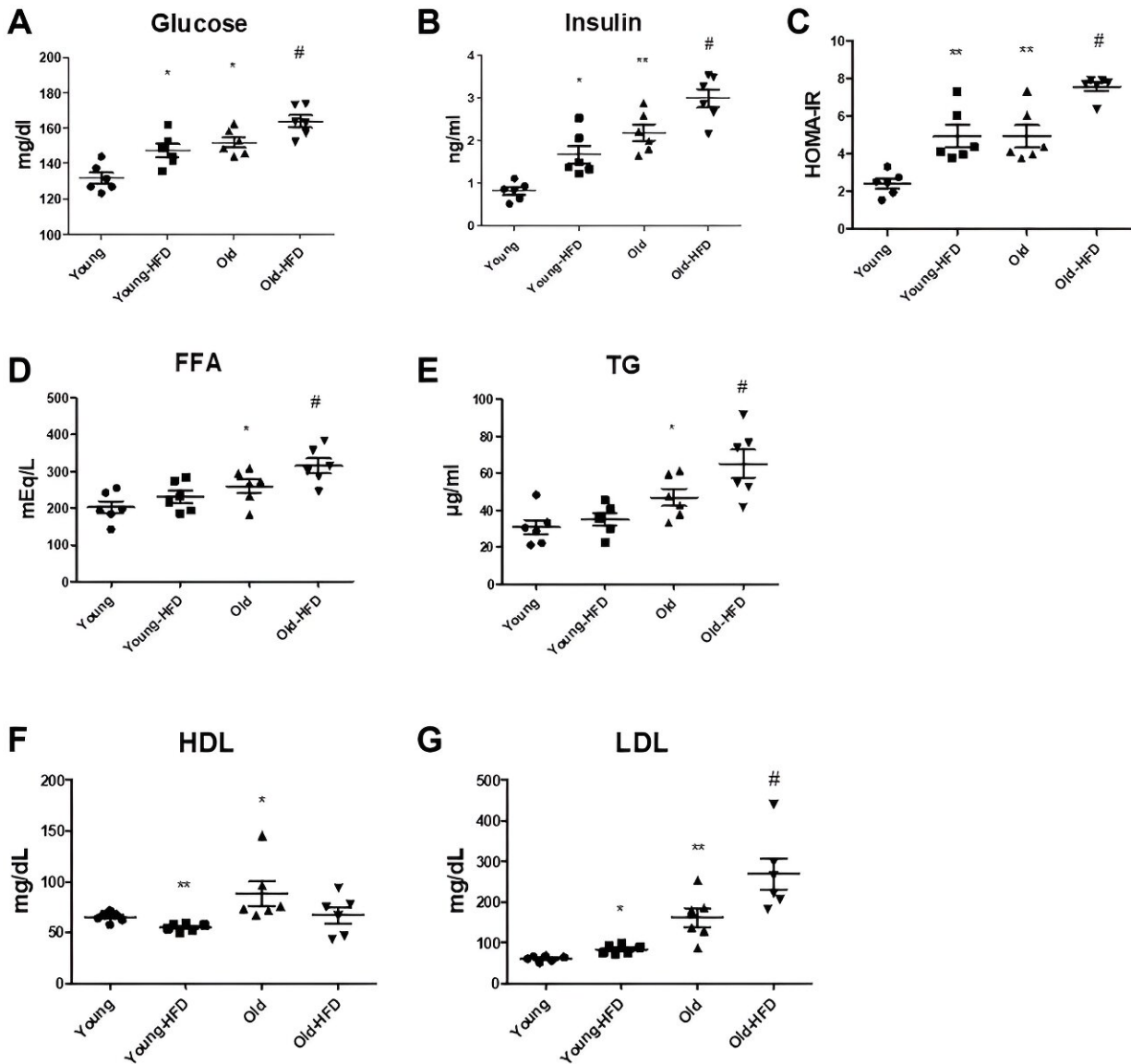


# **FoxO6-mediated ApoC3 upregulation promotes hepatic steatosis and hyperlipidemia in HFD aged rats: Study**

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Aging-related serum changes in insulin resistance and lipogenesis. (A) Glucose levels, (B) insulin levels, and (C) HOMA-IR scores were determined. (D) FFA (free fatty acid), (E) TG, (F) HDL, and (G) LDL levels in the serum of HFD-fed aged rats (each n = 6). Results of one-factor ANOVA: \*p Aging (2024). DOI: 10.18632/aging.205610

A new research paper titled "FoxO6-mediated ApoC3 upregulation promotes hepatic steatosis and hyperlipidemia in aged rats fed a high-fat

diet" has been [published](#) in *Aging*.

FoxO6, an identified factor, induces hyperlipidemia and hepatic steatosis during aging by activating hepatic lipoprotein secretion and lipogenesis leading to increased ApoC3 concentrations in the bloodstream. However, the intricate mechanisms underlying hepatic steatosis induced by elevated FoxO6 under hyperglycemic conditions remain intricate and require further elucidation.

In this new study, researchers Dae Hyun Kim, Seulah Lee, Sang Gyun Noh, Jaewon Lee, and Hae Young Chung from Pusan National University aimed to delineate the regulatory pathway involving ApoC3 controlled by FoxO6 and its resultant functional impacts.

The researchers explain, "[...] we employed a spectrum of models including liver cell cultures, aged rats subjected to HFD, [transgenic mice](#) overexpressing FoxO6 (FoxO6-Tg), and FoxO6 knockout mice (FoxO6-KO)."

Their findings indicate that FoxO6 triggered ApoC3-driven lipid accumulation in the livers of aged rats on an HFD and in FoxO6-Tg, consequently leading to hepatic steatosis and hyperglycemia. Conversely, the absence of FoxO6 attenuated the expression of genes involved in lipogenesis, resulting in diminished hepatic lipid accumulation and mitigated hyperlipidemia in murine models.

Additionally, the upregulation of FoxO6 due to elevated [glucose levels](#) led to increased ApoC3 expression, consequently instigating cellular triglyceride mediated lipid accumulation. The transcriptional activation of FoxO6 induced by both the HFD and high glucose levels resulted in hepatic steatosis by upregulating ApoC3 and genes associated with

gluconeogenesis in aged rats and liver cell cultures.

"Our conclusions indicate that the upregulation of ApoC3 by FoxO6 promotes the development of hyperlipidemia, hyperglycemia, and hepatic steatosis in vivo, and in vitro. Taken together, our findings underscore the significance of FoxO6 in driving [hyperlipidemia](#) and [hepatic steatosis](#) specifically under hyperglycemic states by enhancing the expression of ApoC3 in aged rats," the researchers conclude.

**More information:** Dae Hyun Kim et al, FoxO6-mediated ApoC3 upregulation promotes hepatic steatosis and hyperlipidemia in aged rats fed a high-fat diet, *Aging* (2024). [DOI: 10.18632/aging.205610](https://doi.org/10.18632/aging.205610)

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