Early detection of cancer by analysis of nucleosomes and other plasma markers

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OBJECTIVES

1. To review and analyze scientific advances on the use of biomarkers (nucleosomes and nucleic acids) in the early diagnosis of cancer.
2. To demonstrate the utility and feasibility of liquid biopsies through the results of different studies.

ADVANTAGES OF LIQUID BIOPSY

- Non-invasive, fast and low cost
- Lower risk to the animal
- Represents tumour heterogeneity
- Monitors tumour evolution and therapeutic response
- High sensitivity
- Analyse various biomarkers in various fluids

MATERIAL AND METHODS

Bibliographic work performed through three different PubMed search strings after 2018, one for each biomarker. As the number of relevant articles in the field of veterinary medicine was small, it was decided to extend the search to articles in human medicine.

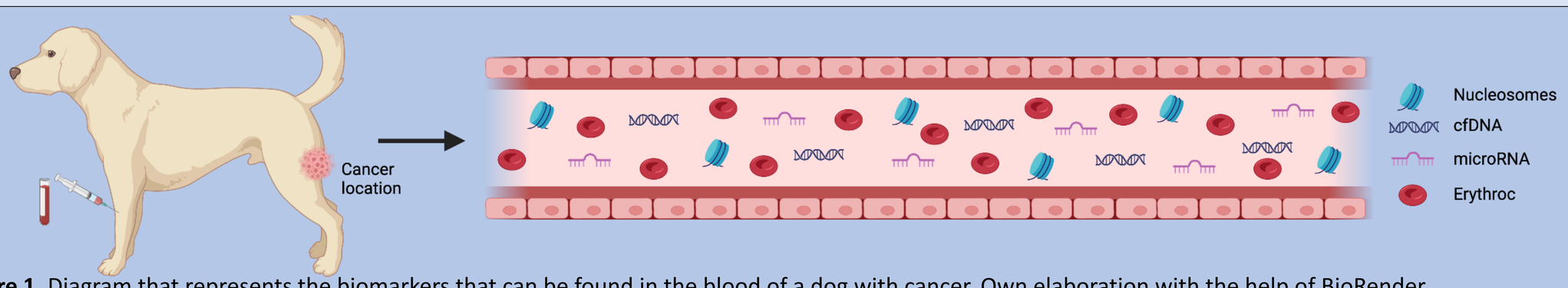

Figure 1. Diagram that represents the biomarkers that can be found in the blood of a dog with cancer. Own elaboration with the help of BioRender.

Table 1. Comparison of various biomarkers used in the diagnosis of cancer.

	Nucleosomes	cfDNA	MicroRNA
Size	Histone octamer + DNA (145 bp)	Small fragments of DNA (150-200 bp)	Small non-coding RNA (22 nucleotides)
Source	Apoptosis or necrosis of normal and pathological cells	Apoptosis or necrosis of normal and pathological cells	Healthy cells and cancer cells or in response to pathological situations
Detection technique	ELISA	qPCR, ddPCR, NGS	qRT-PCR, NGS, dPCR
Advantages	High sensitivity and specificity High stability in plasma Detects cancer in early stages Constant values up to a maximum processing time of 1 hour	High sensitivity and specificity Short half-life ctDNA contains mutations from the original tumour Secreted before it is visible on imaging or shows clinical signs	Early detection of cancer High stability Promising biomarker as a prognostic tool
Disadvantages	Elevated nucleosome level is not only cancer specific (false positives) In serum, *ex vivo* coagulation increases nucleosome concentrations	Elevated nucleosome level is not only cancer-specific Low amount of ctDNA requires very sensitive techniques In some tumours (CNS) biological barriers limit their release into the bloodstream.´ Low stability	Its small size requires sensitive techniques No standardized methods of extraction and sequencing Low specificity

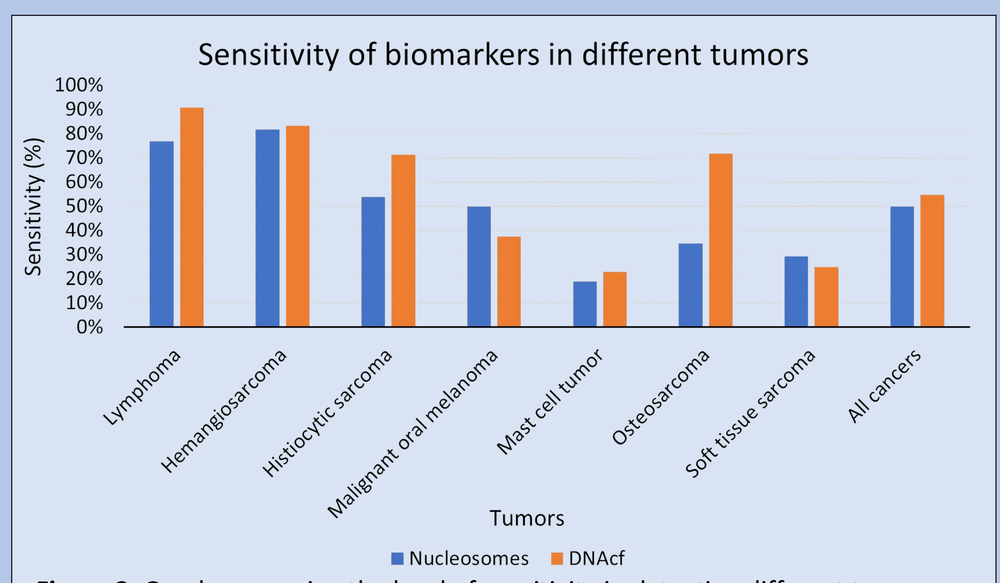

Figure 2. Graph comparing the level of sensitivity in detecting different tumours using both nucleosomes and cfDNA. Own elaboration and adapted from Wilson-Robles et al. 2022 and Flory et al. 2022.

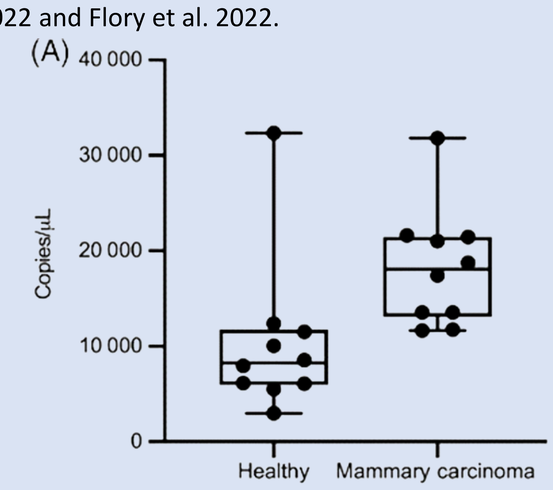

Figure 3. Number of copies/µl in bitches with mammary carcinoma and healthy bitches by dPCR on miE-199b (Fish et al. 2020).

CONCLUSIONS

- Despite the limitations of the studies carried out, it is considered an innovative technique that is attracting attention in oncology. Liquid biopsy could be used in wellness visits for geriatric populations or predisposed breeds to detect a wide variety of cancers early.
- Liquid biopsy should be considered as a complementary test, and a more specific test should be used to determine the final diagnosis, type of cancer and stage.
- Cancers in humans and animals share many characteristics, therefore future research in the veterinary field will also provides useful information in human medicine.

REFERENCES

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Fish EJ, Martinez-Romero EG, DeInnocentes P, Koehler JW, Prasad N, Smith AN, Bird RC. 2020. Circulating microRNA as biomarkers of canine mammary carcinoma in dogs. J Vet Intern Med, 34(3), 1282–1290.