Abstract: 28O

The designer cytokine IC7Fc promotes weight loss by decreasing digestive efficiency in obese mice.

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Background: Obesity is largely a result of an energy imbalance where energy intake exceeds energy expenditure. Notwithstanding a third, but often overlooked, component to energy balance is nutrient absorption/digestive efficiency. Decreased nutrient absorption is one reported mechanism for the weight loss effect of a diet rich in fiber, while the weight loss drug Orlistat®, which inhibits lipase in the gut, works by inhibiting nutrient absorption by approximately 30%(1). We have recently shown that a) activation of the gp130 receptor in the intestinal epithelium can prevent gut barrier deterioration(2) and b) the designer gp130 receptor cytokine IC7Fc can prevent weight gain in mice fed a high fat diet (HFD)(3). Accordingly, in the present study, we tested the hypothesis that one mechanism, for the anti-obesogenic effect of IC7Fc treatment was reduced digestive efficiency.

Methods: Sixteen C57BL/6 mice were fed a HFD from 6 weeks (wk) of age for 8 wk and injected intraperitoneally with 1 mg/kg IC7Fc (n=8), or an equal volume of saline (n=8), daily for 7 days (d). Food intake was measured over the course of the intervention and body weight was measured every 2 d throughout. Faeces were collected for the final 3 d and measured for faecal output, caloric density and digestive efficiency using a bomb calorimeter.

Results: As we have observed previously(2), treatment with IC7Fc decreased ($P<0.05$) body weight relative to Saline treated animals. No differences in either food intake (g/day) or faecal output (g/day) were observed when comparing IC7Fc with Saline treatment. Importantly, however, treatment with IC7Fc increased faecal caloric density (Kcal/g; $P<0.0001$) and decreased digestive efficiency (%; $P<0.01$) relative to Saline treatment.

Conclusion: The mechanism, in part, for the anti-obesogenic effect of IC7Fc is via decreased digestive efficiency. Importantly, unlike Orlistat®, which is known to increase defecation, urgent bowel movements and diarrhea, limiting its therapeutic utility, IC7Fc treatment does not increase faecal output in mice. Whether IC7Fc can be used as a weight loss drug by affecting nutrient absorption remains to be experimental tested.

References

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