Obesity and Heart Steatosis: the Potential Role of the Receptor for Advanced Glycation End Products (RAGE)

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Obesity is one of the leading risk factors for cardiovascular diseases. Most of the obesity-related complications are due to the ectopic accumulation of fat in tissues different from the adipose one, as liver and heart, a condition that can promote organ damage and dysfunction. The receptor for the advanced glycation end products (RAGE) is up-regulated in many tissues in obesity and has been related to ectopic lipid accumulation in the liver. No data are available about RAGE and heart steatosis, instead.

By using lean (n = 5) and obese non-diabetic (n = 5) Zucker rats (age: 20 weeks) (investigations have been conducted in conformance with the FASEB Statement of Principles for the use of Animals in Research and Education. Protocol Number 325/2015PR - 2015/04/05, Italian Ministry), we tested the hypothesis that in obesity, the accumulation of lipids in the heart may be mediated, at least in part, by RAGE.

Heart tissues were studied in terms of lipid accumulation, RAGE tissue expression, activation/modification of specific genes (n=84) involved in lipid metabolism (RT^2 Profiler PCR Array , PARN-007Z, QIAGEN). The following methods were used: red oil staining, real time RT-PCR and Western blot.

We did not observe any difference in heart fat content between lean and obese rats. Heart RAGE levels, both as gene and protein, were almost the same in the two groups. Among the 84 genes evaluated, 6 genes were significantly up-regulated, of which 4 promoting fatty acid metabolism (Acaa2, Acadl, Acadm, Acot9), 1 fatty acid transport (Crat) and 1 tryacilglycerol metabolism (Gpd1).

Uncomplicated obesity in 20-week old rats is not associated with fat accumulation in the heart. The lack of RAGE hyper-expression and the increased fatty acid metabolism seem to play a protective role against fat-induced heart damage.

Whether fat accumulation may be promoted by aging and the onset of obesity-related complication (*i.e.* diabetes) needs to be explored.