



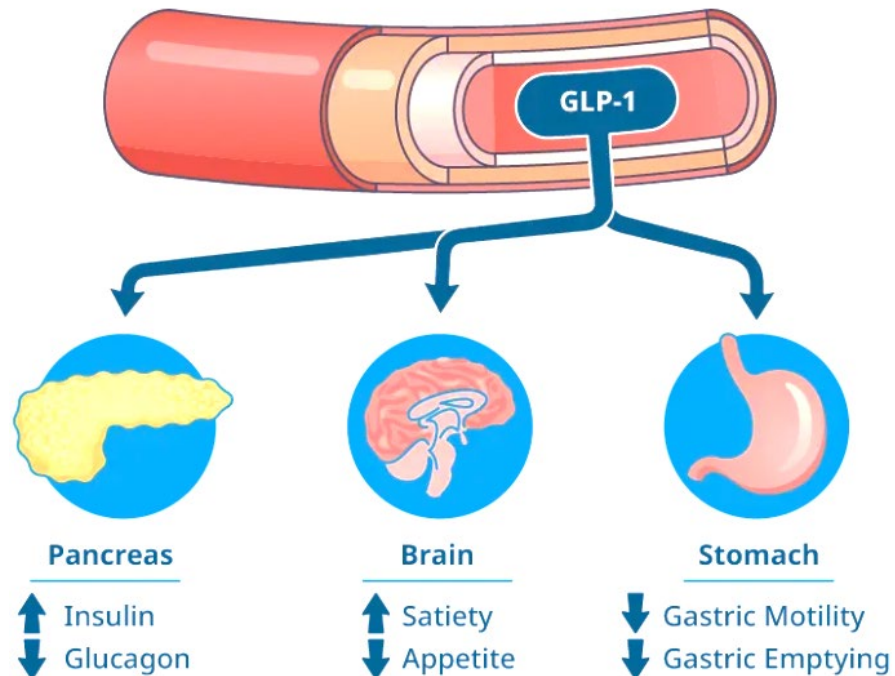
Next-Generation Obesity Treatments

Tam Phuong

GLP-1-Based Therapeutics: Current Status and Advances

Role of GLP-1 in Metabolic Regulation

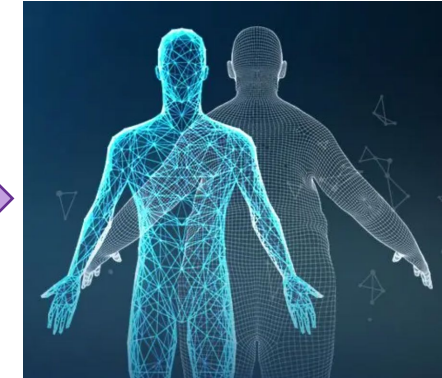
GLP-1 Glucagon-Like Peptide-1



GLP-1 RA is FDA-approved for obesity treatment



AM Rx



Challenges

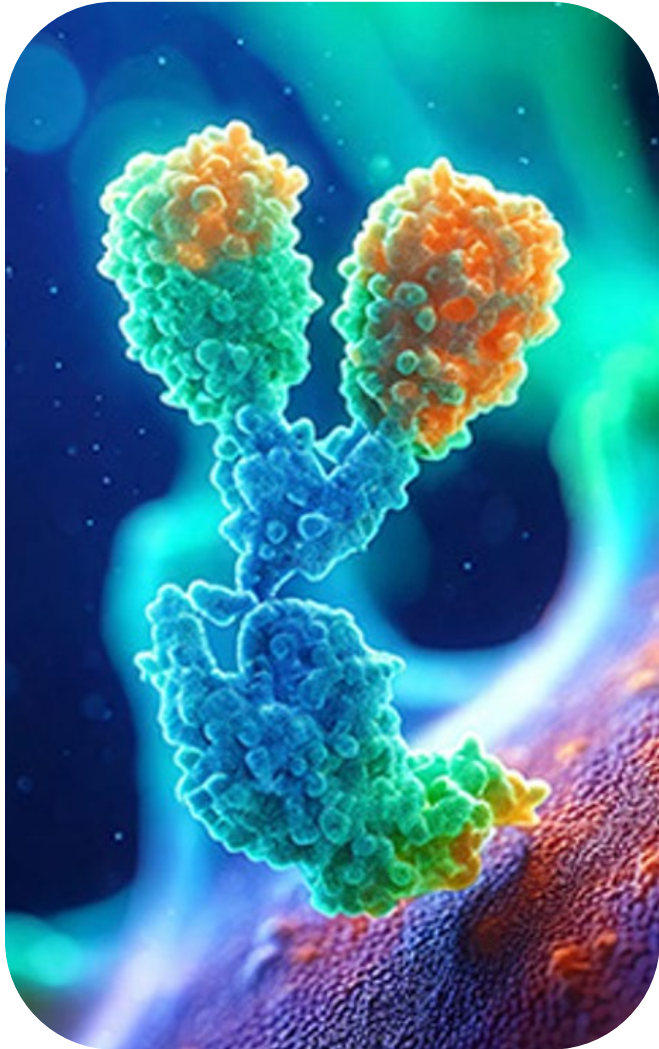
- ❖ **Intolerability:** High dropout rates: **53.6%** of adults prescribed a GLP-1 receptor agonist discontinued therapy within one year, and **72.2%** stopped within two years ¹
- ❖ **Reduce lean mass:** As much as **40%** of the weight dropped on GLP-1 drugs comes from loss of lean mass rather than fat (ADA)²
- ❖ **Rebound:** Patients who stopped taking GLP-1 medications regained about two-thirds of the weight they lost during the trial within one-year.

