

Extracellular Vesicles in Fatty Liver Disease

From Contributors to disease pathogenesis to novel biomarkers

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Disclosures

Co-inventor on pending and issued patents filed by the Cleveland Clinic and UCSD that refer to the use of biomarkers in fatty liver disorders.
And

Scientific Advisory Board: Gilead, Takeda, Mitsubishi-Tanabe, Raptor, Conatus

And

My presentation does not include discussion of off-label or investigational use

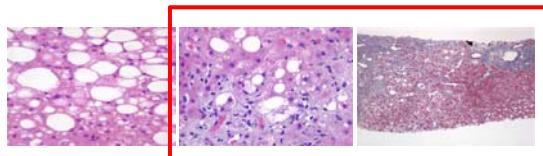
Outline

- NAFLD: Clinical Spectrum
- Pathogenic Pathways
 - Lipotoxicity
 - Hepatocyte Derived Extracellular Vesicles
 - Mediators of Angiogenesis and Fibrosis in NASH
 - Circulating Biomarkers
- Summary and Conclusions

Non-Alcoholic Fatty Liver Disease (NAFLD)

• Spectrum of disease

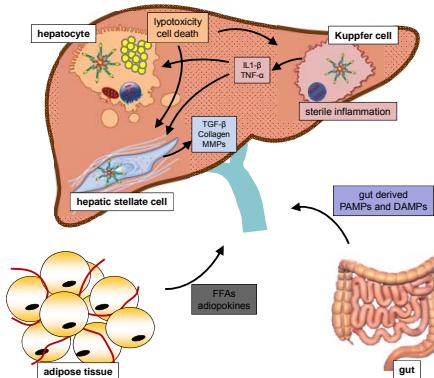
- NAFL: fatty liver (steatosis)
- NASH: steatosis + inflammation + liver injury
- Fibrotic NASH: steatosis + inflammation + liver injury + fibrosis



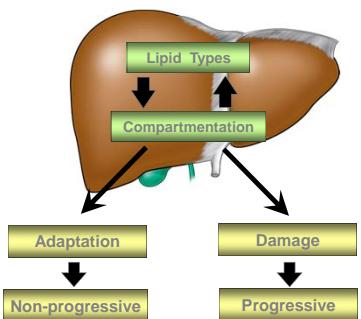
Angulo P et al. N Engl J Med 2002;346:1221-31

Angulo P et al. Gastroenterology. 2015 Aug;149(2):389-397

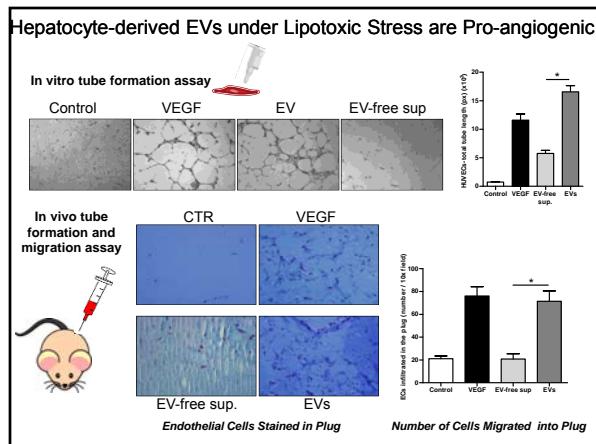
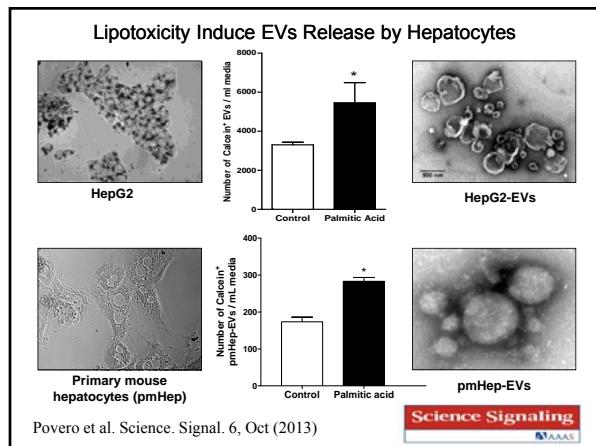
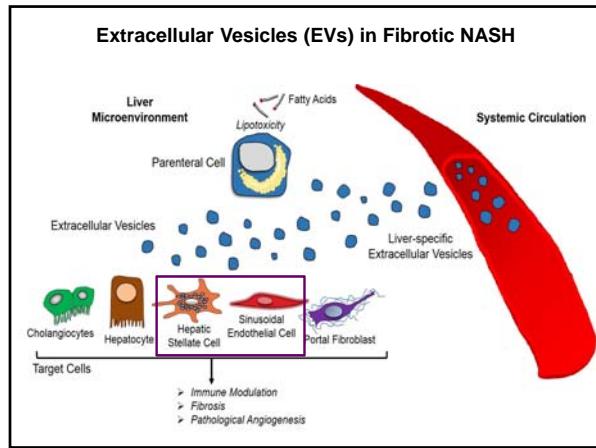
NAFLD Pathogenesis: complex interaction and crosstalk between environmental factors, host genetics and gut microflora

