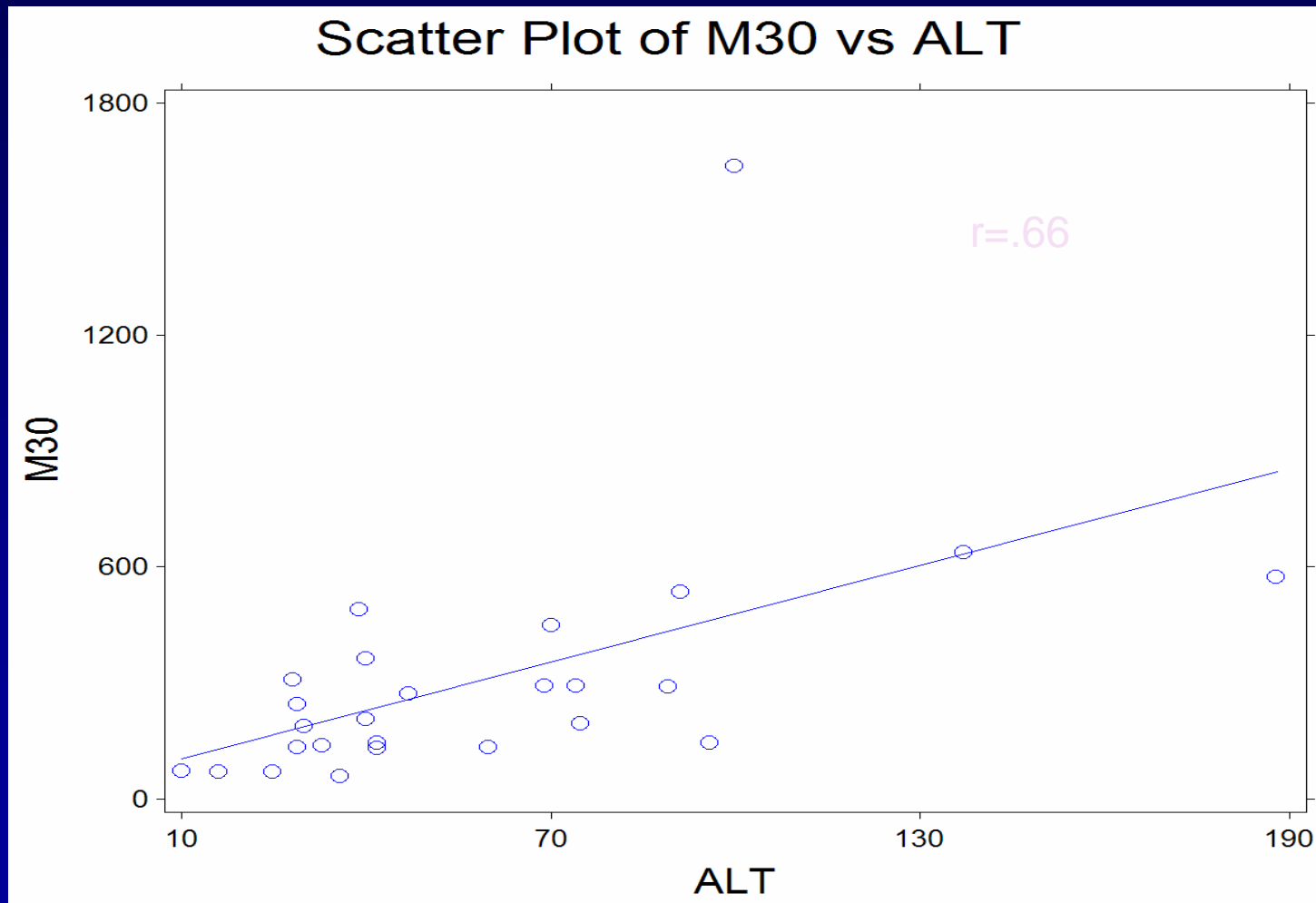
	HCV (n=10)	HCV/HIV (n=17)
Age (mean)	39.5	37.6
Male Gender	8 (80 %)	15 (88%)
Race	Caucasian=8; AA=2	Caucasian=10;AA =7
ALT (mean)	62.2	100.5
Fibrosis score	1.5	2.0
HCV Genotype	1=5;2/3=5	1/4=13;2=3(*)