(1) [Discontinuation and Reinitiation of Dual-Labeled GLP-1 Receptor Agonists Among US Adults With Overweight or Obesity | Nutrition, Obesity, Exercise | JAMA Network Open | JAMA Network](#)

(2) [Studies Address Muscle Loss Caused By GLP-1 Drugs, such as Ozempic and Zepbound - Drugs.com MedNews](#)



Advancing Next-Generation Therapies for Obesity and Weight Management



Designed to Improve Quality of Weight Loss Not Met by Current GLP-1 Drugs

Prevention of muscle mass loss

Reduce side effects leading to discontinuation

Sustainment of weight loss

Decrease **dosing frequency**



Complete Portfolio Approach to Obesity with Highly Validated Targets

Focusing on Fat-specific weight reduction

Targeting **calories and energy** with less side effects

Preserving and increasing muscle mass

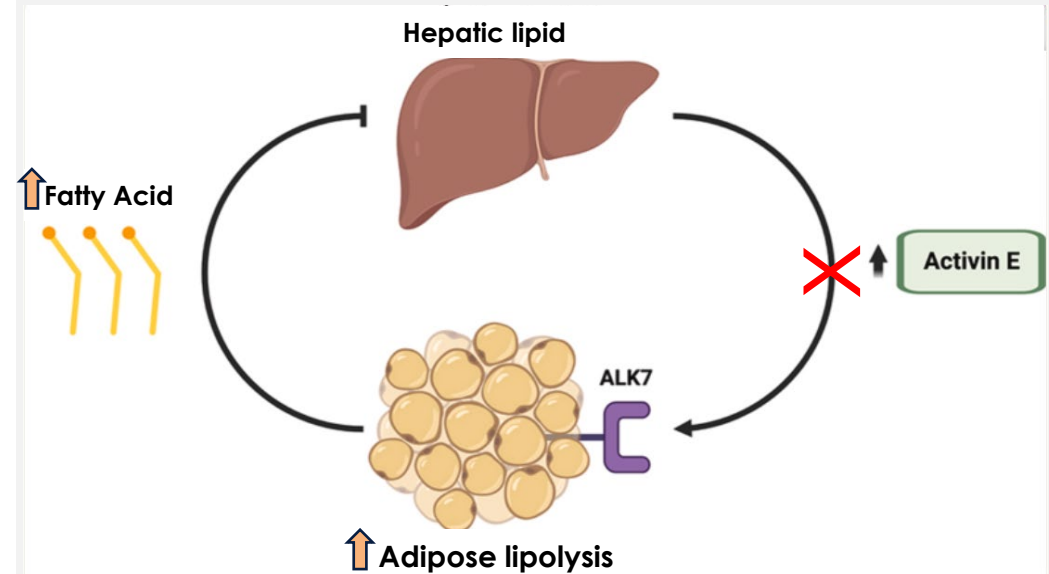
Activin E Potential Next-Generation Therapeutic for Obesity and Weight Management



Why targeting Activin E?

