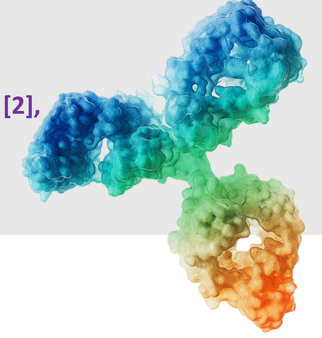
Activin E Neutralization Drives Healthy Fat Loss

Tam Phuong [1]*, Coutney Zour [1], Cory Schwartz [1], Cody Moore [1], Alexander Taguchi [1], Tom Hsu [1], Hongyu Zhang [1], Matthew Dent [1], Arjan Hada [1], Justin DiMartino [2], Patrick Crutcher [2], and Martin Brenner [1]

[1]. iBio Inc., 11750 Sorrento Valley Road, San Diego, California, 92121; [2]. AstralBio. Inc. Boston, Massachusetts; * Presenter



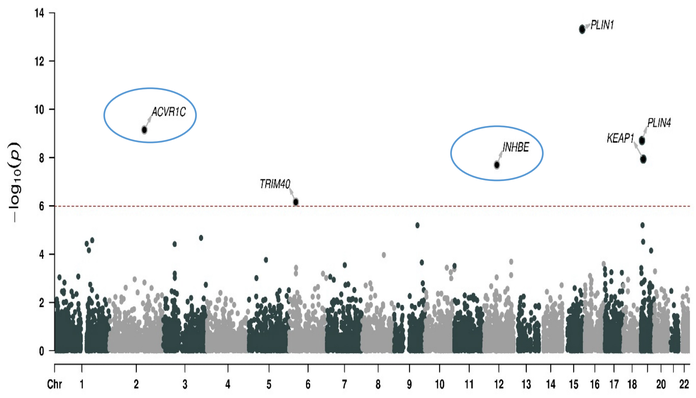
Introduction

Visceral adiposity is a major driver of insulin resistance, cardiometabolic disease, type 2 diabetes, and mortality, highlighting the need for therapies that selectively reduce visceral fat while preserving lean mass. Human loss-of-function variants in Activin E are associated with a lower waist-to-hip ratio independent of BMI and reduced type 2 diabetes risk, supporting Activin E as a therapeutic target.

In a diet-induced obesity mouse model, neutralization of Activin E significantly reduced body weight through selective loss of visceral adiposity while preserving lean mass. Treatment markedly decreased mesenteric and epididymal fat, reduced pro-inflammatory M1 macrophages, and enhanced thermogenic and metabolic gene expression in visceral fat.

Together, these findings establish Activin E neutralization as a promising strategy for targeted visceral fat reduction and metabolic improvement.

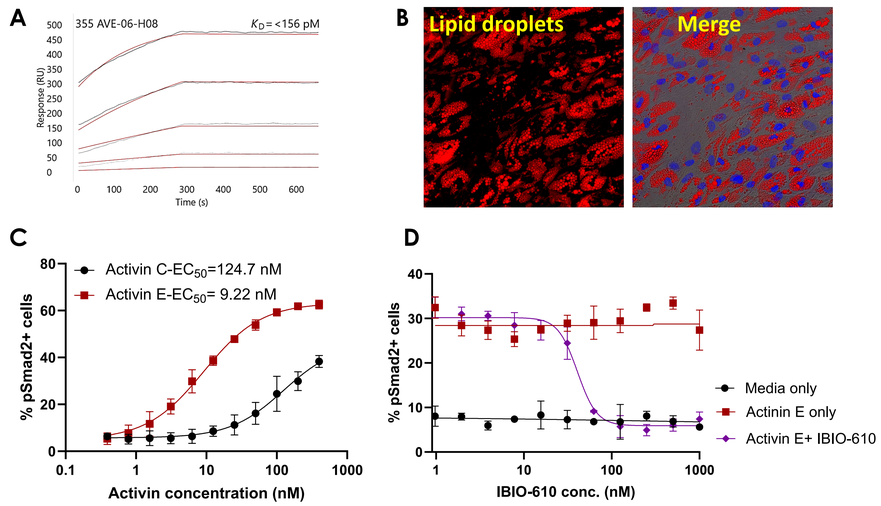
Waist-to-hip ratio adjusted for BMI: Loss of function and missense variants



Deaton, A. M. et al. Nat Commun (2022)

Results

Figure 1: IBIO-610 blocks Activin E – induced pSmad2 in human adipocytes.



(A) The binding of Activin E antibody was characterized using a Carterra LSA. (B) Representative image of the lipid droplet in an adipocyte differentiated for 8 days from a human visceral pre-adipocyte. (C) Activin E induced pSmad2 signaling in a dose-dependent manner. (D) The IBIO-610 blocked Activin E-induced pSmad2 signaling in a dose-dependent manner in human differentiated adipocytes.

