DOWNREGULATION OF COMPLEMENT C3 AND C3aR EXPRESSION IN SUBCUTANEOUS ADIPOSE TISSUE IN OBESE CAUCASIAN WOMEN

Abhishek Gupta[1,2], Reza Rezvani[1], Marc Lapointe[1], Pegah Poursharifi[1], Picard Marceau[1], Sunita Tiwari[2], Andre Tchernof[1], , Katherine Cianflone[1]

[1]Centre de Recherche Institut Universitaire de Cardiologie & Pneumologie de Québec, Université Laval, Québec, Canada
[2]Department of Physiology, King George's Medical University, Lucknow, Uttar Pradesh, India

Abstract:

Background: The central component of the complement system, C3, is associated with obesity, type 2 diabetes and cardiovascular disease however the underlying reasons are unknown. In the present study we evaluated gene expression of C3, the cleavage product C3a and its cognate receptor C3aR in subcutaneous and omental adipose tissue in women.
Methods: Women (n=140, 21-69 years, BMI 19.5-79 kg/m^2) were evaluated for anthropometric and blood parameters, and adipose tissue gene expression.
Results: Subjects were separated into groups (n=33-36) according to obesity: normal/overweight (≤ 30kg/m^2), obese I (≤45 kg/m^2), obese II (≤51 kg/m^2), and obese III (≤80 kg/m^2). Overall, while omental expression remained unchanged, subcutaneous C3 and C3aR gene expression decreased with increasing adiposity (2-way ANOVA, $p<0.01$), with a concomitant decrease in SC/OM ratio ($p<0.001$). In subcutaneous adipose, both C3 and C3aR expression correlated with apoB, and apoA1 and inversely with waist circumference and blood pressure, while C3aR also correlated with glucose ($p<0.05$-0.0001).
While omental C3aR expression did not correlate with any factor, omental C3 correlated with waist circumference, glucose and apoB (all $p<0.05$). Further, while plasma C3a/C3adesArg increased and adiponectin decreased with increasing BMI, both correlated (C3a negatively and adiponectin positively) with subcutaneous C3 and C3aR expression ($p<0.05$-0.001) or less).
Conclusions: The obesity-induced down-regulation of complement C3 and C3aR which is specific to subcutaneous adipose tissue, coupled to the strong correlations with multiple anthropometric, plasma and adipokine variables support a potential role for complement in immunometabolism.

KEYWORDS
Complement C3, C3a receptor, C3a/C3adesArg, adipose tissue, body mass index, obesity