Letter to the Editor: GLP-1 and exendin-4: not simply two of a kind

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TO THE EDITOR: We read with great interest the recently published study by DeNicola et al. (2), entitled “Stimulation of glucagon-like peptide-1 receptor through exendin-4 preserves myocardial performance and prevents cardiac remodeling in infarcted myocardium”. The authors demonstrated that systemic treatment with exendin-4 attenuated left ventricular remodeling and improved survival in mice with myocardial infarction. In cardiomyoblasts subjected to oxidant stress, they showed that exendin-4 reduced ROS production and preserved mitochondrial function and cell survival. While the authors provided strong evidence for the cardioprotective effects of exendin-4, they omitted an important aspect that may affect the interpretation of the results.

Exendin-4 has been generally considered a potent agonist of the glucagon-like peptide-1 receptor (GLP-1R). However, there is accumulating evidence questioning its specificity. Exendin-4, but not GLP-1, was shown to improve insulin sensitivity in adipocytes (3). Furthermore, Ban et al. (1) reported direct cardioprotective effects of exendin-4 in mice lacking the GLP-1R. Finally, we (4) recently demonstrated in rat hearts that the effects of exendin-4 on myocardial glucose utilization and contractility differed from those of GLP-1 and were unaffected by blocking the GLP-1R with exendin 9–39. In light of these data, it is of particular importance to discriminate between the effects of exendin-4 and those of GLP-1, and the involvement of the GLP-1R in treatments with exendin-4 should not be taken for granted.

DISCLOSURES
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