- Activin E is a hepatokine, produced in liver a member of the TGF β family.
- Activin E and its receptor are highly genetically validated.
- Genetic loss of function decreases adiposity and risk for diabetes/ Cardiovascular Disease.
- 2 siRNA targeting molecules provide pharmacological validation.

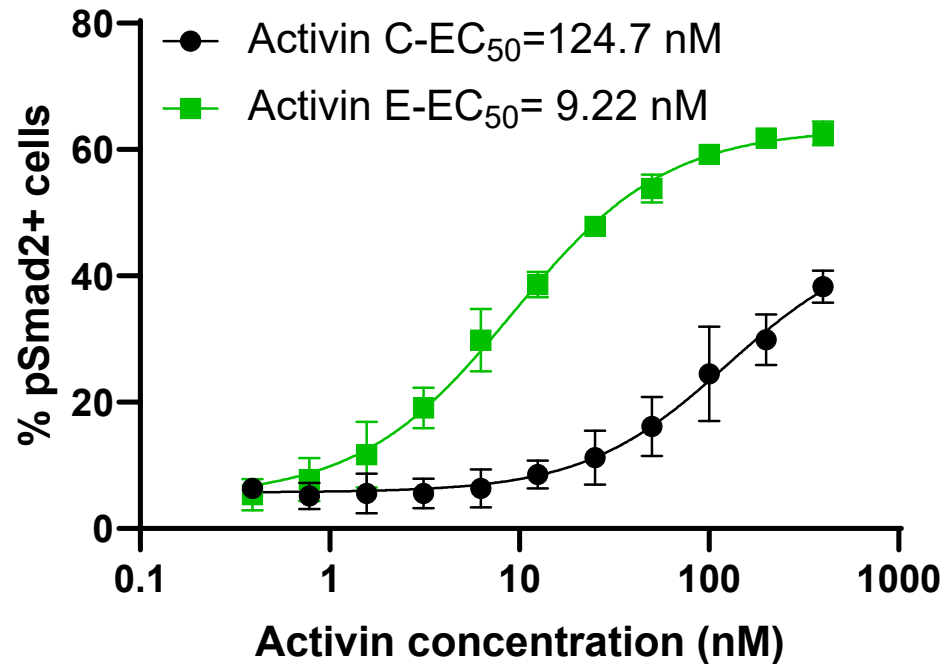
Activin E -Mode of action



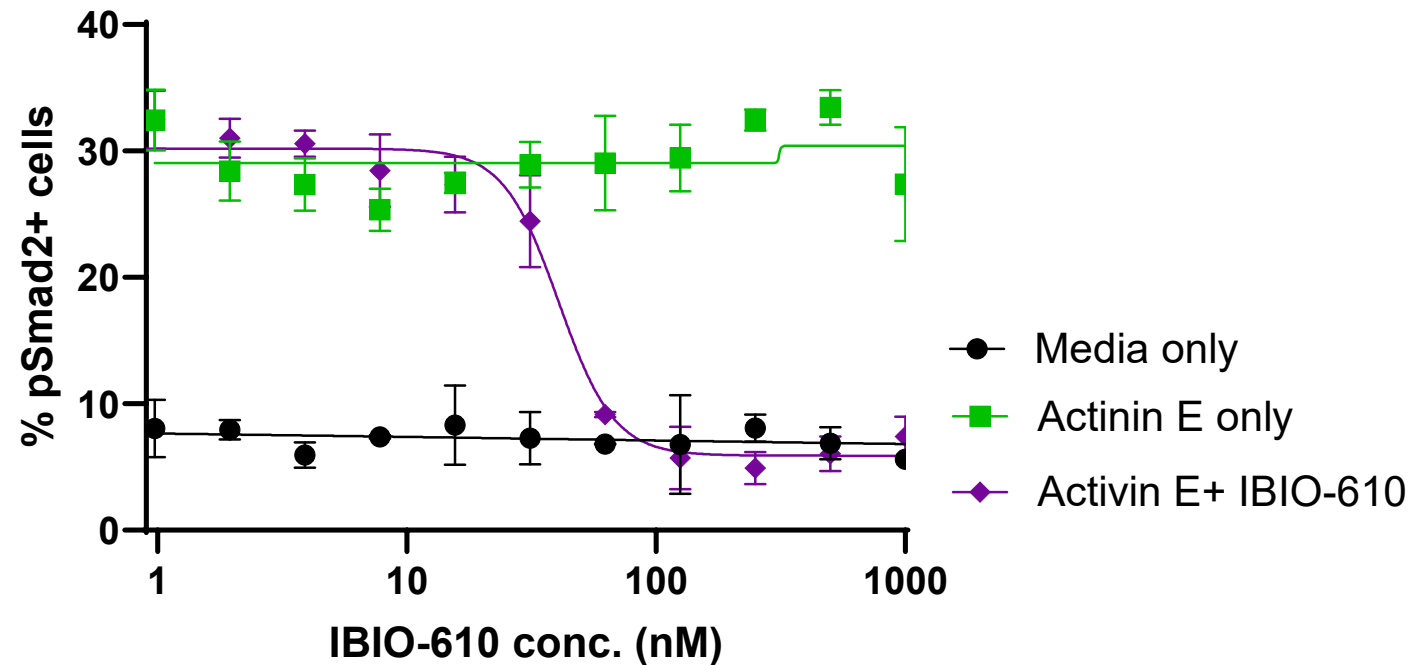
Anti-Activin E antibody (IBIO-610) strongly blocks Activin E – induced pSmad2 in human adipocytes.



