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December 20, 2011

Ms. Donna Schmack-Rose
Ms. Chelle Zulick
C/O Yorkie Angel Patrol
206 Md. Terry Lane
Dunn, NC 28334

Dear Donna and Chelle:

We want to express our sincere thanks and appreciation for the recent \$1000.00 donation from you and the Yorkie Angel Patrol for funding to help expand the CREATE fund at the North Carolina State University-College of Veterinary Medicine. Although you will also receive direct confirmation of receipt of the funding from the North Carolina Veterinary Medical Foundation, we also wanted to extend our personal thanks for all that both of you continue to do, as well as all of the members of the Yorkie Angel Patrol, are doing to combat GME!

We continue to be amazed at the outpouring of energy, time and enthusiasm that all involved with the Yorkie Angel Patrol are doing to turn what has been a personally challenging loss of a canine companion(s) into a positive program for many pets and their owners, not only at NCSU-CVM, but at other Universities as well. We were also so honored to have you both as guests at the new Terry Center this past fall!

We have put together a brief summary of some of the projects that are either in progress, or that we have plans to pursue:

- Dr. Chris Mariani, Director of The Comparative Neuroimmunology and Neurooncology Laboratory (Mariani Lab) is involved in the investigation of canine meningoencephalitis (ME). This encompasses a number of disease processes, including granulomatous meningoencephalitis (GME) and necrotizing meningoencephalitis (NME). This work is proceeding on several fronts:

1) We are trying to unravel the mechanisms underlying the development of inflammatory brain and spinal cord disease. As infectious agents are rarely identified in dogs, these diseases are thought to be immune-mediated; that is related to an “overactive” immune system. We are investigating the interactions between the immune system and nervous system, including analyzing immune cell populations within the nervous system, draining lymph nodes and peripheral blood, and cytokine concentrations within the spinal fluid and blood. We have also been pursuing studies of specific at-risk breeds such as Maltese and Yorkshire Terriers, to try and identify underlying genetic causes of these diseases.

2) The laboratory is also interested in biomarkers of disease. These are compounds that can be sampled from patients (e.g., from the blood, urine or spinal fluid) and provide information about the disease process and burden of disease. Such biomarkers ideally provide information helpful in making a diagnosis, in monitoring the response of the disease to treatment, and in forming an accurate prognosis. We have investigated and are continuing to work on a number of biomarkers for canine ME including c-reactive protein, matrix metalloproteinases (MMPs), neopterin, and vascular endothelial growth factor (VEGF).

3) We are also keenly interested in improving the therapy for these diseases, which usually involves suppression of the immune system. We have recently been examining the ability of specific immunosuppressive drugs to interfere with immune cell populations in an experimental setting. This might be useful in the future both to guide selection of the best drug in clinical patients as well as to monitor ongoing treatment.

4) Finally, we have been involved in clinical investigations of several immunosuppressive medications to try and establish optimal treatment protocols for these diseases. These clinical studies are both lab-based, with a Cytosar Pharmacokinetic study completed in 2011 and a clinical-based Cytosar project that is ongoing into 2012. Dr. Katherine Crook, one of our Neurology Residents that you met during your visit, along with faculty Drs. Peter Early and Karen Munana, are in the process of finalizing these projects. In addition, both residents and clinical faculty are sharing this information at regional, state and nationwide veterinary meetings.

- In addition to the above, we have been able to help a couple of patients this past year with costs associated with GME diagnosis and medical care.
- Also, we are continuing to develop a CSF sample bank of affected dogs, to pursue additional studies.

It has been very exciting in many ways to be taking part in both clinical and laboratory based research related to GME and other neurological disorders affecting our companions. It has also been an honor to again be the recipient of dollars raised for

additional research dedicated towards the CREATE fund. It has been pet-owners such as both of you, and the entire Yorkie Angel Patrol, that is truly driving some of this research and education forward.

On behalf of Dr. Chris Mariani, Dr. Karen Munana, myself and the entire NCSU-CVM Neurology Service, we all wish to extend our sincere appreciation for all that you have done, and continue to do, to support funding to help fight the battle against GME.

May you have a wonderful Holiday Season!

Dr. Chris Mariani

Dr. Karen Munana

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