

Human melanoma is the fastest growing cancer currently in USA and worldwide. Melanoma accounts for 5% of all skin cancers but 71% of all skin cancer deaths. The risk for melanoma has steadily increased since 1935 when the risk was 1:1,500. Today one in 74 people are diagnosed with melanoma. The mechanism for melanoma initiation is unknown and no significant advances in medical therapies (survival) for patients with advanced melanoma have occurred in the past 30 years. Additional research and drug development are required. Miniswine offer insights into the genetics, immunology and pathogenesis of malignant melanoma. At birth, 54% of Sinclair miniswine have primary melanomas, which increases to 85% at one year (Goldberg et al., 2004). Over 70% of primary lesions result in metastasis to regional lymph nodes and have remarkable histological similarity to human melanoma.

Sinclair Miniature Swine

A sub-strain of Sinclair miniature swine develops an aggressive form of melanoma very similar to the human counterpart. This aggressive melanoma has the unique attribute of spontaneously regressing after a complete metastatic phase. Within this clinically relevant animal model, scientists have a rare opportunity to study development, regression, and therapeutic compounds in a spontaneously occurring malignant cancer.

Availability

Sinclair miniswine were derived from pigs originally developed at the Hormel Institute in Minnesota. The Sinclair swine melanoma was first observed in 1967 in one animal of the Sinclair miniature swine breeding herd. Experimental breeding herds of melanoma swine currently are maintained at the Sinclair Bio Resources, Columbia, Missouri.

Immune Response in Sinclair Miniature Swine

Sinclair miniswine display cutaneous melanoma lesions at birth or develop lesions shortly thereafter. Most, if not all, subsequently remain free of tumors. The tumor regression observed in Sinclair miniswine appears to be associated with an increase in host leukocyte mediated activity. Examination of swine melanoma lesions during the latter stages of melanoma growth has revealed that large numbers of pigment-laden macrophages have invaded the lesions with an apparent decline in the number of cells. Furthermore, other studies have reported that the melanoma bearing swine exhibited enhanced leukocyte reactivity to 3 M KCl extracts of swine melanoma cells using an antigen stimulated active rosette assay. This in vitro leukocyte reactivity appeared to correlate with tumor volume as leukocyte activity was greater in swine with a lower rate of tumor growth and lower tumor volume. This Sinclair miniswine developed an immune response to the melanoma.

Comparison to Human Disease

The Sinclair miniswine melanoma model has many features in common with its human counterpart: 1). Tumors develop spontaneously; 2). Swine possess a wide spectrum of benign melanocytic lesions capable of malignant transformation; 3). Melanomas in pigs histopathologically resemble human superficial spreading melanoma; 4). Metastatic disease is correlated with deeply invasive cutaneous tumors; 5). The pattern of metastatic spread is analogous to the distribution of metastases in human melanoma; 6). The histopathology of cutaneous regression is similar; 7). A tumor-related immune response occurs in the host; 8). A genetic component is readily apparent that is comparable to the genetic component of some melanomas in man.

Usefulness of the Model

Sinclair miniswine melanoma provides a unique opportunity to investigate host-tumor-cell interactions in a clinically relevant system. The miniswine melanoma model has many features in common with human malignant melanoma. Furthermore, substantial evidence exists that host immunological factors play a role in the development, growth, and regression of this neoplasm. The Sinclair miniswine melanoma model also provides an excellent system in which to investigate the progressive cellular changes during the transition from normal, through pre-malignant, to malignant and to metastatic melanoma, as well as the cellular change occur during the spontaneous regression of melanoma lesions. Sinclair miniswine melanomas take a variety of histopathologic forms in vivo. We have found that when these lesions are adapted to grow in vitro, the primary cultures are also morphologically variable. This finding, together with the observation that several swine melanoma lesions can progress and regress simultaneously in a single pig, suggests that tumor heterogeneity may play a significant role in the natural history of swine melanoma.

Sentinel Lymph Node Mapping for Resection

Tanaka et al. (2006) [Ann Surg Oncol Dec 13(122): 1671-81] of Beth Israel Deaconess Medical Center, Boston, MA, have developed a novel invisible near-infrared (NIR) fluorescent method for in vivo sentinel lymph node (SLN) mapping and resection using the spontaneous melanoma large animal model (Sinclair Miniature Swine). This method improves visualizing tumor metastasis for oncologic surgical resection.