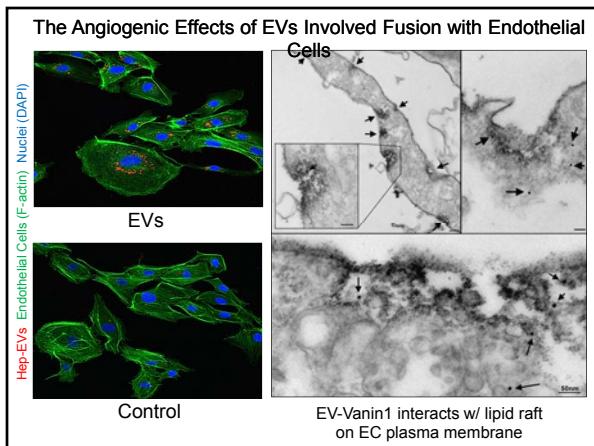
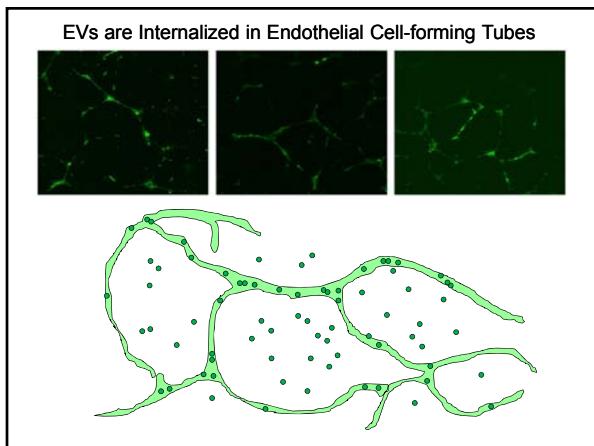
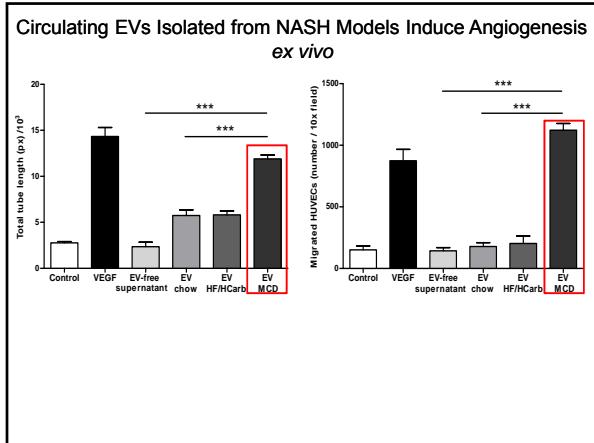


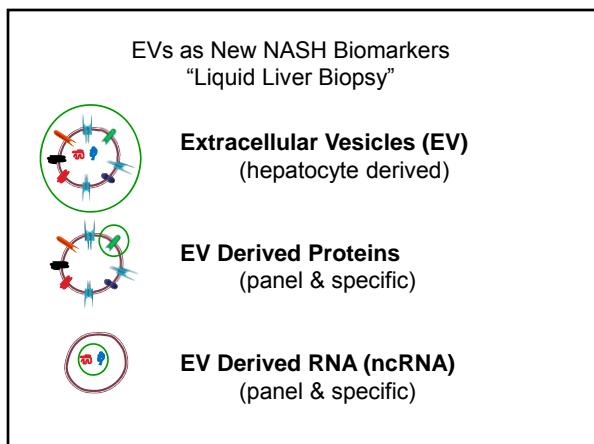
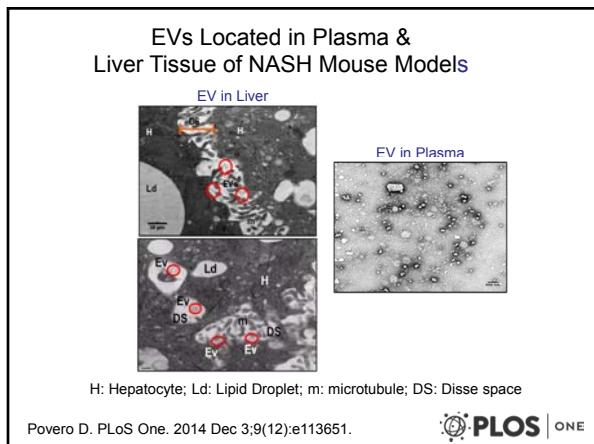
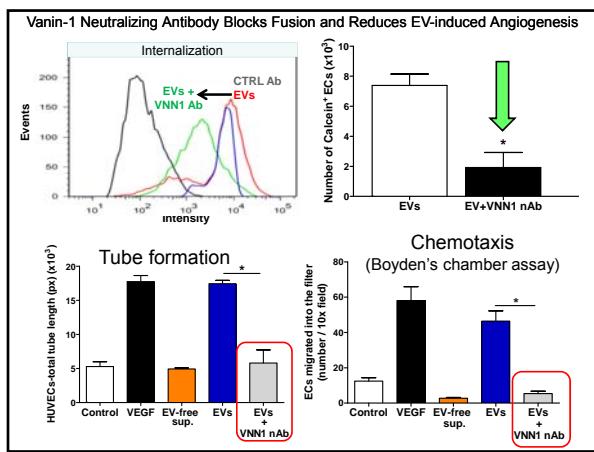
Lipid Partitioning and Disease Progression

