Research Institute of Cellular Diagnostics and Mitochondrial Medicine, LMB Clinic

UNCOUPLING OF RIBOSOMAL AND MITOCHONDRIAL FUNCTIONS IN LEUKOCYTES DURING GLP-1–INDUCED WEIGHT

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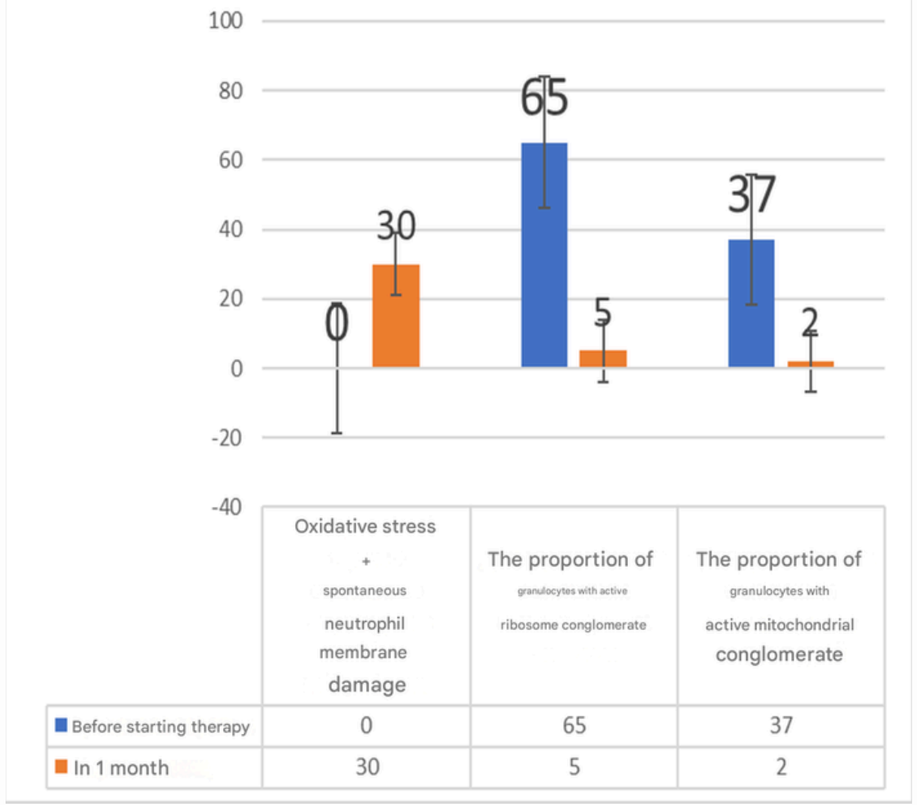
RICDMM LMB CLINIC

1. BACKGROUND & AIM

GLP-1 agonists have transformed obesity care but may favor sarcopenic weight loss over metabolic rejuvenation (1). Preservation of ribosomal capacity and mitochondrial resilience in granulocytes has emerged as a blood-accessible hallmark of healthy aging (2).

To investigate whether GLP-1-induced changes in leukocyte ribosomal RNA (translational capacity) and mitochondrial function can serve as a live-cell biomarker of weight loss "quality," and to evaluate the efficacy of combining GLP-1 agonists with targeted mitochondrial boosters to prevent sarcopenia.

