COL6A3 expression in adipocytes associates with insulin resistance and depends on PPAR? and adipocyte size.

Abstract:
COL6A3 may modulate adipose tissue function in obesity and insulin resistance. A role for human adipocytes linking COL6A3 with insulin resistance warrants exploration. COL6A3 mRNA in abdominal subcutaneous adipose samples was compared between (1) BMI-matched obese subjects resistant or sensitive to insulin (surgical whole tissue biopsies, n = 30/group), (2) lean/overweight and obese subjects (isolated adipocytes from collagenase-treated surgical biopsies, n = 11/group), (3) developing primary human adipocytes with/without knockdown of the insulin-sensitizing adipogenic gene PPARG (collagenase-treated lipoaspirate, n = 5), and (4) small and large adipocytes from lean/overweight subjects (collagenase-treated surgical biopsies or lipoaspirate, n = 10). Insulin resistance and sensitivity were assessed by euglycemic-hyperinsulinemic clamp (glucose infusion rate 70 ?mol kg(-1) min(-1), respectively) (1), or by HOMA-IR and TG/HDL ratio (2). Whole tissue COL6A3 mRNA was 2.6-fold higher in insulin resistant compared to sensitive subjects (P < 0.001). In isolated adipocytes, COL6A3 mRNA
correlated positively with BMI (P = 0.007), HOMA-IR (P = 0.039), and TG/HDL (P = 0.004). PPARG knockdown in developing adipocytes increased COL6A3 mRNA 1.5-fold (P = 0.043). The inverse relationship with adipocyte development was further supported by 2.8-fold higher COL6A3 mRNA in small compared to large adipocytes (P = 0.004). Increased adipocyte COL6A3 expression associates with insulin resistance in humans, which may involve impaired PPAR?-mediated adipocyte development.