

Body Composition Changes in Female APOE*3Leiden.CETP Transgenic Mice After 5-week Injection of Resveratrol-encapsulated Liposomes to Inguinal White Adipose Tissue (P21-041-19)

Zeynep Goktas,¹ Md Shahjalal Hossain Khan,² Yujiao Zu,² Lei Hao,² and Shu Wang²

¹Texas Tech University, Hacettepe University; and ²Texas Tech University

Objectives: Many cell culture and animal studies have demonstrated that *Trans*-resveratrol (R) has the potential to induce beige cell formation and activity. Although human studies indicate that R can maintain metabolic health, evidence is inconclusive regarding its browning effectiveness mainly due to its low aqueous solubility and high hepatic metabolism in humans. To combat the shortcomings of R, we have successfully synthesized biocompatible and biodegradable R-encapsulated liposomes (Rlipo). We will directly inject Rlipo into inguinal white adipose tissue (iWAT) in this project. The purpose of this study to evaluate the anti-obesity effects of **resveratrol-encapsulated liposomes** in female APOE*3Leiden.CETP transgenic mice, which have human-like lipoprotein metabolism.

Methods: Rlipo was prepared using R and soy phosphatidylcholine (soy-PC) dissolved in ethanol. After mixing and drying with nitrogen, deionized water was added followed by a sonication step. Ultrafiltration

was used to remove any unencapsulated R. The void liposomes (Vlipo) were prepared using only soy-PC.

Female APOE*3Leiden.CETP mice ($n = 40$) were fed with a high fat diet (45% of calorie from fat) throughout the study. After 4 weeks of the high-fat diet administration, mice were randomly divided into 4 groups ($n = 10$) and received iWAT injections of **Rlipo**, **Vlipo**, **free R** and **saline** (control) once per week for 5 weeks. **R** concentration was 17.5 mg/kg body weight/week. Body weight and food intake were measured weekly. Body composition of mice was measured using an EchoMRI™ every other week. Paired sample t-test and One-way ANOVA were used to analyze differences between means.

Results: After 5-weeks of treatment compared to baseline, fat percentage differences were $1.99 \pm 0.93\%$, $1.85 \pm 0.58\%$, $1.45 \pm 0.67\%$, and $1.40 \pm 0.68\%$ in **control**, **free R**, **Vlipo** and **Rlipo** groups, respectively. Body weight and fat mass showed a similar trend of change. Although control group showed an increase in lean mass (0.25 ± 0.95 g), Rlipo group showed a decrease (-0.14 ± 0.52 g). Food intake was similar among four groups.

Conclusions: Nanoencapsulation of R can enhance R's anti-obesity effects. However longer treatment time might be necessary to see more prominent results.

Funding Sources: NIH/NCCIH (Grant R15AT008733).