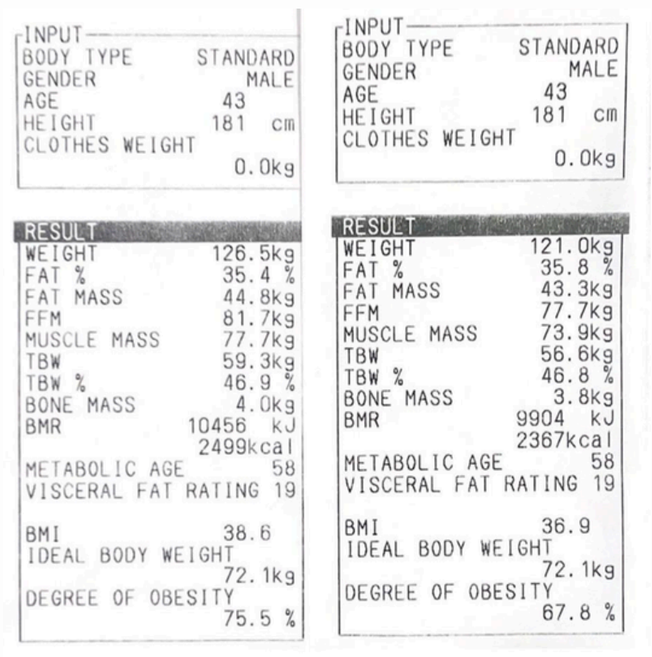


	Oxidative stress + spontaneous neutrophil membrane damage	The proportion of granulocytes with active ribosome conglomerate	The proportion of granulocytes with active mitochondrial conglomerate
Before starting therapy	0	65	37
In 1 month	30	5	2

2. MATERIALS & METHODS

Study Design: 12-week prospective, randomized study.
Participants: 40 overweight women (Age 27–37, BMI > 25, hyperinsulinemia >20 µU/ml).
Intervention:
Control Group: Semaglutide 2.4 mg/week (monotherapy).
Experimental Group: Semaglutide 2.4 mg/week + Mitochondrial Boosters (Fulvic-humic complex & 100 mg/day transdermal trans-resveratrol).

Assessments:
Body Composition: Visbody bioimpedance (muscle vs. visceral fat loss).
Live-Cell Profiling: . Leukocyte RNA was assessed by quantitative fluorescence microscopy using Pyronin Y (PY; CAS 92-32-0), mitochondrial membranes by NAO (CAS 75168-11-5) staining

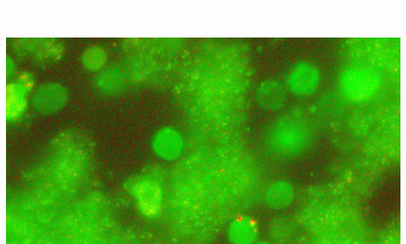


INPUT	
BODY TYPE	STANDARD
GENDER	MALE
AGE	43
HEIGHT	181 cm
CLOTHES WEIGHT	0.0kg

RESULT	
WEIGHT	126.5kg
FAT %	35.4 %
FAT MASS	44.8kg
FFM	81.7kg
MUSCLE MASS	77.7kg
TBW	59.3kg
TBW %	46.9 %
BONE MASS	4.0kg
BMR	10456 kJ 2499kcal
METABOLIC AGE	58
VISCERAL FAT RATING	19
BMI	38.6
IDEAL BODY WEIGHT	72.1kg
DEGREE OF OBESITY	75.5 %

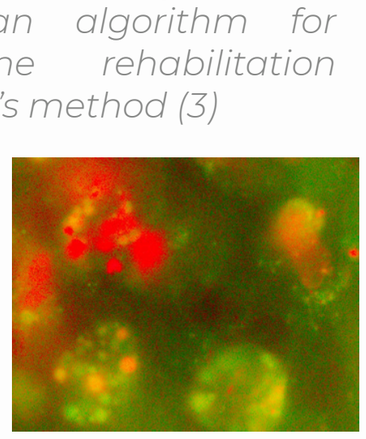
INPUT	
BODY TYPE	STANDARD
GENDER	MALE
AGE	43
HEIGHT	181 cm
CLOTHES WEIGHT	0.0kg

RESULT	
WEIGHT	121.0kg
FAT %	35.8 %
FAT MASS	43.3kg
FFM	77.7kg
MUSCLE MASS	73.9kg
TBW	56.6kg
TBW %	46.8 %
BONE MASS	3.8kg
BMR	9904 kJ 2367kcal
METABOLIC AGE	58
VISCERAL FAT RATING	19
BMI	36.9
IDEAL BODY WEIGHT	72.1kg
DEGREE OF OBESITY	67.8 %