Activin E induce pSmad2 in human differentiated adipocyte



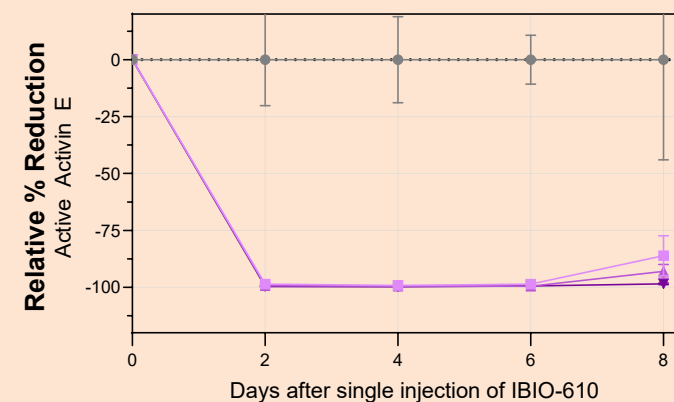
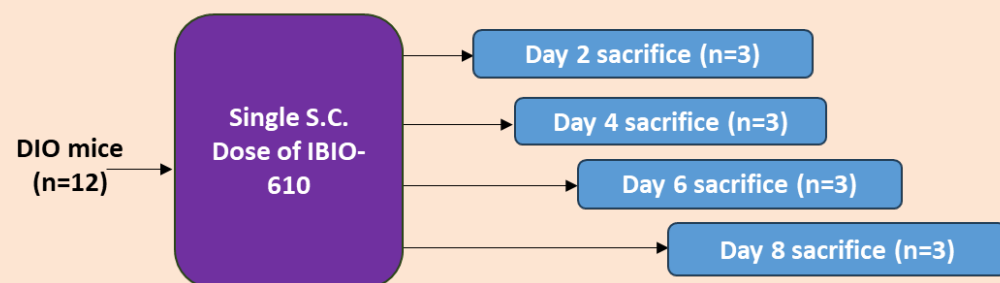
IBIO-610 block activin E induce pSmad2 in human differentiated adipocyte



