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Use of UCHL1 Gene Expression to Estimate Adipocyte Size

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Abstract

Adipocyte size is linked to insulin resistance and the risk of developing type 2 diabetes. We aimed to generate a surrogate method to estimate adipocyte size by measuring adipose tissue gene expression using quantitative real-time PCR (qRT-PCR), which could be used alongside systemic measures of insulin sensitivity to predict type 2 diabetes risk. We examined the relationship of 40,591 genes with abdominal subcutaneous adipocyte size in 132 adults and validated the findings in additional cohorts with available transcriptomic and adipocyte size data. qRT-PCR analysis of gene expression in abdominal adipose tissue biopsies was used to develop a standardized adipocyte size estimate. This estimate was compared alongside systemic and adipose insulin sensitivity measures, including adipocyte lipogenesis, hyperinsulinemic-euglycemic clamp, adipose insulin resistance, and HOMA. Transcriptome-wide analyses found that UCHL1 gene expression strongly correlated with adipocyte size, independent of other genes and additional cofactors, such as insulin resistance (beta coefficient 0.32; P < 0.002). Using qRT-PCR, UCHL1 expression accurately estimated adipocyte size across a wide range of adipocyte volumes with high precision (receiver operating characteristic area under the curve 0.94) and showed strong correlations with all insulin sensitivity measures (adjusted R² = 0.2-0.6; P < 0.0001). We scaled the measurement of UCHL1 expression to 25-mg adipose biopsies and provided a standard operating procedure for routinely estimating adipocyte size. In summary, we provide a simple, accurate, and accessible surrogate measure to estimate an individual's adipocyte size, which may be useful in clinical insulin resistance studies.

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Use of UCHL1 Gene Expression to Estimate Adipocyte Size.
Schormals, Katharina; Zhong, Jiawei; Ricci, Laura D.R.; Wang, Na; Dahlman, Ingrid; Amer, Peter; Kent, Alastair G.
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Adipocyte size is linked to insulin resistance and the risk of developing type 2 diabetes. We aimed to generate a surrogate method to estimate adipocyte size by measuring adipose tissue gene expression using quantitative real-time PCR (qRT-PCR), which could be used alongside systemic measures of insulin sensitivity to predict type 2 diabetes risk. We examined the relationship of α -SPT genes with abdominal subcutaneous adipocyte size in 132 adults and validated the findings in additional cohorts with available transcriptomic and adipocyte size data. qRT-PCR analysis of gene expression in abdominal adipose tissue biopsies was used to develop a standardized adipocyte size estimate. This estimate was compared alongside systemic and adipose insulin sensitivity measures, including adipocyte lipogenesis, hyperinsulinemic-euglycemic clamp, adipose insulin resistance, and HOMA. Transcriptome-wide analyses found that UCHL1 gene expression strongly correlated with adipocyte size, independent of other genes and additional cofactors, such as insulin resistance (beta coefficient 0.20, $P = 0.002$). Using qRT-PCR, UCHL1 expression accurately estimated adipocyte size across a wide range of adipocyte volumes with high precision (receiver operating characteristic area under the curve 0.94) and showed strong correlations with all insulin sensitivity measures (adjusted $r^2 = 0.2$ – 0.6 , $P < 0.0005$). We scaled the measurement of UCHL1 expression to 25-mg adipose biopsies and provided a standard operating procedure for routinely estimating adipocyte size. In summary, we provide a simple, accurate, and accessible surrogate measure to estimate an individual's adipocyte size, which may be useful in clinical insulin resistance studies.

Article Highlights:
* Adipocyte size is linked to insulin resistance and the risk of developing type 2 diabetes.
* A surrogate method was generated to estimate adipocyte size by measuring adipose tissue gene expression using quantitative real-time PCR.
* UCHL1 expression was found to correlate across a wide range of adipocyte cell volumes (38–1420 μ L) and to strongly and independently correlate with measured adipocyte volume when examined alongside measures for insulin resistance.
* Clinicians can use this method to estimate adipocyte size from an adipose tissue needle biopsy and routine quantitative real-time PCR measurement using the provided equation and methodological framework.
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