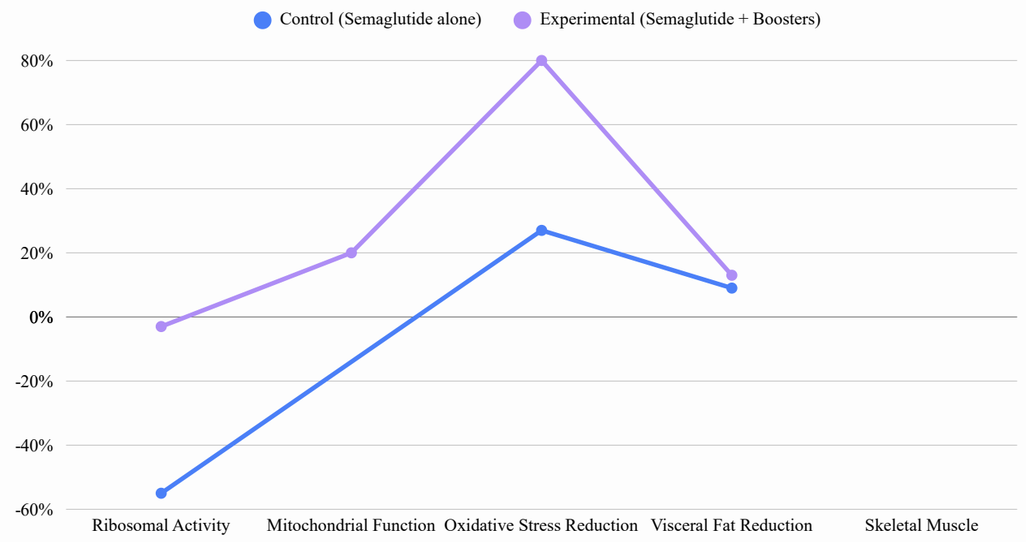


In the absence of signs of growth of the formation into the deep layers of the skin and low energy values according to Electrophoton Emission Analysis in combination with identified disturbances in the immune system, we have developed an algorithm for preventive immune rehabilitation based on the author's method (3)

which is carried out under the control of the CD4/CD8 level, NLR, the qualitative state of neutrophil function with the determination of phagocytic tests, stress apoptosis tests and monitoring of the level of mitochondrial activity



3. RESULTS:



Mean weight loss was 14.7–19.1%. The main group showed greater visceral fat reduction (13% vs. 9%) with significantly lower muscle loss. Mitochondrial indices increased (+20% active cells), while ribosomal activity was preserved (−3% vs. −55% in controls). The decrease in PY-high leukocytes paralleled pyruvate dehydrogenase-related changes and correlated with muscle loss (r≈0.55), but not with percentage weight loss.

4. THE "UNCOUPLING" MECHANISM

Our data reveal a critical mechanism, e.g. that GLP-1-induced starvation forces cells to sacrifice highly demanding protein synthesis (ribosomal collapse) to survive energetic stress.

Key finding: The decrease in Pyronin Y-high leukocytes (ribosomal suppression) strictly correlated with skeletal muscle loss (r ≈ 0.55), but not with total percentage weight loss.

This functional uncoupling of oxidative metabolism and translational capacity is the cellular driver of clinical sarcopenia.

CONCLUSIONS

1. *Systemic Stress: Monotherapy with GLP-1 agonists induces severe intracellular metabolic stress, causing functional uncoupling of leukocyte mitochondria and ribosomes.*
2. *A Novel Biomarker: Live-cell profiling of ribosomal RNA (Pyronin Y) serves as a highly sensitive, minimally invasive predictor of sarcopenic risk and "unhealthy" weight loss.*
3. *Therapeutic Synergy: Co-administration of high-bioavailability mitochondrial boosters prevents bioenergetic collapse, preserves muscle mass, and ensures long-term metabolic rejuvenation.*

References:

1. *Pantazopoulos, D. et al. "GLP-1 receptor agonists and sarcopenia: Weight loss at a cost?" *Diabetes Res Clin Pract*. 2025; 229:112924.*
2. *Steffen, K.K., Dillin, A. "A Ribosomal Perspective on Proteostasis and Aging." *Cell Metabolism*. 2016; 23(6):1004-1012.*
3. *Panov S.A., Baltabekov N.T. Utility Model Patent No. 6180, KZ, 2021.*