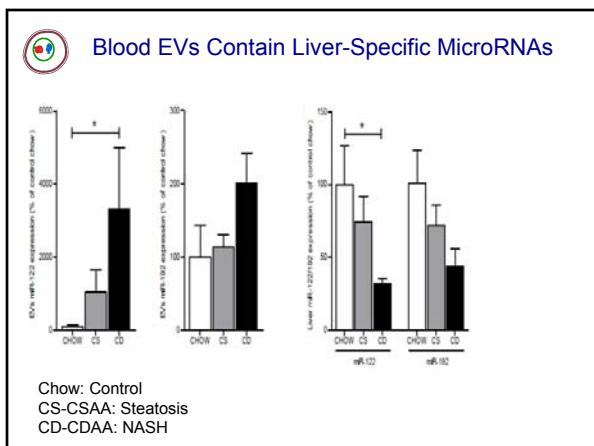
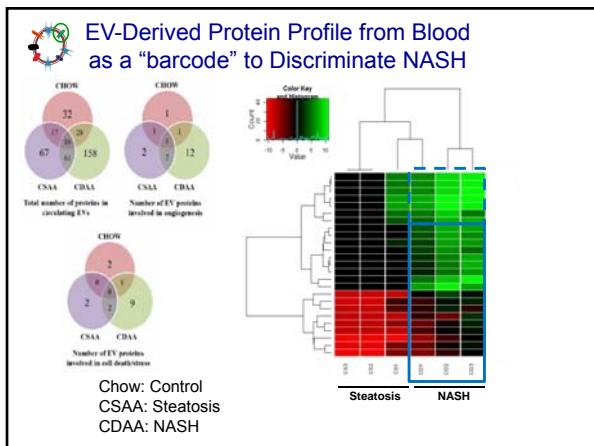
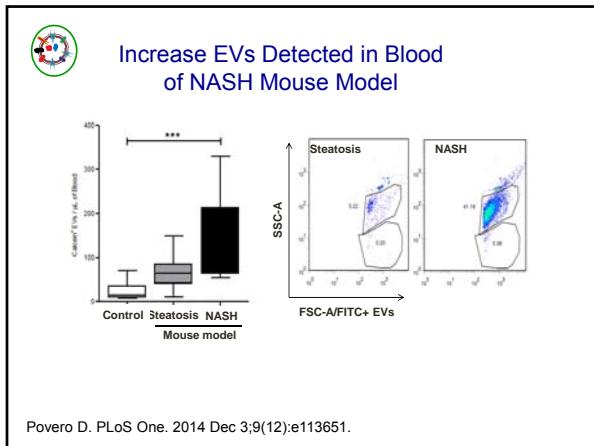


