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Summary

Targeting metabolic age: Mechanisms across the lifespan

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UEG Week Barcelona 2026 | Presentation

Mechanisms & Personalised Medicine

October 19, 2026

The speaker discussed metabolic flexibility in aging, focusing on hormonal regulators FGF19 and FGF21 in postprandial and fasting states, and presented unpublished data showing age-related uncoupling of metabolic biomarkers from muscle and liver parameters.

KEY POINTS

- FGF19 is secreted by the terminal ileum at the end of digestion, while FGF21 is the main fasting-state hormone that drives lipid oxidation and lipolysis, acting via beta-klotho in the brain to reduce appetite.
- The speaker stated that GLP-1 agonists lack hepatocyte receptors and suggested their liver effects may be systemic or paracrine, with semaglutide showing phase 3 efficacy and FGF21 activation improving liver fibrosis in mice.
- Unpublished biobank data from 3000 patients showed that metabolic correlations present in younger dysfunctional patients, such as between muscle and vascular parameters or insulin resistance, are lost by age 70.
- The speaker reported that with aging, ALT decreases and FIB-4 increases, raising concern that high FIB-4 at age 75 may not directly reflect fibrosis and suggesting age-specific reference values may be needed.
- The speaker recommended fasting in the evening and eating at breakfast and lunch, stating that consuming carbohydrates in the evening produces insulin at the wrong circadian time and drives lipogenesis.

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