Evaluation of plasma nucleosome concentrations as a tool for treatment and disease monitoring in cancer bearing dogs.

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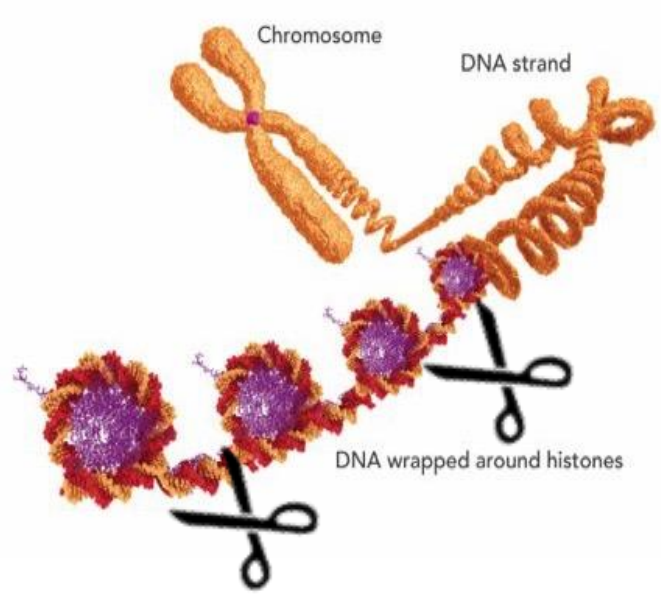
VETERINARY MEDICINE
& BIOMEDICAL SCIENCES
TEXAS A&M UNIVERSITY

Introduction



Prediction of response to neoadjuvant chemotherapy in breast cancer patients by circulating apoptotic biomarkers nucleosomes, DNAse, cytokeratin-18 fragments and survivin

Oliver J Stoetzer [1], Debora M I Fersching, Christoph Salat, Oliver Steinkohl, Christian J Gabka, Ulrich Hamann, Michael Braun, Axel-Mario Feller, Volker Heinemann, Barbara Siegele, Dorothea Nagel, Stefan Holdenrieder

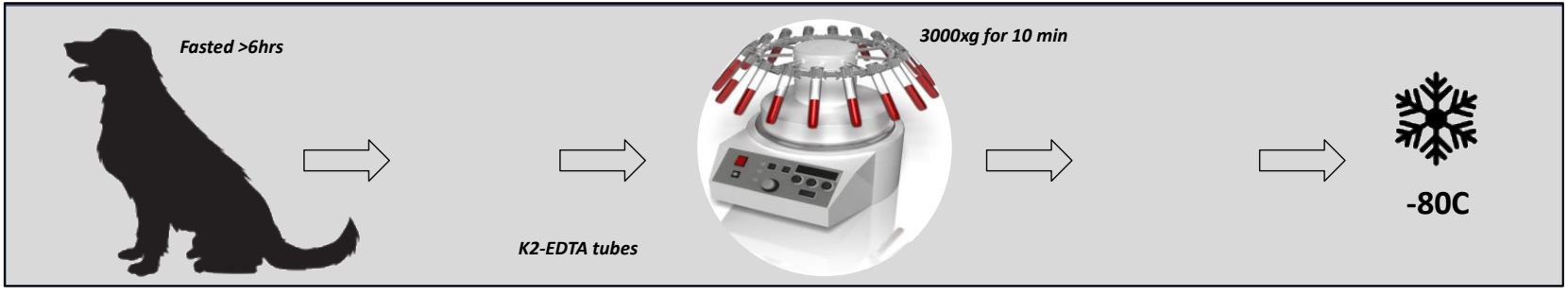
Circulating nucleosomes predict the response to chemotherapy in patients with advanced non-small cell lung cancer

Stefan Holdenrieder [1], Petra Stieber, Joachim von Pawel, Hannelore Raith, Dorothea Nagel, Knut Feldmann, Dietrich Seidel

Predictive and prognostic value of circulating nucleosomes and serum biomarkers in patients with metastasized colorectal cancer undergoing Selective Internal Radiation Therapy

