Update for the Mach-Gaensslen Foundation - 2009
Dr. Lynn Megeney, The Mach-Gaensslen Chair in Cardiac Research.

This past year has been exceedingly productive for my research group, on both the academic side as well as with regards to commercialization activities. In terms of academic progress, our laboratory has published 3 original research papers (Fernando et al. 2009, Miyake et al. 2009 and Guevel et al. 2009), as well as an invited book chapter (Puente et al. 2009 in Phospho-Proteomics) for 2009. Moreover, we have recently completed an additional invited book chapter (Evans and Megeney 2010 in Modern Insights into Disease from Molecules to Man: Apoptosis), the text of which will be published in early 2010.

In addition to these publications we have a number of manuscripts in review[1] at high profile journals. All three of these manuscripts deal with the topic of cell death proteins and pathways as key regulators of normal cell function rather than signals for cell death. We discovered over the past 8 years that cell maturation requires the activity of these various 'death only' genes/proteins. These studies from our laboratory were initially greeted with great hostility in the larger scientific community. For example, the 2002 Nobel prize in medicine was awarded to the scientists that discovered the key cell death proteins and pathways. However, our observations are now widely accepted and we are regarded as the leading global authority in this area of research. At the time of last year's update, preliminary observations in the laboratory suggested that these death proteins were required for the normal maturation process of heart muscle cells. Currently we have completed this study and the manuscript has been submitted for publication (Abdul-Ghani et al.)[1]. This is a very important observation as many scientists/clinicians in the field have proposed that therapies should be developed to block these cell death proteins as treatment strategies for various cardiac/heart disease conditions. Our results suggest that such an approach may cause significant unanticipated problems as these cell death factors are required for normal function in the heart.

With regards to commercialization activities, we are poised to make a major breakthrough in the financing of our Biotech start-up company Verio Therapeutics Inc. As you may recall, Verio Therapeutics Inc. is a new venture born from the science that launched our initial commercial vehicle StemPath Inc. Verio is the commercialization vehicle for the translational research that comes from my laboratory as well as that of Dr. Michael Rudnicki. We anticipate a major financing agreement will be in place by year end (2009), an agreement that will be substantial and allow for the movement of 2 programs toward clinical applications. The positioning of Verio for a successful financing has been due in large part to 2 key developments over the preceding year. First, we have been recently informed that patent protection will be issued in the European Union (E.U.) for my groundbreaking work on the characterization of a protein that promotes cardiac stem cell activity and repairs heart muscle damage associated with infarcts/heart attacks[2]. Awarding of the patent in the E.U. offers significant market protection for this very promising discovery. In addition, we anticipate a similar response from the United States Patent Office (USPTO) within the coming months. Second, I have submitted a very promising provisional patent with regards to a drug

treatment for muscular dystrophy[3]. This discovery is of considerable potential impact and we are currently in discussions with the Muscular Dystrophy Association (USA) toward formulating a clinical trial within the coming year.

Finally, I would like to note 2 honors I have received over the preceding year. First, I was selected by my fellow scientists to be the director of the Centre for Neuromuscular Disease (CNMD) at University of Ottawa. The Ottawa area (The OHRI, CHEO and the Univ. of Ottawa) has the largest concentration of muscle disease researchers in North America. The CNMD is a virtual centre that facilitates a common research theme supported by a highly integrated collaborative research environment. I have been selected to lead the CNMD and build the research capacity of the larger group. Second, I have been honored by the Chinese Academy of Sciences (CAS) as a Visiting Senior International Scientist. This prestigious award was granted based on our pioneering work on cell death proteins as noted above and forms the basis of an international collaboration that has been established between my laboratory and one of the premier CAS research centres, The Guangzhou Institute of Biomedicine and Health.

1. Abdul-Ghani, M., Dufort, D., DeRepentigny, Y., Kothary, R., and **Megeney, L.A**. (2009). Wnt11 promotes myocardial development through a caspase dependent suppression of canonical Wnt signals. *Submitted.*

   Larsen, B.D., Rampalli, S., Burns, L., Dilworth, F.J. and **Megeney, L.A.** (2009). Caspase 3/Caspase activated DNase promote cell differentiation by inducing DNA Breaks. *Submitted.*

   Lee, R.E.C., Brunette, S., Puente, L.G., and **Megeney, L.A.** (2009). The yeast caspase YCA1 is required for the clearance of insoluble protein aggregates. *Submitted.*

   Guevel, L., Lavoie, J., Perez-Iratxeta, C., Rouger, K., Dubreil, L., Feron, M., Brand, M., and **Megeney, L.A.** (2009). Quantitative proteomic analysis reveals dramatic metabolic disturbances in the canine model of Duchenne muscular dystrophy. *Submitted.*

2. Use of Cardiotrophin to Modulate Stem Cell Proliferation. Publication number:WO2004113380; Application number:WO2004CA00940 20040625; Priority number(s):US20030482001P 20030625; Publication date:2004-12-29; Inventor: Lynn Megeney.

3. Treatment of Muscle Disease Characterized by Insulin Resistance. New USPTO application. US: Priority Date: 2009-05-24. Inventor(s): Lynn Megeney, Carol Evans.