IBIO-610 Reduces Serum Levels of active Activin E in Mice

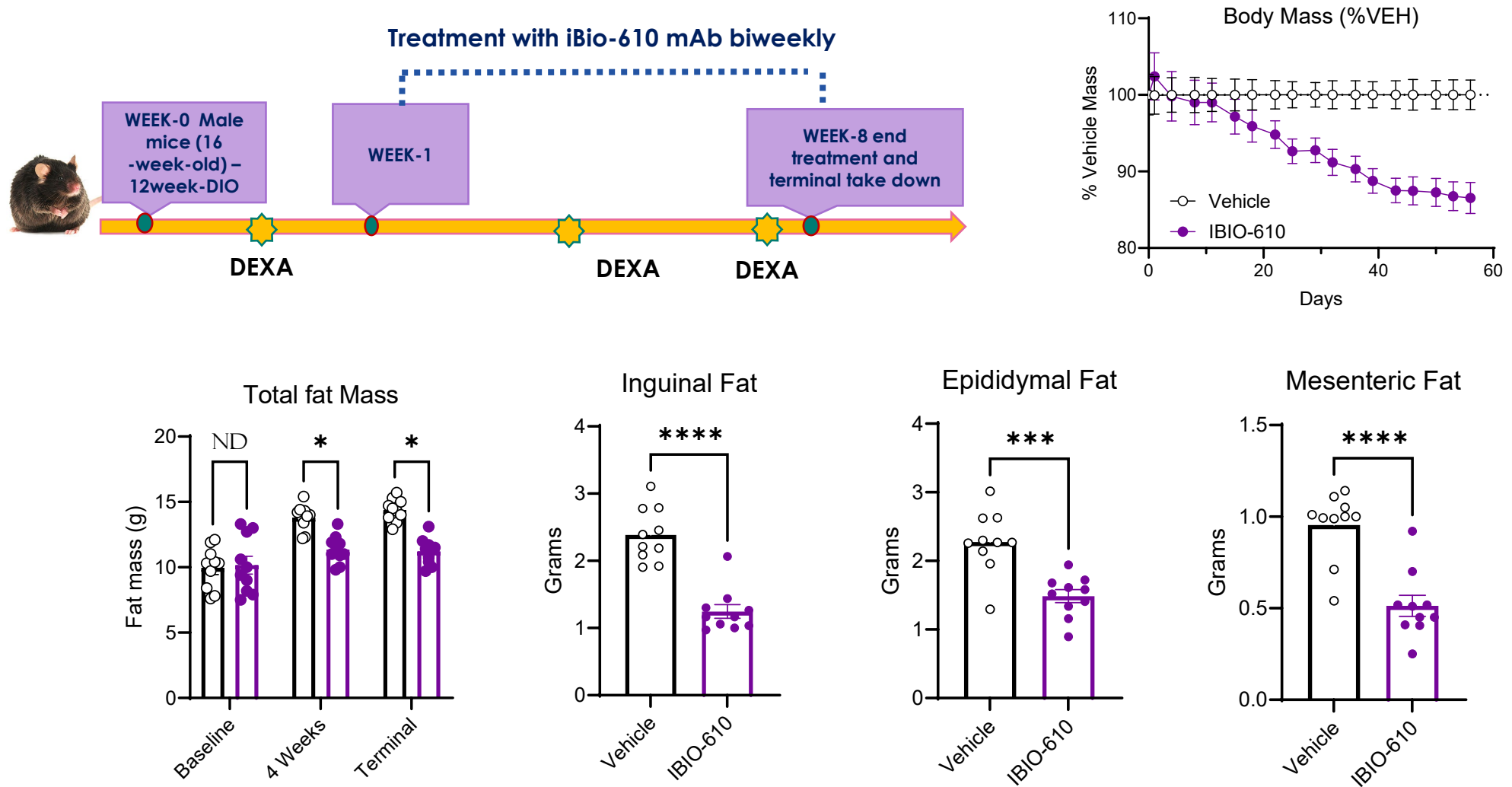
Active Activin E % Reduction – Study Design