Yvonne Nadine Fahmueller,[1] Dorothea Nagel,[1] Ralf-Thorsten Hoffmann,[2,4] Klaus Tatsch,[3,5] Tobias Jakobs,[2,6] Petra Stieber,[1] and Stefan Holdenrieder[1,7]

Methods



Breed	Age at Diagnosis	Body weight (kg)	Gender	Disease/Stage	H3.1 Concentration at Diagnosis
Australian Cattle Dog	11	36	Neutered Male	Lymphoma, B cell, IVa	225.85
Mixed Breed	11	20.4	Neutered Male	Lymphoma, B cell, IVa	525.61
Mixed Breed	9	37.2	Neutered Male	Lymphoma, T cell, Visceral, IVb	397.26
Rottweiler	5	38.4	Spayed Female	Lymphoma, B cell, IVa	224.01
Labrador	7	34.2	Spayed Female	Lymphoma, B cell, IVa	655.4
Labrador	5	35.6	Neutered Male	Lymphoma, B cell, IVa	145.612
Pit Bull Terrier	9	21.2	Spayed Female	Lymphoma, B cell, IIIa	183.52
Min. Schnauzer	6	4.9	Spayed Female	Lymphoma, B cell, IIIa	650.84
Labrador	6	32.2	Neutered Male	Lymphoma, T cell, Cutaneous, Va	224.13
Maltese	8	5.3	Spayed Female	Lymphoma, B cell, IVa	154.67
Rhodesian/Leonberger	5	52.2	Neutered Male	Lymphoma, B cell, IIIa	80.98
Chow Chow	9	34.8	Neutered Male	Multiple Myeloma	71.76
Shetland Sheepdog	10	17.8	Neutered Male	Malignant Melanoma, IV	128.79
German Shepherd	8	35.4	Neutered Male	Nasal Chondrosarcoma, III	109.25
St. Bernard	9	43	Spayed Female	Osteosarcoma IIb	40.8
Catahoola	12	26	Neutered Male	Hemangiosarcoma (SC), III	646.65
Labrador	10	19.4	Neutered Male	Hemangiosarcoma (Rt. Auricle), II	249.47
German Shepherd	10	33	Spayed Female	Hemangiosarcoma (Spleen), III	93.66
Poodle	12	4.6	Neutered Male	High grade pulmonary carcinoma, IV	76.27
Siberian Husky	7	29.8	Spayed Female	AGASACA, III	101.22
Goldendoodle	10	33.8	Neutered Male	AGASACA, I	816.2

Disease monitoring: H3.1	% of dogs <67.4 ng/mL		H3.1 (ng/mL) at CR	Time to lowest H3.1	Time from CR to lowest H3.1	Time to CR
Round Cell Tumors	12/12	Mean	294.97 (71.6-655.4)	49.5 (6-210)	35.8 (13-125)	28.1 (6-85)
	100%	Median	224.07	19.5	16	23
Sarcomas	3/5	Mean	227.97 (40.8-646.6)	181.5 (81-282)	129 (24-282)	123.6 (7-282)
	60%	Median	109.25	181.5	81	82
Carcinomas	3/3	Mean	331.23 (76.3-816.2)	20 (14-28)	20 (14-28)	23 (18-28)
	100%	Median	101.22	18	18	23
All Cancers	19/21	Mean	95.3 (40.8-816.2)	55.1 (6-282)	51.1 (13-282)	44.35 (6-282)
	90.4%	Median	42.7	23	19.5	24

