

Cancer Stem Cells: A New Way to Look at an Old Disease

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Dr. Modiano called cancer stem cells the “evil twin sister” of therapeutic stem cells, but said the similarity is no reason to doubt or fear the possibilities of regenerative therapy using stem cells.

Noting that dogs and humans have a common concern with cancer, he asked for a show of hands from those who had not been affected in some way by cancer, either human or canine. Only a few participants raised their hands.

Cancer is a conglomerate of conditions that represents a huge public health problem, Dr. Modiano said. It is the primary cause of death for adults under age 85, and the secondary cause for adults over 85 and for children.

He described cancer as the uncontrolled proliferation of cell growth, starting with a single cell. Playing a short video clip of a tumor’s progression, he said that cancer cells continue to divide at the expense of normal cells around them. They grow, and then recruit blood vessels, and in the final stage, called metastasis, the tumor cells invade the bloodstream and travel along vessels to infect other tissues.

Dr. Modiano said that while he has been told by many lay people that cancer is caused by walking under power lines, using a cell phone, being zapped by cosmic rays, or eating commercial dog food, the actual cause is life. Being alive means an inherent risk for cancer with every cell division, he said, and life itself is the biggest risk factor for cancer. He gave what he called the Breen/Modiano Axiom: “Cancer is an inevitable consequence of mammalian evolution.”

Because nature has limited tools to work with, Dr. Modiano said, cells might try to revert to an earlier state. That may be where cancer starts. A long life exponentially increases the risk of cancer.

The lifetime risk for cancer in both dogs and people is between 30% and 50%, and cancer represents the leading cause of death for 50% of dogs aged seven and up. For some breeds, it is also the most common cause among diseases leading to death. For example, he said, one study showed that 60% of Golden Retriever deaths are from cancer.

While most cancer is treatable, the majority of cancers are not preventable with current strategies. It is possible to reduce the risk of some cancers—for example by using sunscreen, and quitting, or never starting, smoking. Some studies show that lean, fit animals have a reduced incidence and fewer problems with cancer, suggesting that a good diet and regular exercise also help.

“For humans, it’s hard to get a handle on genetic factors,” Dr. Modiano said. “That’s where dogs come in.” Statistics show that certain breeds, such as Boxers, Golden Retrievers, Labrador Retrievers, Basset Hounds, Doberman Pinschers, and German Shepherds, are at higher relative risk of lymphoma. Others, including mixed breeds, Pomeranians, Poodles and Chihuahuas, are at a lower risk. Dr. Modiano said researchers have speculated that small breeds may have less risk because they require fewer cell divisions to grow their smaller frames, but more research is needed. Recent research into insulin-like growth factors suggests that the risk of cancer in dogs may increase with body mass, but this hypothesis has not been proven.

One study that looked at 1,262 dogs of various breeds found that the average age for all dogs developing lymphoma was 9.5 years. Some breeds had a lower average age, including Golden Retrievers at 8.5 years and Rottweilers at 6.8 years. These numbers represent statistically significant deviations from the average, Dr. Modiano said, and could be evidence of less genetic diversity within a given breed. He noted that the study suggests a risk resulting from whatever makes up a breed’s genetics. A study of 100 dogs with osteosarcoma showed similar numbers and age distributions. However, Dr. Modiano said, the meaning of these differences is still unknown.

Another osteosarcoma study tracked the survival of dogs with the disease over time according to the type of treatment received. Dogs receiving no treatment survived for less than one month; those receiving palliative treatment did not fare much better. Dogs with amputations survived longer, and those receiving the current standard of care had the best results of the four options studied. Dr. Modiano said researchers have found some genetic markers that seem to predict which dogs will do well and which will not.

Cancer cells are characterized by a series of mutations, self-sufficiency, reduced sensitivity to anti-growth signals, limitless replication, and the ability to evade apoptosis, programmed cell death or “suicide.” A study at Johns Hopkins that sequenced 22 human tumors found that on average, each cancer cell contained 90 mutations, Dr. Modiano said.

Although many urban myths circulate regarding cancer, no single cause can be pinpointed. Toxic compounds can increase susceptibility, but even so, they are not a sure predictor. For example, Dr. Modiano said, only 20% of smokers get cancer. “There are many risk factors, but they only come together to produce cancer in one of five in this group.”

While the existence of cancer stem cells is supported by compelling information, Dr. Modiano said, how they are formed is still unknown. If cancer stem cells really are like stem cells, they should be able to self-renew and give rise to heterogeneous reproduction. Studies of human chronic myelogenous leukemia done in Denmark and in Texas have shown that cancer stem cells do share these properties.

Dr. Modiano noted that this has implications for the conventional model for resistance and relapse, in which cancer returns after treatments kills the cancer cells. One

hypothesis is that if treatments introduce mutations in cancer stem cells, they may become resistant to therapy, return, and then metastasize. If this is the case, Dr. Modiano said, researchers should try to develop treatments that specifically target cancer stem cells.

One small study of nine dogs showed that the presence of more stem cells was linked to a shorter survival time, suggesting that the presence of these cells may be predictive.