

# TUMOR MARKERS FOR DIAGNOSIS OF NEOPLASMS IN ANIMALS

**Bineesh P.P.**

Veterinary Surgeon,  
Veterinary Dispensary,  
Koorachundu  
Kozhikode

Tumor markers (TM) are widely used in human diagnostic field for the diagnosis and treatment of the neoplasms (fig 1). The usefulness of tumor markers in animals for the better treatment and diagnosis is yet to be established for which studies are in progress worldwide. Different methods are adopted in cancer detection. The main methods are pathology techniques and the imaging techniques like X-ray and CT Scan and are widely used in cancer detection. Their ability to locate the tumor in the body is unquestionable. However, such techniques have limitations; firstly, all cancers cannot be detected using X-ray or CT Scan; secondly, the pathological methods are invasive and it requires biopsy for examination. In addition, locating the tumor by imaging techniques is a prerequisite for biopsy to be advised for pathological examination. While the third method, the biochemical methods detects and measures tumor markers (can be detected by immunohistochemical techniques-fig 2 also in pathological methods) and predicts the development of tumor based on marker concentration which is an easier technique and is useful in detection of the tumor well before they attain a considerable size that could be detected by imaging or biopsy techniques.

## What are tumor markers?

They are generally proteins which could be an antigen, hormone, enzyme or immunoglobulin which are identified in blood, tissues, urine or feces of the animals or man which are secreted by tumor cells or are the part of the cell structures released in another words the tumor markers are the substances that can be detected in the blood or body fluids of animals having an underlying malignancy. The markers are made by the tumor and released into the circulation but it should be kept in mind that they may be produced by normal tissues in response to tumor.

The Kochian postulates of tumor markers outlines the criteria for a substance to be considered as a marker. They are:

- 1) circulating level of TM must be abnormal in presence of neoplastic process
- 2) the circulating level of TM has direct relationship to tumor progression or regression
- 3) the tumor tissue itself must contain the tumor marker.

The hormones does not fulfill the criteria whereas, the CEA and AFP are identified within the tumor tissues.

More precisely, a tumor marker must be specific and sensitive.

A TM will be **specific** when it is produced only by cells of a particular malignancy and not by other cancers or benign conditions and a marker will be **sensitive** when it is produced in all patients with similar malignancies and the get produced in amounts that correlate with the tumor burden. It should be born in mind that the specificity will be affected

- 1 by false positive results,
- 2 by detection of substance other than the index marker by the assay used to detect,
- 3 the chances of more than one malignancy producing the same marker
- 4 the chances of conditions other than malignancy producing that marker.

While taking the aspect of sensitivity of the assay detecting the marker will be greatly influenced by the frequency of the production or shedding of markers by the tumors and the least amount of tumor which should be present for the marker to be detected by the assay. An ideal marker will be present early in the disease before the clinical evidence of the disease that increase with advancing tumor and decrease with effective therapy and must be test reproducible, available and cost effective. Studies revealed that no marker satisfies all these criteria. It is also disappointing that, the tumor marker level alone is insufficient to diagnose a tumor because,

- 1 their level can be elevated in benign conditions also,
- 2 their level is not elevated in all patients with tumor,
- 3 many markers are not specific to particular type of cancer
- 4 their level can be elevated by more than one type of cancer.

## What are the uses of tumor markers?

Briefly, the tumor markers are used

- 1 for screening,
- 2 as an aid in diagnosis,
- 3 to know the stage of tumor,
- 4 to determine the prognosis,
- 5 to guide and monitor the treatment
- 6 to determine the recurrence of tumors.

## What are the types of tumor markers?

Earlier the markers were classified as tumor specific and tumor associated antigens but the modern system classifies the markers based on their molecular structure and source of antigens.