Repeated for each dose level, including vehicle

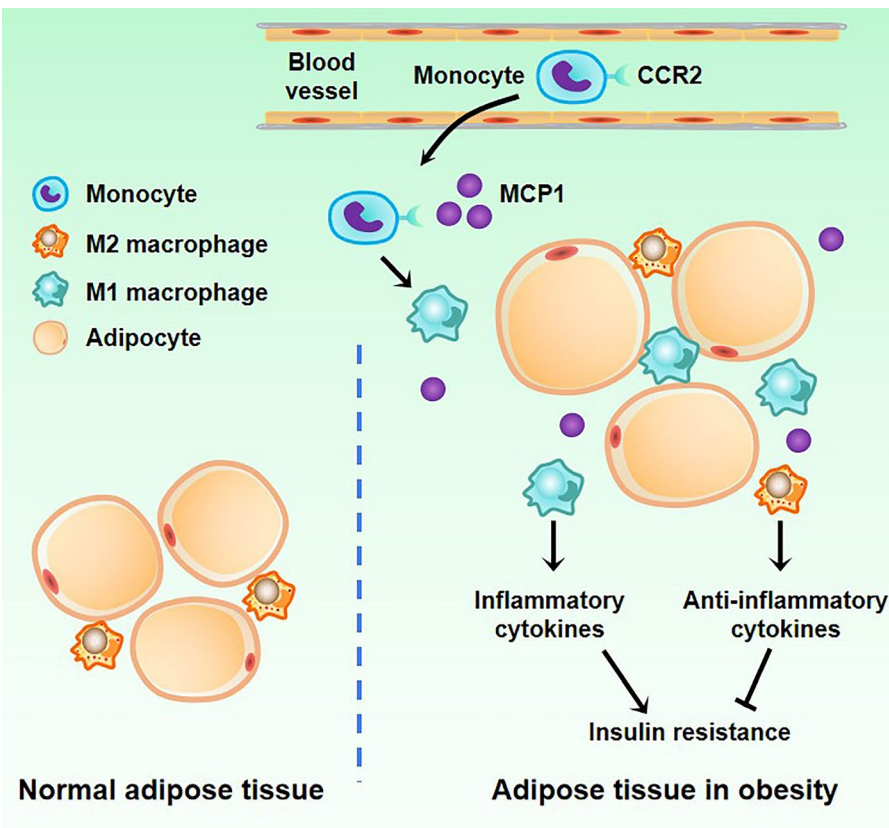


	% Reduction	
	Day 4	Day 8
Vehicle	0%	0%
Low Dose	-99.2%	-86.1%
Medium Dose	-99.6%	-93.0%
High Dose	-99.8%	-98.5%

IBIO-610 treatment drives fat loss but not lean mass loss in DIO mice



Macrophage function in adipose tissue homeostasis and metabolic inflammation



Article

High-Fat Diet-Induced Dysregulation of Immune Cells Correlates with Macrophage Phenotypes and Chronic Inflammation in Adipose Tissue

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High-fat diet-induced adipose tissue-resident macrophages, T cells, and dendritic cells modulate chronic inflammation and adipogenesis during obesity

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Macrophage infiltration into obese adipose tissues suppresses the induction of UCP1 level in mice

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High-fat diet triggers obesity-related early infiltration of macrophages into adipose tissue and transient reduction of blood monocyte count

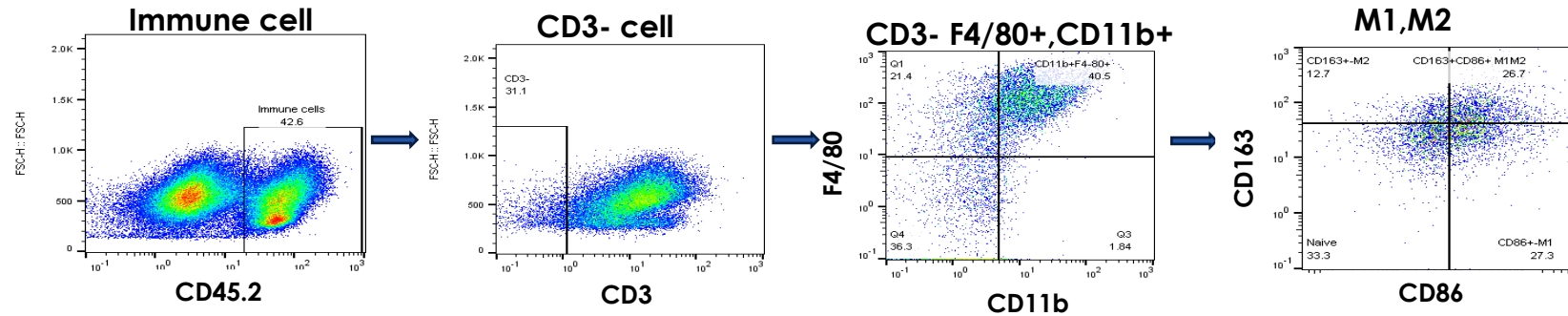
Yanxia Liu^a, Xinping Lu^b, Xialian Li^a, Peijie Du^a, Guijun Qin^{a,*}

