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PROTEOMIC ANALYSIS OF LIPOPROTEIN LIPASE CHARGE ISOFORMS

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Lipoprotein lipase (LPL) is a glycoprotein enzyme that plays a pivotal role in lipid metabolism. Abnormalities in LPL function have been associated with a number of pathophysiological conditions, including atherosclerosis, obesity, Alzheimer's disease, and diabetes. A large number of LPL studies have been performed in rat, although the amount of information derived from direct study of the protein in this species is limited. Here we attempted to examine possible modifications of LPL using proteomic tools. By combining high-resolution two-dimensional gel electrophoresis and Western blot with biological mass spectrometry we demonstrate, for the first time, the coexistence of multiple LPL charge isoforms in the rat. We studied the origin of this charge heterogeneity by: (1) comparison with the 2D pattern of LPL from post-heparin rat plasma (as a source of mature LPL); (2) protein dephosphorylation; (3) protein deglycosylation; and (4) partial sequencing of different LPL isoforms by capillary liquid chromatography tandem mass spectrometry. The results reveal that this charge heterogeneity is not due to different stages of intracellular maturation or protein phosphorylation. It can be partially explained by glycosylation, although other post-translational modifications must also be involved. Our findings increase the complexity of LPL studies and data interpretation and open the doors to further research aimed at identifying the molecular differences between LPL isoforms and exploring the potential functional implications of this charge heterogeneity.