GLP-1 receptor agonists reduce liver inflammation in a 3-week Non Alcoholic Steato-Hepatitis Mouse Model

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BACKGROUND:
Glucagon-like peptide 1 (GLP-1) receptor agonists are characterized with anti-inflammatory capacity suitable to treat Non Alcoholic Steato-Hepatitis (NASH) as a novel therapeutic alternative. We here evaluated the effect of GLP-1 receptor agonists on liver inflammation in a rapid mouse model of liver inflammation, i.e. the mouse fed a high fat/high cholesterol diet, where cyclodextrin is co-administered to favor hepatic cholesterol loading, liver inflammation and NASH within 3 weeks.

METHODS:
C57BL6/J mice were fed a 60% high fat, 1.25% cholesterol, 0.5% cholic acid diet with 2% cyclodextrin in drinking water (HFCC/CDX diet) for 3 weeks. An ancillary group of chow fed mice were used as negative control. After 1 week of HFCC/CDX diet, mice were treated intraperitoneally for 2 weeks with vehicle or GLP-1 receptor agonists liraglutide at 100 µg/kg QD or exendin-4 10 µg/kg BID. Data are shown as mean ± SEM.

RESULTS:
HFCC / cyclodextrin combination rapidly induces NASH with strong inflammation

Both liraglutide and exendin-4 reduce cholesterolemia and impacts innate and adaptive immune systems in the liver

CONCLUSION
• Taken together, our data suggest that GLP-1 receptor agonists reduce liver inflammation in our 3-week NASH mouse model.
• This model should be useful to rapidly detect anti-inflammatory effects of novel drugs targeting NASH, including novel GLP-1 analogues.

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