

Swine Melanoma

Introduction

Melanoma is a serious form of skin cancer. It begins in melanocytes, the cells that make the skin pigment called melanin.

In human, melanoma accounts for only about 4% of all skin cancer cases. However, it causes most skin cancer-related deaths. Melanoma is often curable if it is detected and treated in its early stages. In men, it is found most often on the area between the shoulders and hips or on the head and neck. In women, melanoma often develops on the lower legs. It may also appear under the fingernails or toenails or on the palms or soles. The chance of developing melanoma increases with age, but it affects all age groups. In human familial melanoma, three risk susceptibility genes are already known, CDKN2A, CDK4 and MC1R.

Melanocytic neoplasms occur in domestic species, including cattle, sheep and swine as well as laboratory animals. Of these species, Swine melanoma has been very much studied for two reasons. Firstly, some miniature pigs such as Sinclair and MELIM strains, and Duroc breed have a genetic predisposition for melanomas. Secondly, some herds of miniature pigs have served as experimental models for spontaneous cutaneous melanoma in humans. According to Stevenson (1999), cutaneous melanomas in Duroc are often benign and heavily pigmented. Melanomas primarily appear on the skin and may develop metastases to lymphatic tissues and organs.

According to CFIA's "Meat Hygiene Manual of Procedures", the carcass and carcass portions must be condemned when cutaneous melanoma lesions also affect an internal organ or are accompanied by systemic effects. If the cutaneous lesions are ulcerated or invasive or if the lymph nodes are involved (either a hypertrophy of the lymph node or a black tar-like pigmentation), the carcass is held after trimming. The appropriate samples must be sent to the laboratory for histopathological examination. When the results confirm the presence of metastases, the carcass and carcass portions must be condemned.

In practice, the carcasses with melanoma are condemned at the packing plant. Producers don't get paid anything for hogs with melanoma.

Recognition of swine melanoma

Melanoma may include several types of neoplasms in animals. In animal skin melanocytic neoplasms, the most reliable histologic feature for distinguishing malignant from benign is the mitotic index. Neoplastic cell morphology is also a useful discriminating feature. Cytologic features of malignancy include the presence of a large nucleus, variation in nuclear size and shape, hyperchromasia, abnormal chromatin clumping, one or more nucleoli, and atypical mitotic figures (Smith et al. 2002).

Genetics of swine melanoma

Swine melanoma is a heritable cancer. This was demonstrated by statistical analyses of pedigree data and gene mapping studies. Here, some studies are reviewed briefly.

Blangero et al (1996) conducted a complex segregation analysis of a two-locus model and detected an unknown major locus and a second locus that lies within or close to the swine leucocytic antigen (SLA) complex. The loci jointly determine the risk in pedigreed animals.

Tissot et al. (1987) discovered two loci that are involved in the expression of swine melanomas. The first locus lies within the swine major histocompatibility (also called SLA) complex where one particular allele causes the second locus fully penetrant. The second locus segregates independently of the major histocompatibility complex. The melanoma-producing allele at this second locus is inherited in the heterozygous state and requires a mutation of the normal allele to initiate tumor development.

Geffrotin et al (2004) used the MeLiM swine as an animal model of hereditary melanomas of human. They performed a genome scan for linkage to melanoma in swine. Founders of the affected MeLiM stock were crossed with each other and with healthy Duroc pigs, to generate MeLiM F1 and backcross families for the gene mapping study. The results revealed that (1) MeLiM swine melanoma was inherited as an autosomal dominant trait with incomplete penetrance, preferably in black animals, (2) four chromosomal regions potentially involved in melanoma susceptibility were identified on swine chromosomes 1, 2, 7 and 8, respectively, in intervals 44-103, 1.9-18, 59-73 and 47-62 cM of the chromosomes, (3) a fifth region close to MC1R was revealed on SSC 6 by analyzing an individual marker located at position 7.5 cM. (4) CDK4 and BRAF were unlikely to be melanoma susceptibility genes in the MeLiM swine model, and (5) the 3 regions on SSC 1, 6 and 7, respectively, have counterparts on human chromosomes (HSA) 9p, 16q and 6p, harboring melanoma candidate loci. The 2 others, on SSC 2 and 8, have counterparts on HSA 11 and 4.

Müller et al. (2001):

A line of Munich Miniature Swine (MMS) Troll showing a high incidence of spontaneous benign and malignant cutaneous melanocytic lesions has been developed since 1986.

Müller et al. (2001) studied the inheritance of cutaneous melanocytic lesions by establishing the F1-, F2- and reciprocal B1-generations with one melanoma Munich Miniature Swine (MMS) Troll boar and four unaffected German Landrace sows as founders. The MMS Troll showing a high incidence of spontaneous benign and malignant cutaneous melanocytic lesions has been developed since 1986. A total of 176 animals were available, 27 in the F1-, 111 in the F2-, 19 in the B1-DL-, and 14 in the B1-Troll-generation. Benign melanocytic lesions were observed in 42% of F1-, 18% of F2-, 11% of B1-DL- and 50% of B1-Troll-animals. Malignant melanomas developed in 3.6% of F2- and 7.1% of B1-Troll-animals. The result showed that no animal with white coat colour was affected. A mixed major gene model with arbitrary gene action explained the segregation of benign lesions sufficiently well. For melanomas a mixed major gene model

required additional dominant acting suppressor loci to obtain a sufficient fit to the data. The association analysis of the white phenotypes strongly indicated that the dominant allele I at the I-locus suppresses malignant melanocytic lesions. An explanation is the lack of melanocytes in the skin of dominant white pigs caused by a mutation of the KIT-gene, which leads to a failure of melanoblast migration and development.

suggestions

Many studies confirmed that swine melanoma is hereditary. Several candidate genes and loci have been reported. Selection on these genes and loci can lead to reduce the incidence of swine melanomas and related carcass anomalies.

Melanoma begins with the cells that make the skin pigment called melanin. Therefore, coloured animals, such as the black swine (Geffrotin et al 2004) and Duroc (Smith et al. 2002) are more susceptible to melanoma. Müller et al. (2001) noted that no animal with white coat colour was affected in their 176 experimental animals. Müller et al.'s association analysis (2001) strongly indicated that a dominant allele in white phenotypes suppresses the presence of swine melanoma. The explanation is the lack of melanocytes in the skin of dominant white pigs caused by a mutation of the c-KIT gene, which leads to a failure of melanoblast migration and development. Therefore, the dominance allele may be utilized for remedy the issue in commercial level.

In Canada, dam lines are white breeds and sire line, Duroc is coloured. Melanomas should not be a problem at commercial level since commercial hogs are expected to be white. However, the problem is that white dominance gene is not always completely dominant because except c-Kit locus, some other genes such as MC1R also play a role in coat color inheritance. It is not clear how these genes work together with c-Kit gene in determining swine coat color. Some study on c-Kit and MC1R genes needs to be done. Solving this issue is also able to promote the Canadian genetics sale in some Asian countries since uniform coat color has been taken as an indication of breed purity.

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