Figure 2: IBIO-610 neutralized activin E in DIO mice

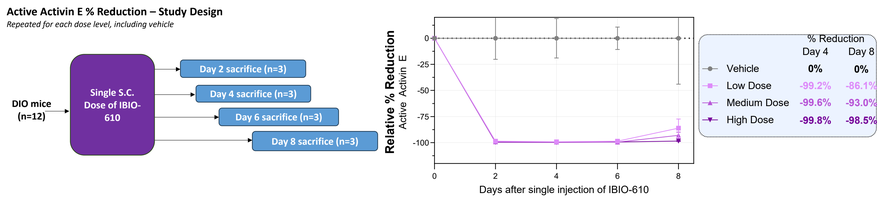
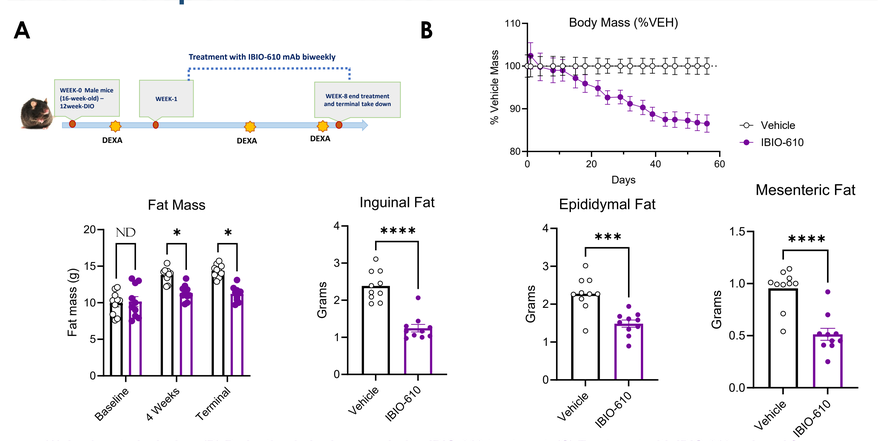
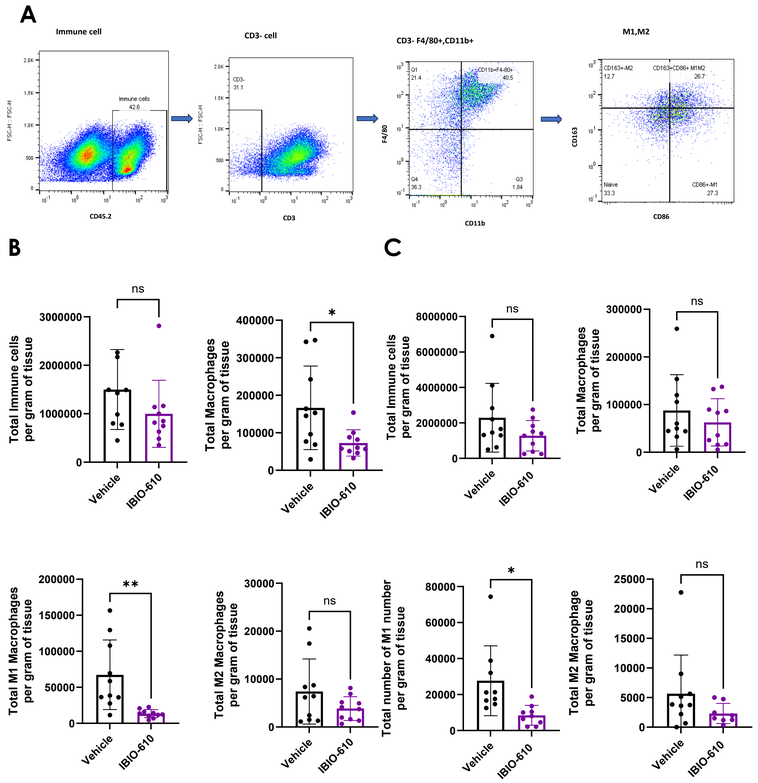


Figure 3: IBIO-610 significantly reduce body weight and fat depots in DIO mice



(A) *In vivo* study design. (B) Reduction in body mass during IBIO-610 treatment. (C) Treatment with IBIO-610 reduced fat mass , as measured by DEXA. (D) Treatment with IBIO-610 reduced fat depots in diet-induced obese (DIO)

Figure 3: IBIO-610 reduce pro-inflammatory macrophage in fat deports



(A) Gating strategy for M1 and M2 Macrophages. IBIO-610 treatment significantly reduce M1 Macrophages in epidermal WAT (B) and in Mesenteric WAT (C) ,

Conclusions

Taken together, the data demonstrate IBIO-610 potently neutralizes activin E both in vitro and in a diet-induced obesity (DIO) mouse model. IBIO-610 treatment significantly reduced body weight, adipose tissue mass, and pro-inflammatory M1 macrophage infiltration in DIO mice. These findings support Activin E neutralization as a promising therapeutic strategy for targeted visceral fat reduction and metabolic improvement. The observed effects on adiposity and adipose inflammation provide a strong biological rationale for advancing IBIO-610 therapy into clinical evaluation for obesity and obesity-related metabolic disease.