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Disease at clinical remission*		Time to CR (days)	H3.1 (ng/mL) at CR	CRP (mg/dL) at CR	TK (ng/mL) CR
Round Cell Tumors	Mean	28.1 (6-85)	294.97 (71.6-655.4)	23.3 (3-75.1)	2.038 (0.74-3.51)
	Median	23	224.07	16.7	1.98
Sarcomas	Mean	123.6 (7-282)	227.97 (40.8-646.6)	11.7 (9.9-15.3)	1.827 (0.19-3.85)
	Median	82	109.25	9.9	1.71
Carcinomas	Mean	23 (18-28)	331.23 (76.3-816.2)	9.9	N/A
	Median	23	101.22	9.9	N/A
All Cancers	Mean	44.35 (6-282)	95.3 (40.8-816.2)	10.8 (3-75.1)	2.5 (0.74-3.85)
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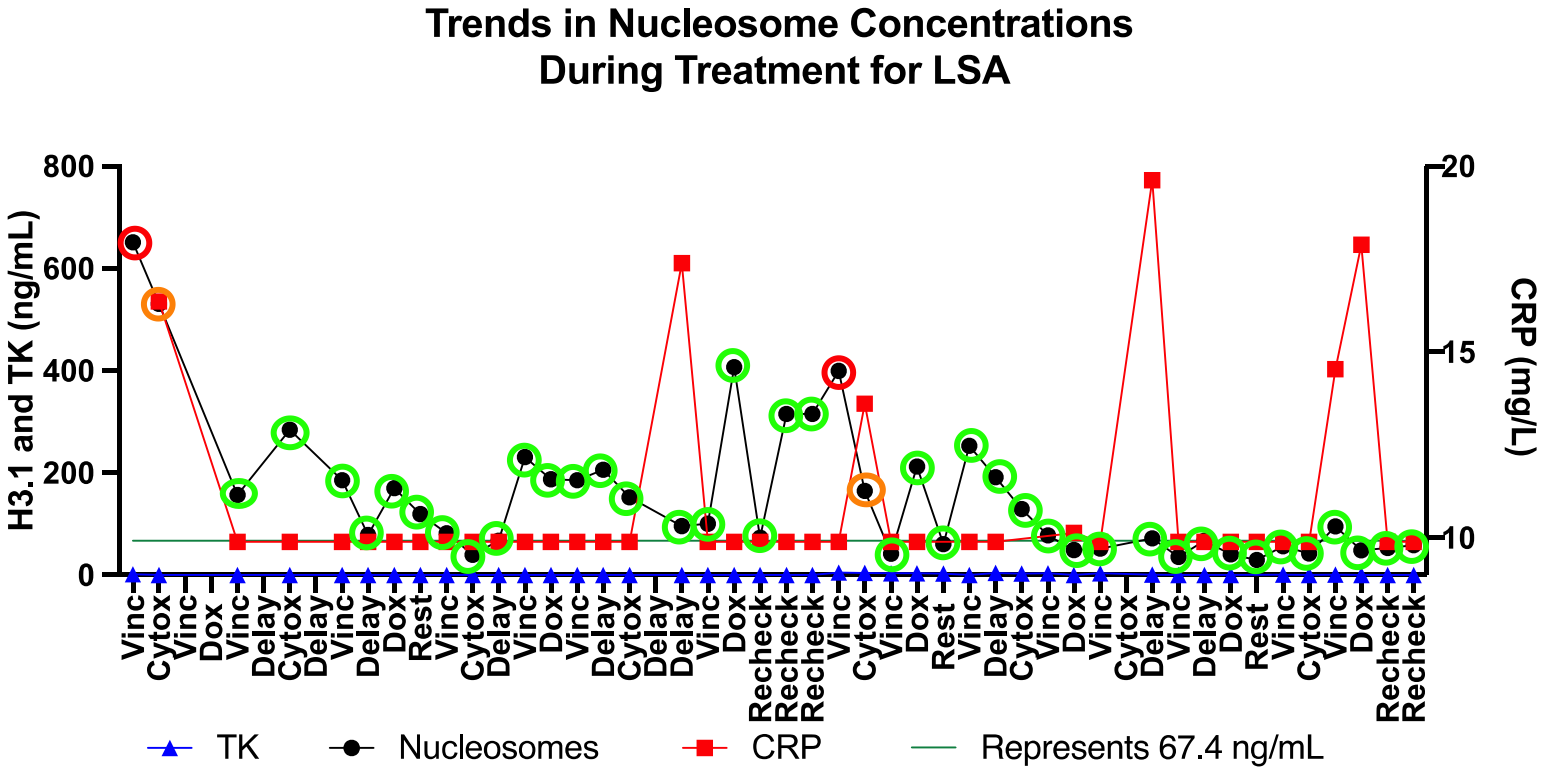
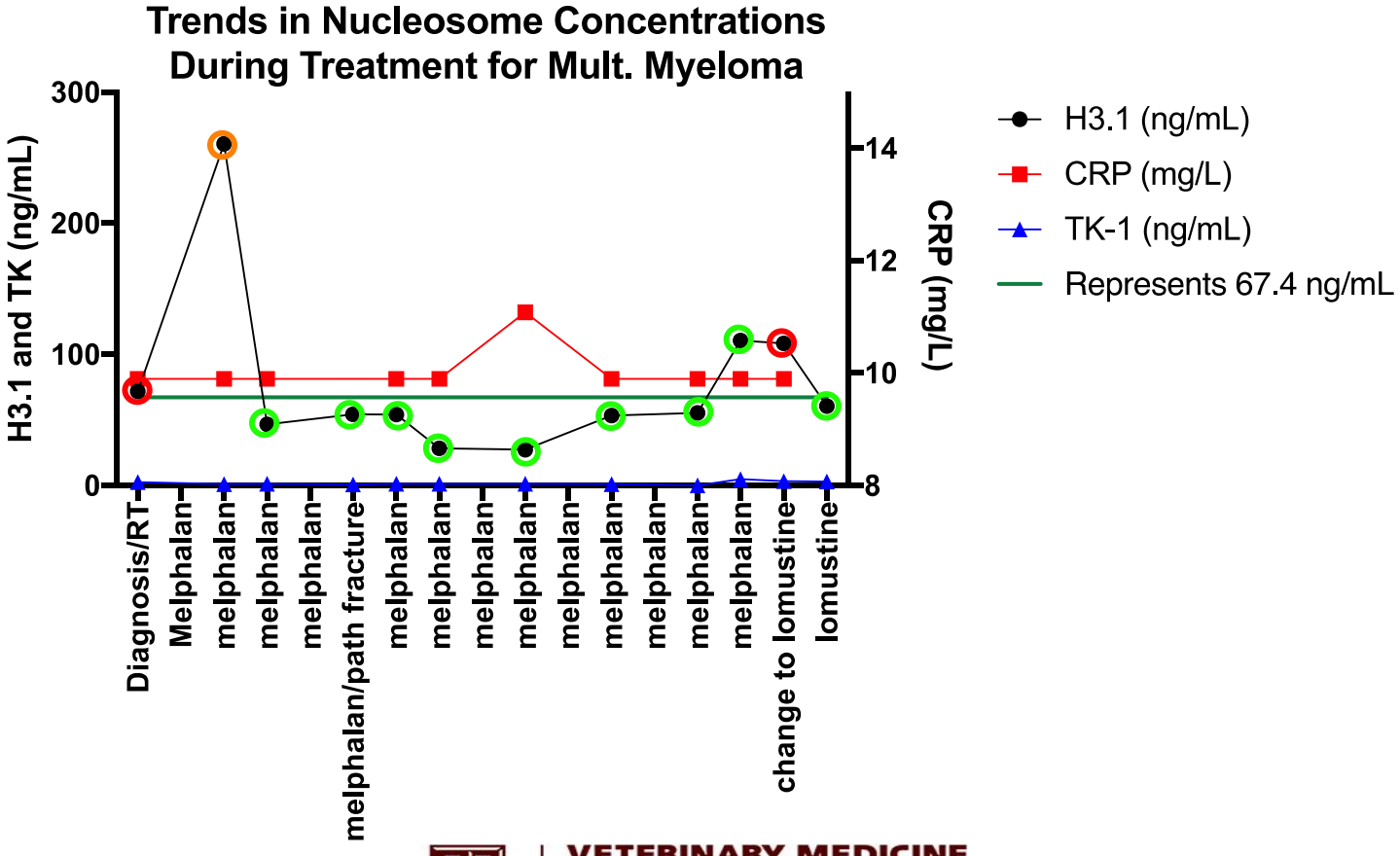
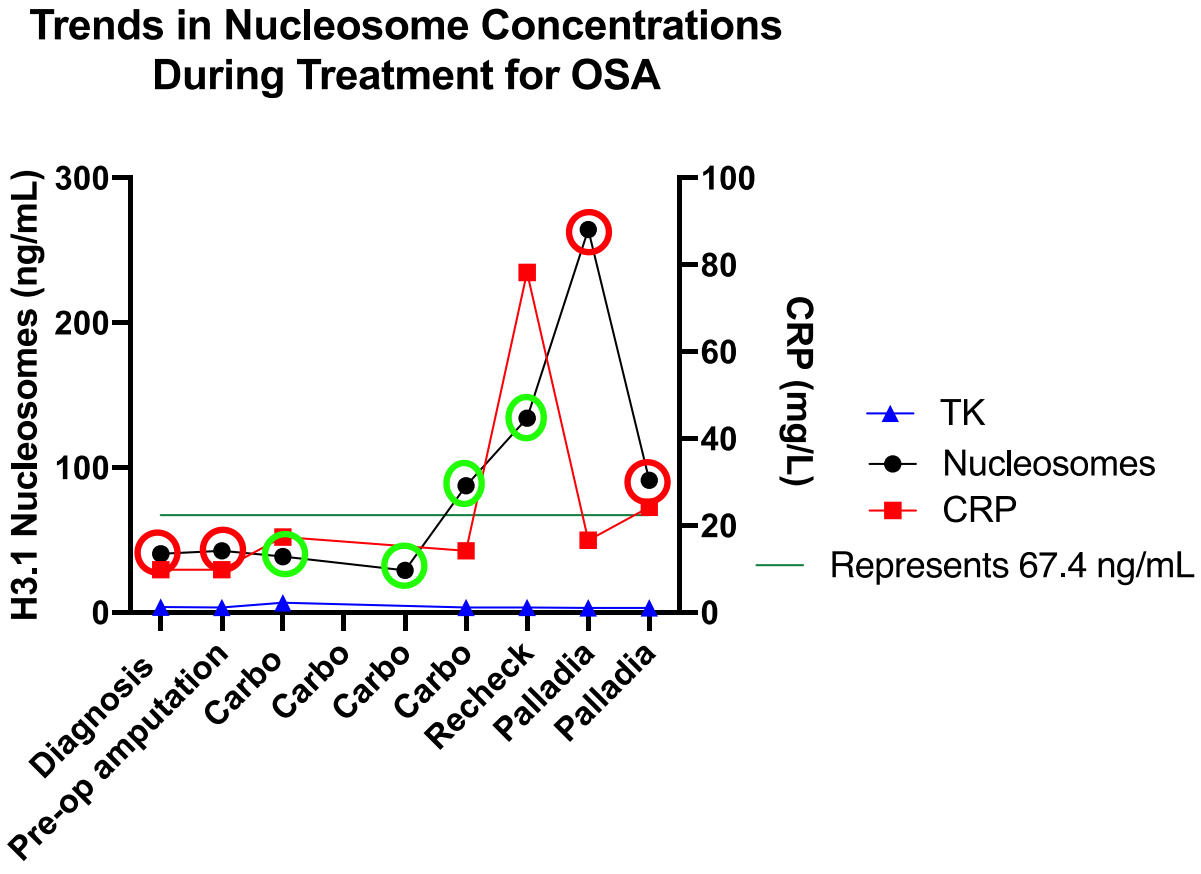
Case Study Examples



