**New Necropsy Lab Available for Investigators**

The Laboratory of Comparative Pathology (LCP) has recently inaugurated a new state-of-the-art necropsy laboratory at its WCMC facility. This lab (C-704) is used by LCP staff, but is also available to investigative staff to perform necropsies on animals of any size, from mice to swine. The room is equipped with a downdraft necropsy table, two backdraft grossing stations, CO₂ for euthanasia of rodents, and a cooler for carcass storage and disposal. For reservation or questions regarding the use of this room, please contact the laboratory at (646) 888-2422 or lcp@med.cornell.edu.

**Comparative Pathology—Important Tool in Scientific Discovery**

Comparative pathology, the study of disease in various species, including humans, has contributed to the advancement of medical knowledge since the cellular basis of disease was first described in the 19th century by Rudolf Virchow, the Father of Modern Pathology. The core of pathology is formed by the study of four aspects of disease: its cause (etiology), mechanisms (pathogenesis), biochemical and morphologic manifestations (molecular and morphologic pathology), and functional consequences (clinical manifestations). Therefore, pathology is an integrative discipline: by combining the basic and clinical sciences, it contributes to a comprehensive understanding of disease. With the rapid growth in the development and use of animal models of human disease, the role of comparative pathology has expanded. As manipulations of the mouse genome has lead to the creation of increasingly sophisticated models, comparative pathology has become essential in their validation and use. Comparative pathologists contribute a

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In February, The American Association for Laboratory Animal Science (AALAS) sponsored Laboratory Animal Technician Appreciation Week or “Tech Week.” Tech Week was created a decade ago to recognize the contributions of animal care technicians by highlighting the important role they play in ensuring the health and well being of research animals. The celebration is officially scheduled for the first week of February in coordination with “Groundhog Day” and is meant to symbolize the technicians “coming out of the shadows”.

For the past 7 years RARC has celebrated this occasion with a department luncheon for the combined WCMC and MSKCC staff. During the luncheon awards are presented to outstanding staff who have gone above and beyond the call of duty. In an effort to further staff education, we also invite guest speakers to discuss their research with animal. This year Dr. Jonathan Dyke, a member of the Citibank Biomedical Imaging Center (CBIC) spoke about his work on atherosclerosis using a guinea pig model and Dr. Pat Zanzonico, Director of MSKCC’s Small Animal Imaging Core (SAIC) detailed the state-of-the-art imaging facilities available to our investigative staff.

Please take a moment to thank the technicians who work in your area each day ensuring your animals are receiving the highest level of care.

**Popular Suture Product Recall- Vicryl Rapide**

ETHICON has expanded a voluntary product recall of VICRYL RAPIDE suture material. This recall includes 37 lots of product that was produced during the May to June 2007 timeframe. The recall was initiated because of a defect in the packaging which could compromise the integrity of the product leading to premature suture degradation or impaired sterility. If you have VICRYL RAPIDE suture, please locate the lot number on the product and contact Veterinary Services (VS) to determine if that particular lot is included in the recall. VS can assist you with the return and replacement of this product.

**Important Notice:**

**VICRYL RECALL!**

Contact RARC Vet Services for details.
Infusion Technology Update, cont.

A tethered system may be more appropriate for studies which require long term access (days to months) to a catheter for drug delivery or blood withdrawal.(5) Tethered systems also allow for simple alterations to infusion rates and solutions without anesthesia or surgery. These systems are available for animals ranging from mice to non-human primates. Rats are the most commonly used species for tethered infusion.(6) Specialized equipment and in some instances specialized caging is required for this technology.

The tethered catheter can be placed into any vessel, visceras or other cavity. Vascular access is most commonly achieved through the vena cava, tail vein or femoral vein.(5) After placement into the desired location, the distal portion of the catheter is exposed outside of the animal. A tether system then anchors and protects the catheter. These systems come in the form of jackets, harnesses, implantable buttons or tail cuffs. The externalized portion of the catheter extends to a pump delivery system, and requires protection against animal entanglement or chewing. This is achieved by running the catheter through a flexible metal spring attached to a swivel and lever arm that permits animal movement. This configuration prevents many rodent tethered systems from fitting within microisolator caging systems.

A syringe or peristaltic pump is required to drive the experimental compound through the catheter. Syringe pumps are better for low volumes and flow rates. These external pumps allow easy adjustment to the infusion rate and replacement of the infusion solution to test another compound or provide a washout period. Unlike osmotic pumps, the initial set-up cost of these tethered systems is substantial, but long term costs can be low.