*Tumor specific antigens* are unique to the tumor cells and do not occur in normal cells, are presented with class I MHC molecules and capable of inducing CMI response (PSA) while the *tumor associated antigens* are expressed at extremely low levels on normal cells and in much higher levels on tumor cells (CEA, AFP)

In modern classification the tumor markers are 1) *the products of mutated oncogenes and tumor suppressor genes* (oncogenes and tumor suppressor genes) 2) *products of over expressed genes* (tyrosinase in melanoma) 3) *products of genes that are silent in most of the normal tissues* (MAGE, GAGE and BAGE proteins) 4) *products of other mutated genes* (mutation by carcinogens- tumor specific transplantation antigens) 5) *tumor antigens encoded by genomes of oncogenic viruses* 6) *oncofetal antigens* (CEA, AFP) 7) *altered glycolipid and glycoprotein antigens* (gangliosides, bloodgroup antigens, mucins) 8) *hormones* 9) *tissue specific differentiation antigens* (CD10 and CD20 in B cell lymphomas) 10) *enzymes* (histaminase in medullary carcinoma of lungs, amylase in lung carcinoma) 12) *immunoglobulins* (in multiple myelomas) 13) *apoptosis index* (in canine mammary tumor)

fig1: Tumor markers in use in man

fig 2: Tumor marker detection by immunohistochemistry technique

Based on the use, the tumor markers are classified as

- 1) *diagnostic*- which aid in detection of malignant disease (PSA)
- 2) *prognostic*-aid in the estimation of recurrence and cancer related death PAI-I in breast cancer
- 3) *predictive*- which foretells the response to a given therapy (estrogen receptors in endocrine therapy prediction).

### Tumor markers detected in animals

Several studies are being carried out all over the world in animals to detect the presence of various markers in the neoplasms

of animals. A large number of tumor markers have been identified so far in animals, however their usage and role in the day today clinical diagnosis and treatment of neoplasms is yet to be standardized. Some of the important tumor markers detected in animals are telomerase (telomerase activity is detected in 95% of the canine tumors and found that it can be used as a therapeutic target and a useful diagnostic tool), C143 in enzootic bovine leucosis, COX2 over expression in canine epithelial nasal tumors, melan A in canine amelanotic melanomas, panleukocyte markers like CD 18 in lymphomas, lysozyme, CD 68, CD 117 and Ki67 in cutaneous histiocytoma in canines, CD 31, 3B5 in ureteral mast cell tumors in canines, apoptosis index in canine mammary tumor, PCNA in cholangiocarcinoma in avian liver, cytokeratins in epithelial cell skin tumors, CEA in primary liver and pancreatic tumors in animals, vimentin and myoglobin in sarcomas, actin in rhabdomyosarcomas, vonWillebrand factor in haemangiomas and hemangiosarcomas, CD31, CD34 and FACTOR 8 in vasculo endothelial tumors, S100 in melanoma and neurogenic sarcoma, melan A in canine oral melanoma, GFAP in neuroendocrine tumors, PCNA and Ki 67 in canine malignant lymphomas, Bcl-2 over-expression in feline neoplasias, P53 in canine cutaneous mast cell tumors and feline neoplasias, estrogen receptors in feline mammary gland tumors, COX 2 in canine TCC and canine renal carcinoma and p glycoprotein in canine lymphomas are a few of the recently discovered tumor markers in animal neoplasms

### Tumor marker utility grading system (TMUGS)

In 1996, the american society of clinical oncology put forward a system which basically aimed at more cost efficient investigation and application of the tumor markers. The main objectives of the system are standardization of the protocols and operating procedures and establish as standard analytic technique to evaluate the clinical utility of known and future tumor markers. Success is definite in this efforts and let us hope that the tumor markers may evolve as most sensitive, specific and cheap diagnostic and prognostic tool in the veterinary field too that may help in relieving the pain of our patients suffering from tumors.



## TESTOSTERONE GIVES MALE BIRDS THEIR COLOR

New research suggests that as testosterone in male birds increases, so does the level of carotenoids, the chemicals that create the bright coloring on birds' feathers, beaks, and legs. The brilliant reds, yellows, and oranges serve as indicators of sexual competitiveness, signaling to females that the bearer is healthy and a potentially good mate. Scientists already knew that testosterone in male birds brings out their macho best, making them sing more sweetly and court with added vigor—other key indicators of males' health and sexual appeal. But until now the relationship between bird coloring and testosterone had eluded biologists. Researcher Julio Blas, a biologist at the University of Saskatchewan in Saskatoon, Canada, and colleagues decided to tackle the issue through experiments in Spain with native red-legged partridges.