Driving Forward Research and Education on Longevity and Cancer Avoidance in Rottweilers: A Report to the Rottweiler Health Foundation June 20, 2012

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In 2007, the Rottweiler Health Foundation awarded Dr. Waters' research team a 5-year grant to pursue factors that impact exceptional longevity and cancer resistance in Rottweilers. Five years later, the collaborative effort has proved highly successful in 3 domains: Scientific progress; Education of veterinarians and pet owners; and Generating goodwill for the Rottweiler breed. In order to build upon this far-reaching achievement, Dr. Waters' research program at the Murphy Foundation's Center for Exceptional Longevity Studies is seeking financial support directly from members of the Rottweiler community. Dr. Waters summarizes below his 5-year progress and outlines the key areas of inquiry that his team intends to pursue.

Scientific Progress

In 2005, we established the Exceptional Longevity Data Base of exceptionally long-lived Rottweilers, representing the first systematic study of successful aging in pet dogs. As of January 2012, we have gathered extensive data from more than 230 Rottweilers who have lived at least 13 years of age, equivalent to 100-year-old people. The scope of this work stretches nationwide, with the Data Base capturing Rottweilers from 41 states and Canada. Thanks to Rottweilers, pet dogs are beginning to be recognized as powerful tools for deepening our understanding of human aging. In 2010, Dr. Waters was invited by the National Academies of Sciences to write a paper on the opportunities and challenges of research on dog aging. This paper, entitled "Aging Research 2011: Exploring the Pet Dog Paradigm", was published in the *ILAR Journal* in February 2011 as part of a special issue devoted to benchmarking the most useful animal models of aging research. The scientific community is turning its attention to Rottweilers as new tools. This is exciting because new tools mean new hope – hope that the research can lead to longer, healthier lives for both pets and people.

Since 2009, we have published four (4) peer-reviewed, scientific papers from our work on aging. Our first paper coming from the Exceptional Longevity Data Base was published in December 2009 in *Aging Cell*, the highest impact journal in the world among the 57 scientific journals dedicated to gerontology and geriatrics. This paper, entitled "Exploring Mechanisms of Sex Differences in Longevity: Lifetime Ovary Exposure and Exceptional Longevity in Dogs", reported our discovery in Rottweilers of a previously overlooked ovary-longevity connection. Our findings in Rottweilers mirror the results of emerging research in women showing that women who keep their ovaries for at least 50 years live longer. In 2011, we published two papers in veterinary journals read by theriogenologists (experts in veterinary reproduction). In the first paper, entitled "Probing the Perils of Dichotomous Binning", we explored the methods previous investigators had used to study spaying and longevity and presented a more rigorous, technically demanding method of performing this type of research. This is very

important so that future studies in this area will generate more reliable results, providing more clarity than confusion. In the other paper, entitled "In Search of a Strategic Disturbance: Some Thoughts on the Timing of Spaying", we urged veterinarians to acknowledge spaying (the removal of hormone-producing endocrine organs) as a physiological disturbance. We reasoned that, if we can agree upon this, then the question is no longer whether spaying is good or bad, but rather a new sort of question: Can we make spaying a *strategic* disturbance? This new way of thinking redirects emphasis toward pursuing the critical issue of finding the timing of spaying that will benefit pets the most.

The Rottweiler community should see publication of our work in top-flight scientific journals to be of prime importance. This is because publication witnesses the scientist passing the sternest test of accountability – not the peer review by a grant committee of an idea that the scientist hopes to pursue, but instead the peer-review of the methods the investigator actually used to complete the research and the importance of the results found. Until 2009, there had never been a paper published in *Aging Cell* on dog aging. That has all changed now, made possible by our persistent efforts.

In addition to these scientific achievements, we have established the Biorepository at Murphy (BAM), a one-of-a-kind biorepository of tissues, DNA, and blood samples from the oldest-old Rottweilers. This collection of biological specimens represents a rare opportunity to pursue research questions about what it takes to live long and avoid cancer, and positions the Murphy Foundation to make further and unique contributions to the science of successful aging.

Education of DVMs and Pet Owners

Our research progress, leading us to re-conceptualize ovaries as endocrine organs, not just reproductive organs, challenges pre-existing beliefs about the timing of spaying that optimizes overall healthy longevity. Since no veterinarians are trained in the biology of aging as part of their DVM curriculum, the veterinary profession is ill-equipped to discuss new research on aging and longevity. Recognizing an unmet need, the Murphy Foundation developed the first Gerontology Training Program for graduate veterinarians in 2007.

