HEALTH RESEARCH ABSTRACT SUBMISSIONS #17

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College *	College of Medicine
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Title of Research *	The Balance Between Life and Death: A Study of Cardiomyocyte Apoptosis in Offspring of Diabetic Mothers
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Introduction & Purpose *	Pregnancies complicated by gestational diabetes have resulted in adult offspring with altered metabolic and vascular function due to oxidative stress on the developing fetus, resulting in diabetes mellitus and hypertension. We hypothesize that cardiomyocytes of adult offspring of diabetic mothers (ODM) show similar susceptibility to oxidative stress, resulting altered expression of cell death markers, including Jun N-terminal kinase (JNK), and of cell survival markers, including Extracellular signal regulated kinases 1 and 2 (ERK1/2).

Experimental Design *

Pregnant Sprague-Dawley rats made diabetic with streptozotocin on day 12 of gestation were supplemented with insulin to maintain glucose levels in the 200-400 mg/dl range during pregnancy. Cells from the hearts of the offspring were isolated and exposed to 0, 20, and 60 µM hydrogen peroxide for 15 min. A control group of cells was also used. Following the peroxide treatment, an ELISA was performed to characterize the amount of apoptosis in each of the samples. The results were analyzed such that the values for the 20 and 60 µM hydrogen peroxide treatments were normalized to the 0 µM treatment. Western blot analysis including ERK1/2, pERK1/2, JNK, and pJNK of both control and ODM cardiomyocytes treated similarly as the ELISA samples was also performed.

Results *

With a 60 µM hydrogen peroxide treatment, control hearts tend to have reduced apoptosis as opposed to ODM hearts ($p = 0.11$). Control hearts also show less apoptosis after the 60 µM treatment as compared with the 20 µM treatment ($p = 0.023$), whereas ODM hearts do not show this same relationship ($p = 0.94$). With regard to ERK1/2 and pERK1/2 protein expression, ODM cardiomyocytes appear to upregulate these proteins with increased oxidative stress (ERK1/2 $p=0.10$; pERK1/2 $p=0.10$). A similar upregulation is seen in ODM cardiomyocytes with respect to JNK and pJNK protein expression (JNK $p=0.09$; pJNK $p= 0.07$). In addition, ODM cardiomyocytes appear to upregulate pJNK expression with increased oxidative stress as compared to baseline ($p=0.09$).

Conclusions *	The studies in this paper support the theory of developmental programming, where disturbances in the intrauterine environment may alter phenotypic expression of a single genotype. It appears that as a result of gestational diabetes, the ODM cardiomyocytes' response to

oxidative stress is altered. However, more studies are warranted to elucidate exactly how the balance between cardiomyocyte cell death and survival is affected in this population.

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