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Diet-induced obesity and NASH aggravate SARS-CoV-2 infection in golden Syrian hamsters

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Abstract

Background: Patients with obesity and nonalcoholic steatohepatitis (NASH) are prone to severe forms of COVID-19. Novel drugs are urgently needed and may be evaluated in the Golden Syrian hamster, a relevant preclinical model for SARS-CoV-2 infection. To better replicate the human context, we recently set-up a nutritional hamster model that develops obesity and metabolic comorbidities including dyslipidemia, NASH, and heart failure with preserved ejection fraction.

Objective: We compared the deleterious effects of SARS-CoV-2 infection in lean versus obese hamsters.

Methods: Lean or diet-induced obese/NASH hamsters were intranasally infected with SARS-CoV-2. Hamsters were sacrificed at 4-, 7-, 10-, and 25-days post-infection for serum and organs collection, biochemistry, and histology analysis.

Results: Obese hamsters did not recover their initial body weight at day 25 post-infection, while lean individuals did. During infection, obese hamsters remained dyslipidemic and kept a significantly higher liver histopathological score, versus lean hamsters. Lung viral load and inflammatory genes expression were not different between lean and obese hamsters. However, obese hamsters had significantly higher lung histopathological scoring at 10 days post-infection ($p<0.05$ vs. lean). Additionally, lung and liver fibrosis were higher in obese hamsters at 25 days post-infection (both $p<0.01$). These greater lesions were concomitant with higher serum monocyte chemoattractant protein-1 and Angiotensin II levels, a component known to favor lung inflammation, fibrosis, and oedema.

Conclusion: Diet-induced obesity and NASH aggravated SARS-CoV-2 infection in golden Syrian hamsters. This model will be useful to evaluate novel drugs targeting the severe forms of COVID-19 seen in patients with obesity and NASH.

Keywords: obesity, nonalcoholic steatohepatitis, COVID-19, hamster

Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; COVID-19, coronavirus disease 2019; NASH, nonalcoholic steatohepatitis

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