Programmable, ambulatory infusion pump technology has existed in human medicine for decades.(7) Its use in animal research has been reserved for animals of two to three kilograms or greater due to pump size.(7) An implantable, tetherless, refillable, programmable system has been developed for animals ranging in size from rats to larger species (iPRECIO™, Primetech Corporation, Tokyo, Japan). Use in mice is precluded as each pump weighs approximately ten grams. The company believes that a lighter pump will be available within the next few years (C. Whelan, personal communication, April 10, 2010). This electromechanical infusion pump uses peristaltic action to deliver pharmaceutical agents according to a programmable infusion protocol.(8) Agents can be delivered at a continuous or variable rate. Up to ten variable flow rates (from 1.0 μl/hour to 30 μl/hour with 0.1 μl/hour increments) can be repeated in cycle loops to increase the number of variations in the infusion protocol. These programs can mimic bolus dosing or create dose response curves among other study designs. Also programmable are start and stop times and time delays to allow agent exchange. The life of the battery driven pump is determined by flow rate. The greater the set flow rate, the shorter the available infusion time, i.e. at 30 μl/hour the battery life is approximately 1 week, at 1 μl/hour, the battery life is approximately 6 months.(8)

The pump is designed to fit within the subcutaneous space of the animal. This superficial placement allows percutaneous access to the pump refill septum and underlying reservoir. Under sedation, the reservoir can be refilled to extend the experimental delivery period or emptied and refilled again to change experimental compounds or create washout periods. Two pumps can fit within the subcutaneous space of a rat to increase the amount of compound delivered, and pumps can be replaced as battery life expires. Pump replacement requires surgery.

This technology is still in its initial stages with few publications and proof of principle available. These pumps are associated with considerable cost. At start up, management software must be purchased to program the pumps and each pump is approximately $250.00. However, further development of this technology resulting in smaller, programmable, refillable pumps could be of great benefit to research.

Comparative Pathology, continued from page 1

unique perspective to biomedical research, as they are trained in veterinary or human medicine and pathology, and have a broad knowledge of the anatomy, physiology, and spontaneous pathology of a wide variety of animal species and strains. However, the number of pathologists trained in investigative comparative pathology and devoted to this discipline is small. In an article on the role of comparative pathology in research, Cardiff, Ward, and Barthold (1), noted: “Many investigators are forced to rely on their own ‘Do-it-yourself’ (DIY) pathology or on a local, albeit inexperienced, pathologist. As a result, the scientific literature is replete with erroneous interpretation of phenotype by DIY pathologists lacking expertise in mouse pathology. [This situation] has led to embarrassing and egregious errors. These are not trivial misinterpretations. Some … have had expensive consequences”. This excerpt is followed by examples of unsubstantiated lesions, erroneous phenotypes, and misinterpretation of normal anatomical structures as lesions, which were published in high impact journals.

The interpretation of neoplastic and preneoplastic lesions in genetically engineered mice (GEMs) is an example that illustrates this problem. The study of GEM models of cancer represents a unique opportunity for understating the natural history of cancers: the correlation of molecular alterations with morphologic evidence of neoplastic transformation and progression can yield critical insights into cancer pathogenesis. However, preneoplastic and neoplastic lesions in new GEMs often represent a diagnostic challenge, even to the most experienced pathologists, and interpretation by untrained investigators has lead to erroneous conclusions (1). For this reason, funding agencies and editorial boards increasingly require the participation of a pathologist in cancer studies involving animal models. Additionally, the recognition of specific “genetic signatures” in animal tumors has become an interesting aspect of comparative pathology (2). As wisely stated by Rosai (3) as he discussed the value of H&E sections, “The amount of information that the examination of these samples [by a skilled observer] has provided is staggering. This should not be too surprising. After all, the microscopic appearance of a tumor … represents the grand synthesis of thousands of genes working in concert and sometimes in opposition”.

Pathology has become essential in the phenotyping of new GEMs, not only for cancer models but for a wide variety of disease processes. By adopting a comprehensive approach which includes macroscopic and microscopic examination of all organ systems, standardized documentation and diagnosis of lesions, and incorporation of hematology and serum chemistry data, pathology contributes to the complete characterization of new GEMs. This approach has often led to the discovery of unexpected phenotypes which may not have been recognized by other methods.

CCMP’s Laboratory of Comparative Pathology provides services and expertise in pathology and all major disciplines of laboratory medicine. The staff of the LCP is composed of three anatomic pathologists who are board certified by the American College of Veterinary Pathologists (ACVP), a consultant ACVP-certified clinical pathologist, one resident and one fellow in comparative pathology, and eight technologists with expertise in necropsy, histology, immunohistochemistry, hematology, serum chemistry, microbiology, parasitology, and serology. The primary role of the LCP staff is to provide analysis and diagnostic interpretation on animal specimens, but they are also available for consultation on the planning of studies and the choice of animal models, as they are familiar with the anatomy, physiology, and naturally occurring pathology of a wide variety of species and strains.

The LCP is open from Monday to Friday, 9 am to 5 pm, and can be reached at 646-888-2422 or lcp@med.cornell.edu. Additional information is available at http://intranet.med.cornell.edu/research/rarc/pat_lab/radl.html

References:
3. Rosai J. Why microscopy will remain a cornerstone of surgical pathology. Lab Invest 2007; 87:403-408.