

Current Progress in Understanding and Treatment of Equine Melanomas

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Melanomas are malignant tumors derived from melanocytes that may arise from the skin or subcutaneous tissues. While melanomas are relatively uncommon in horses, they pose a serious medical problem in horses with graying hair coat. More than 80% of horses with pigmented skin and graying hair coat will develop melanomas that eventually metastasize to other organs.

Analysis of mutations (Genetic “fingerprints”) in melanoma-associated genes and gene associated with graying hair coat revealed that melanoma tumors are genetically different depending on their location and clinical appearance. Mapping specific mutations of melanoma tumors using modern genetic mapping techniques to catalog the genetic defects associated with equine melanomas is in progress. The findings, that will be presented, may help provide a rationale for selective breeding to improve prevention and for drug development to target individual genetic pathways.

Although melanomas are often neglected because of their apparent slow growth rate, they are known to be resistant to traditional forms of treatment including surgery, chemotherapy and radiation therapy. Understanding the central role that the immune system plays in recognizing and fighting tumor cells has led to immunotherapy, which is a form of treatment designed to boost the natural attack of tumors cells by the immune system. Immunotherapy involves the use of tumor-vaccines to immunize the patient against the tumor cells and biologic response modifiers (primarily interleukins) to stimulate immune response against the tumors. Tumor-vaccines train the body to recognize and destroy cancer cells that already exist within its tissues and to keep killing those malignant cells long after treatment has ended. Different types of tumor vaccines including autologous and polyvalent cell-culture derived vaccines as well as recombinant DNA vaccines have been under investigation at UCD-VMTH for several years. Despite variable results, the message is clear: a horse's own immune system can be effectively enlisted to help combat melanoma. The most vexing issue is, however, the inability to obtain a consistent response to tumor immunization due to immune tolerance--or the immune system's reluctance to attack its own normal and tumor cells. In order to eliminate this obstacle, clinical trials using equine interleukin-12 (Eq-IL-12) and interleukin-2 (Eq-IL-2) are underway at UCD-VMTH. These interleukins are intracellular signaling molecules that control the actual killing by the effector cells of the immune system and can override immune tolerance to tumor cells. The drugs are injected directly into tumors which results in high concentrations within the tumor and low systemic toxicity. Results of these clinical trials will be presented.

Better understanding of the disease's link to graying of the hair coat and specific mutations, together with new therapeutic melanoma vaccines now being tested have set the scene for new approaches to the treatment of melanoma in Equidae

BIOGRAPHICAL SKETCH

NAME Alain P. Théon		POSITION TITLE Professor	
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
École Nationale Vétérinaire d'Alfort, France	Veterinary degree	1982	Veterinary Medicine
École Nationale Vétérinaire d'Alfort, France	DEDV	1983	Veterinary Thesis
Faculté de Médecine de Créteil, France	Doctorate (PhD)	1986	Radiation Biology
University of California, Davis, CA	Residency	1988	Radiology –Radiation Therapy
University of California, Davis, CA	MS	1989	Comparative Pathology

1. Positions

1990–1995 Assistant Professor, Department of Radiological Sciences, School of Veterinary Medicine, University of California, Davis, CA

1995- 2000 Associate Professor, Department of Surgery and Radiology, School of Veterinary Medicine, University of California, Davis, California

2000-present Professor, Department of Surgery and Radiology, School of Veterinary Medicine, University of California, Davis, California

2002- present Oncology Service Chief, Veterinary Medical Teaching Hospital, UC-Davis

1995-present Director of Veterinary Radiation Oncology Residency training program

B. Professional Specialty

Diplomate, American College of Veterinary Radiology - Radiation Oncology

Member of the Veterinary Cancer Society, American Society for Therapeutic Radiology and Oncology European Society of Internal medicine – Oncology