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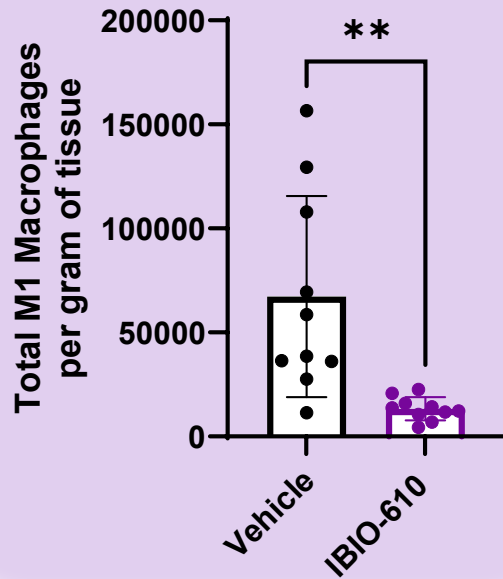
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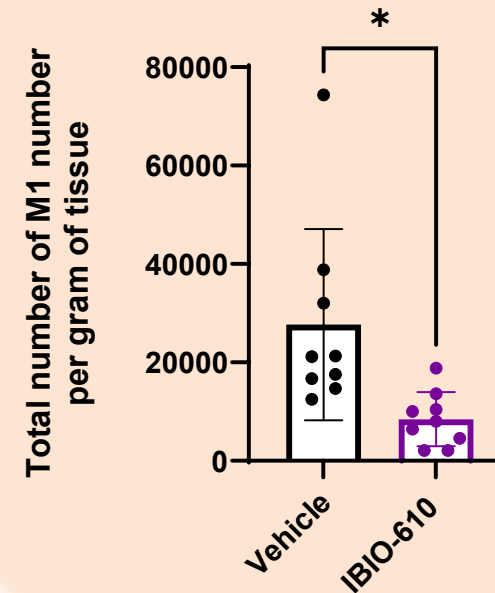
Treatment with IBIO-610, reduce the pro-inflammatory Macrophage (M1) in Visceral fat depots



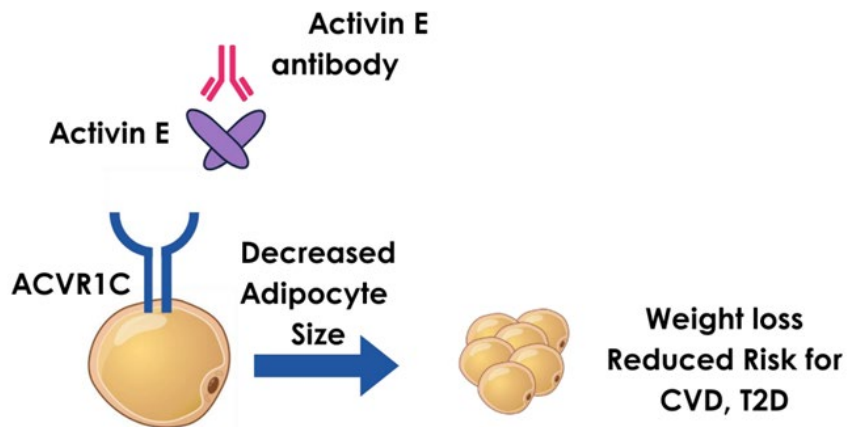
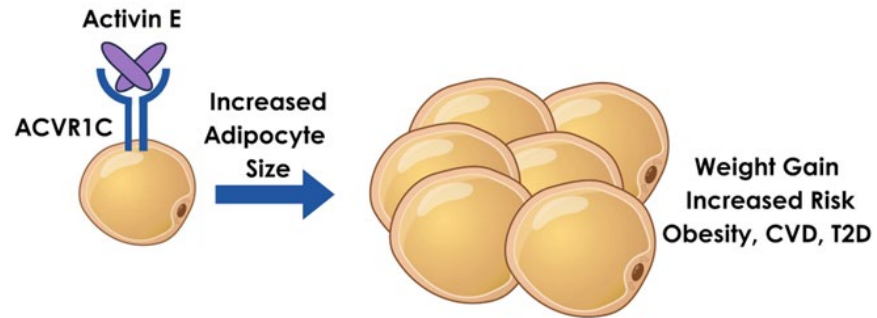
Epididymal -WAT



Mesenteric -WAT



Take home message



- IBIO-610 strongly neutralizing circulating activin E in DIO mice
- IBIO-610 significantly reduce body weight, visceral fat deposits
- IBIO-610 reduces pro-inflammatory M1 macrophages in the visceral fat deposits in DIO mice.



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Thanks for your attention

Q&A