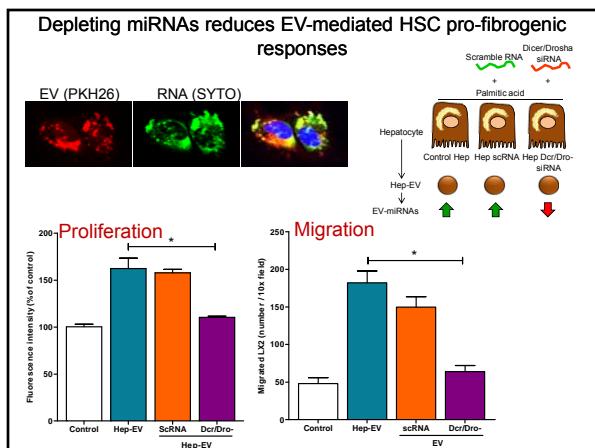
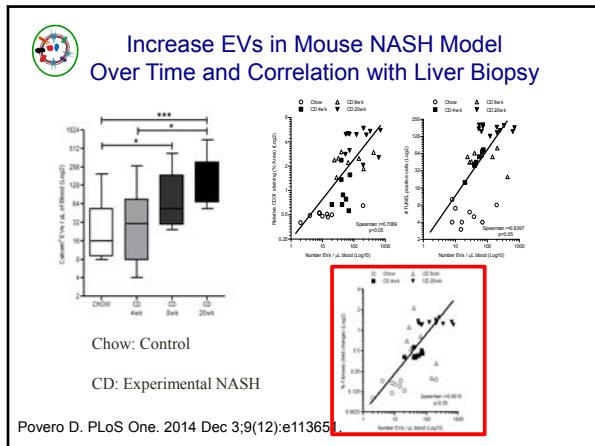
Modified from Feldstein. Semin Liver Dis. 2010 Nov;30(4):391-401.

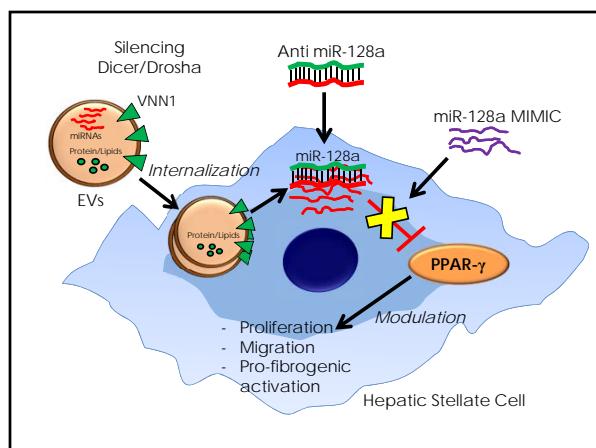
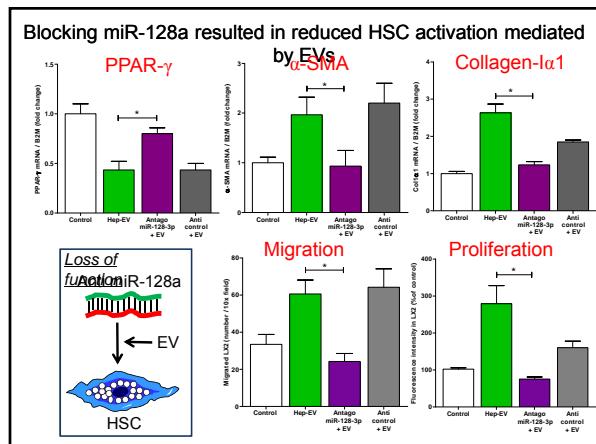
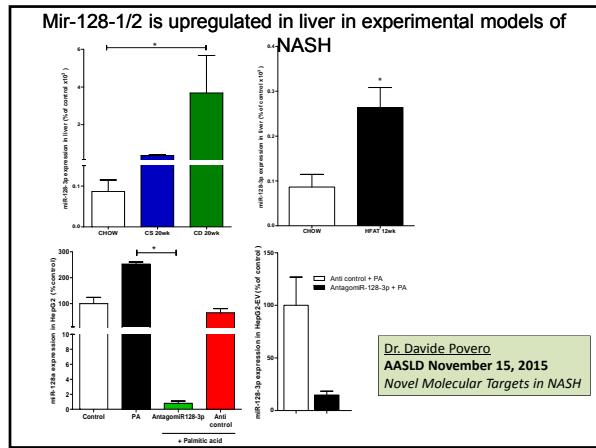












Summary / Conclusion

- NAFLD Pathogenesis involves a complex interaction between environmental factors, host genetics and gut microflora and depends on both intrahepatic and extrahepatic events
- Lipid accumulation in hepatocytes may result in lipotoxicity
- A key consequence of lipotoxicity is the formation and release of extracellular vesicles (EVs)
- EVs may act on neighboring cells and trigger angiogenic and fibrotic responses.
- EVs also carry a footprint of the cell/tissue of origin and are released into the bloodstream suggesting that monitoring EVs in circulation as a promising novel disease biomarker



Collaborators

- Stanley Hazen (CC)
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- Rohit Kohli (Univ. of Cincinnati)
- Sonia Caprio (Yale University)
- Susan Fisher-Hoch (UT Houston)
- Michael Fallon (UT Houston)
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- Ekihiro Seki (UCSD)
- Hal Hoffman (UCSD)
- Vivian Hook (UCSD)
- Michael Karin (UCSD)

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