

0138 - NOT ALL OBESITY AGES EQUALLY: EPIGENETIC RESILIENCE IN EARLY-ONSET OBESITY MEDIATED BY THE IGF-1/FGF-21 AXIS

Mode: Research paper

Thematic Unit: Obesity

Thematic Unit 2: Insulin Resistance

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Background/Objectives: Pediatric obesity is classically linked to accelerated biological aging. However, clinical trajectories are strikingly heterogeneous. We hypothesized the existence of a biologically resilient phenotype in which chronic obesity does not translate into accelerated aging, driven by active regulatory mechanisms rather than absence of risk

Methods: We performed deep phenotyping in three groups (n=45): healthy controls, obese individuals with accelerated aging, and obese individuals with epigenetic resilience nested within a well-characterized historical cohort with long-term follow-up from birth onwards (Santiago Longitudinal Study). We integrated epigenetic clocks (Horvath, GrimAge), telomere length, and key metabolic signaling biomarkers (IGF-1, GDF-15, FGF-21) via Luminex. Multivariable models, partial correlations, and network analyses were used to identify regulatory nodes. Untargeted plasma proteomics (LC-MS) was used for orthogonal pathway validation.

Results: A dominant protective axis centered on IGF-1 emerged as a master regulator of biological stability, associated with telomere preservation ($\rho=0.80$, p

Conclusion: Obesity does not inherently drive accelerated aging; rather, biological aging depends on the integrity of specific regulatory endocrine axes. Convergent multi-omic evidence identifies an IGF-1/FGF-21-mediated resilient phenotype characterized by selective suppression of senescence pathways, reframing pediatric obesity as a biologically heterogeneous condition and highlighting metabolic resilience as a target for risk stratification and intervention. Funding: ACT210006-FONDECYT1210283-NIH-HL088530.