But our education efforts do not stop there. Our efforts in education on the biology of aging for breeders and pet owners (ARC National Show in Lancaster, May 2011; The Eukanuba Breeders Championship in Orlando, Dec 2011; Rose City Classic in Portland, Feb 2012), and for DVMs at some of the world's largest veterinary conferences (American College of Theriogenology, Sept 2010; American College of Veterinary Internal Medicine, July 2011; North American Veterinary Conference, Jan 2012; Western Veterinary Conference, Feb 2012; American Veterinary Medical Association, Aug 2012) are unprecedented. At these prestigious venues, we are *not just presenting facts about aging, but instead presenting a new angle of vision* – new ways of seeing the promises and pitfalls of aging research. During the period from August 2011 to August 2012 alone, Dr. Waters will address more than 1000 DVMs and pet owners about the importance of taking a life-course perspective to highly successful aging and the value of whole-organism thinking. This means that we shouldn't wait until too late, when our pets are old, to start thinking about how to promote longevity. Too often, veterinarians tend to focus on their favorite organ or favorite disease. By advocating that we must pay closer attention to whole organism thinking, we look beyond any one particular disease, and remind ourselves that there will always be trade-offs – every choice we make has some upside and downside. This means that decisions like taking antioxidant supplements or spaying should never be considered "good" or "bad", but instead always considered "good" AND "bad".

These are bold new ideas that will require some time to take hold. But people are listening closely. In February 2012, our work on longevity in Rottweilers was cited by a panel of experts in the American Animal Hospital Association's Canine Life Stage Guidelines, a document intended to shape guidelines for practicing veterinarians to design individualized wellness plans *for pets of all breeds* (*Bartges et al, J Amer Anim Hosp Assoc 2012; 48:1-11*). We see this education activity as vital to preparing the ground for future progress. We need not only tip-top research, but also tip-top communication within the veterinary profession and with pet owners, to achieve the most impact.

Generating Goodwill for the Rottweiler Breed

During the last 5 years, our work has also shaped in a positive way how the public perceives the Rottweiler breed. In 2010, my 22-day, nationwide trek to study 15 of the oldest-living Rottweilers in their homes captured the imagination of people across the country. Not only did it signal a new and innovative way of doing aging research – taking research out of the ivory tower of universities and laboratories and into the very places where these exceptional dogs lived – but also enabled outsiders to see Rottweilers in a positive light. The too-often portrayed negative image of a Rottweiler as threatening was replaced by a gang of Rotties leading an effort to find out what it takes to age successfully. The images of "The Old Grey Muzzle Tour" earned widespread media attention, featured on *Good Morning America, USA Today,* and *AARP Bulletin*. As we continue our trailblazing longevity research on Rottweilers, we expect to occupy the minds of the public with positive images deserving of the Rottweiler breed.

Looking Ahead to Drive Forward Research and Education on Longevity and Cancer Resistance in Rottweilers

Looking ahead, Dr. Waters and the Murphy Foundation's Center for Exceptional Longevity Studies will need the support of the Rottweiler community to sustain research and education progress in at least 3 key areas:

Discovering the Mechanisms of Cancer Resistance

The Rottweilers in our Exceptional Longevity Data Base are resistant to cancer mortality. By conducting detailed autopsy examinations, we will gain a better understanding of what it takes to be cancer resistant.

Probing the Relationship Between Response to Stress and Successful Aging

We will continue to gather data on the stress responses of exceptionally long-lived Rottweilers to determine if we can design new ways to side-step the age-related decline in how the body copes with stress.

Defining the Window of Lifetime Ovary Exposure that Optimizes Healthy Longevity

This line of investigation will move us closer to making smarter recommendations regarding the timing of spaying that optimizes health and longevity.

Concluding Perspective

In 2007, the Rottweiler Health Foundation took a bold step entrusting the Murphy Foundation to advance the science behind aging and cancer in Rottweilers. At that time, there was no ovary-longevity story on the blackboard, no dream of an Old Grey Muzzle Tour, no biorepository of valuable Rottweiler tissue and blood specimens in sight. Today all of these products are in clear view, a testimony to our trailblazing efforts in health investigation. Now, instead of focusing on the funding of a single project, *Dr. Waters is setting out to create a cycle of success* – finding recurrent support from members of the Rottweiler community who have been inspired by his work. Securing the support that will fuel a program that integrates our effort, leading to notable intellectual progress and community impact. We invite members of the Rottweiler community to be a part of this success and further our mission, investing your trust in Dr. Waters' abilities and commitment to sustain healthy progress in the areas of healthy aging and cancer avoidance in Rottweilers. Dr. Waters will be reaching out to you. We encourage you to reach out to Dr. Waters.