* 1 Genotype missing

Gender and M30 levels



M30 levels and ALT



Regression Model

M30 Level

- Factors Evaluated

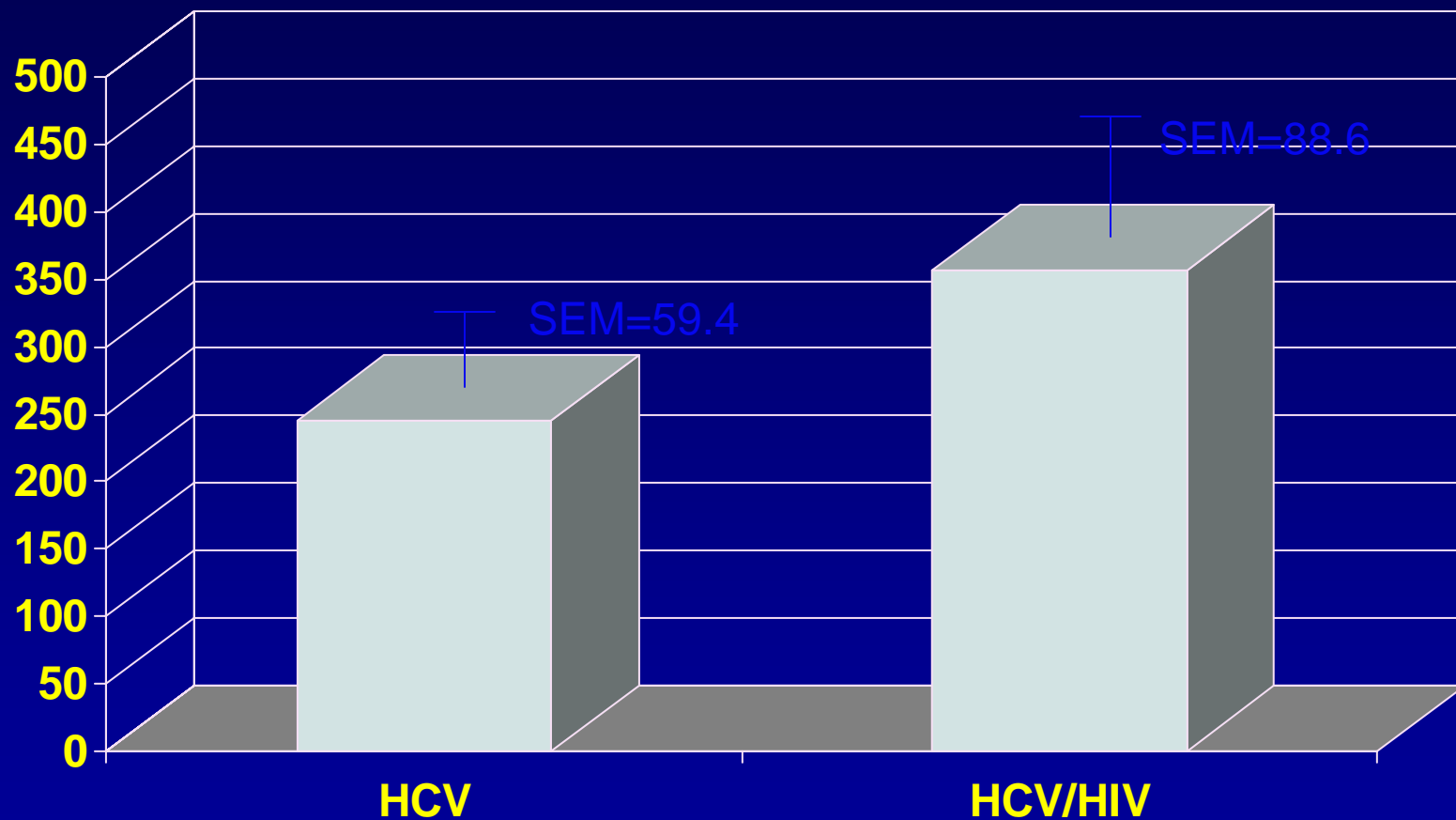
- Age
- Gender
- HCV Genotype
- ALT
- Race
- Fibrosis
- Coinfection Status

- Significant Factors

- Age
- HCV Genotype

M30

Levels by HIV Serostatus



$p = 0.3$

Summary

- M30 levels were similar in HCV and HCV/HIV coinfecting patients
- There was no difference in M30 levels between African-American and Caucasian subjects
- ALT is correlated with apoptotic activity
- Age and genotype may be associated but further evaluation in larger cohorts is needed to validate this observation

Conclusions

- In contrast to other reports, we fail to find an association between an apoptosis marker and presence of HCV/HIV coinfection
- Larger studies may help elucidate the role of genotype and other factors in hepatic apoptosis

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