AFM Characterization of Diabetic Cardiomyocytes

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ABSTRACT:

Dynamic mode atomic force microscopy was used to investigate diabetic cardiomyocytes in order to visually elucidate the development of chronic diabetic heart disease. Diabetes is widely recognized as a major risk factor for developing cardiovascular disease. A significant number of patients with either type 1 or 2 diabetes develop a cardiomyopathy (i.e., abnormal muscle cell function) independent of coronary artery disease. We have evidence that nonesterified fatty acids, which represent one metabolic condition associated with diabetes. play a role in the pathogenesis of diabetic cardiomyopathy. We also have evidence that there are distinct cellular changes (i.e., blebs) in isolated cardiomyocytes due to exposure to fatty acids, which appear to be associated with abnormal mechanical function. These blebs are visible with phase contrast light microscopy. Determining the nature and location of these changes was the primary focus of this investigation.

We developed techniques to visualize the plasma membrane and subcellular topography in fixed adult rat cardiac myocytes cultured overnight in normal or high fatty acid conditions using atomic force microscopy. Atomic force microscopy is a near-field imaging technology with the capacity to resolve structures at the molecular level on the relatively flat surfaces of the myocytes. Dynamic mode atomic force microscopy (a.k.a. "tapping mode" or "intermittent contact" atomic force microscopy) is capable of high resolution imaging without exerting constant destructive sheer forces on the sample that can damage and smear subtle biological features. The exquisite vertical sensitivity of the atomic force microscopy (<1 nm) allows for observation of critical membrane features. Exploring fixed cells at resolutions ten to one hundred times greater than can be achieved by optical techniques, while examining changes in membrane and subcellular structures in the context of diabetic cardiomyopathy, represents a novel addition to diabetes research.