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High-fat diet-induced obesity is associated with increased cardiac telomerase expression but not cell proliferation in the rat

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Obesity is a condition of low-grade, chronic inflammation, defined as elevated body weight due to abnormally increased adiposity, commonly from increased dietary intake of saturated fats. Although there are suggested links between obesity, increased cardiovascular mortality and low telomere length[(1)], no direct relationships between obesity, telomere length and telomerase expression in cardiac tissue have yet been shown[(2)]. On the other hand, cardiac hypertrophy has been linked to higher circulating levels of telomerase and reduced telomere length[(3)], but not to a change in cardiac myocyte proliferation. Two phenomenological studies were carried out to explore relationships between obesity and cardiac tissue telomerase gene expression and cell proliferation.

Age-matched male Wistar rats (~250 g, Charles River, Margate, U.K.) were stratified by body weight and randomly assigned to groups fed for 8 weeks on diets differently enriched in saturated fatty acids (Research Diets, Inc., N.J., U.S.A.; $n = 8$/group). In Study 1, experimental rats received a high-fat diet (HFD), and in Study 2, a very high-fat diet (VHFD), providing 40% and 60% of energy from fat, respectively. In both studies, control groups received low-fat diets providing 10% of energy from fat. All diets contained equal concentrations of antioxidants. Study 1 rats received the cell proliferation tracer, 5-bromo-2-deoxyuridine (BrdU; Sigma), in their drinking water (1 mg/ml) for the final week of the study. Terminal body weight was measured and white adipose tissue depots dissected and weighed. Samples of left ventricular free wall were dissected and processed histologically for BrdU uptake, as assessed using signal intensity immunofluorescent (IF) measurements (Volocity™) (Study 1), or by QT-PCR for telomerase (TERT) mRNA expression referenced to 18S rRNA expression (Study 2).

	Study 1					Study 2			
	% fat mass		BrdU-IF			% fat mass		TERT mRNA	
Diet	Mean	SEM	Mean	SEM	Diet	Mean	SEM	Mean	SEM
Control	0.775	0.076	43.9	4.5	Control	1.032	0.081	5.11×10^{-6}	8.52×10^{-7}
HFD	1.136*	0.116	45.2	5.2	VHFD	1.449**	0.010	1.11×10^{-5}*	2.0×10^{-7}

Adiposity was calculated as % epididymal fat mass relative to final body weight. Significance of within-study differences between diet groups were determined by Student's two-sample *t*-test: *$p<0.05$; **$p<0.01$ *vs.* controls.

Both high-fat diets induced obesity (increased adiposity). This was associated with increased cardiac telomerase gene expression, but not cell proliferation. Future work will examine how the two might be related in the same model and whether increased telomerase expression is an adaptive response to obesity.

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