Case Study Examples



Case Study Examples



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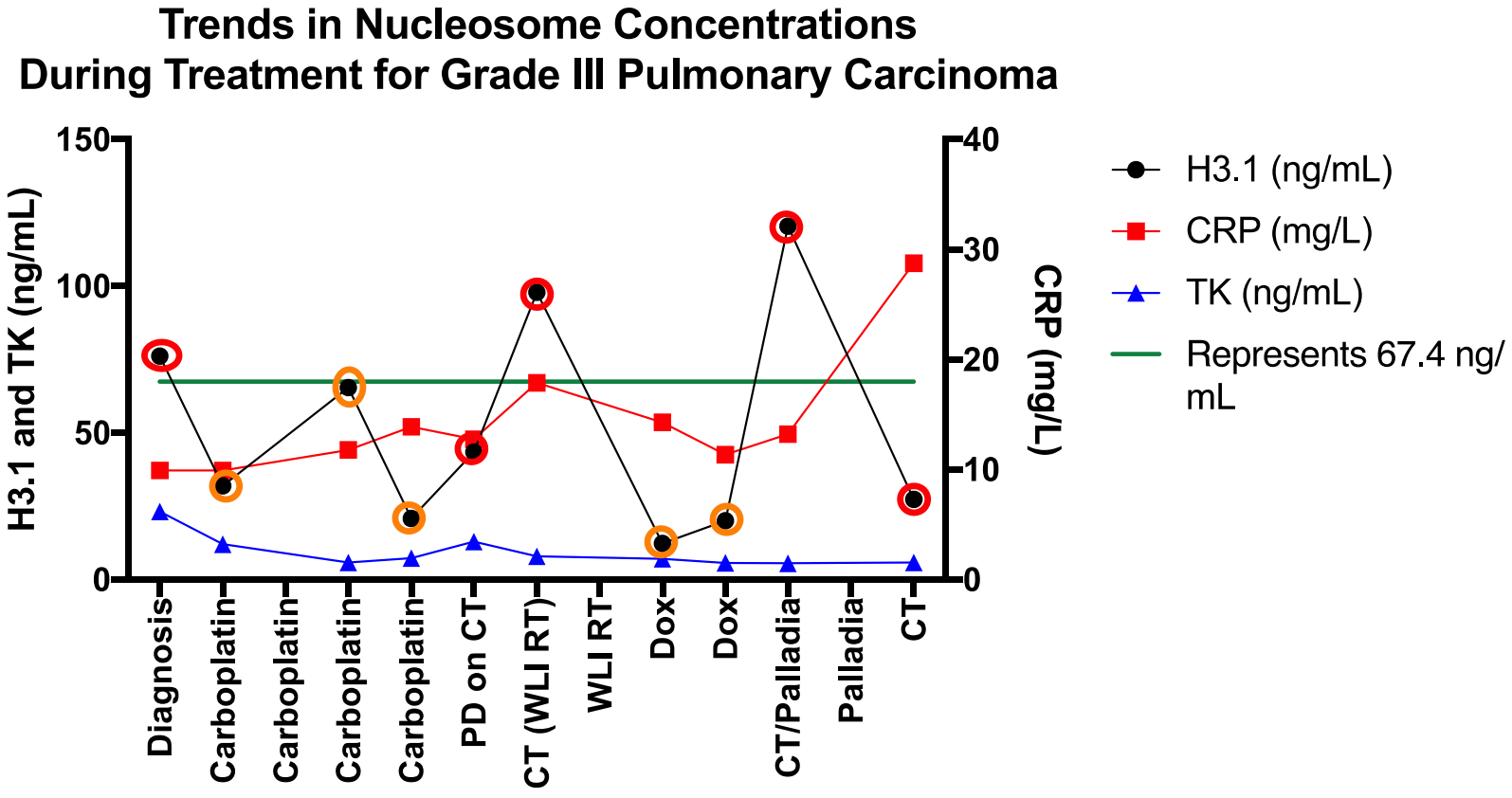

Results and Conclusions

- Nu.Q® can be used to monitor for disease response and progression.
- H3.1 concentrations reached normal levels below 67.4 ng/mL in most patients achieving clinical remission.
- H3.1 concentrations lag behind physical exam findings for clinical remission and may serve as a more sensitive measurement of residual disease.
- H3.1 elevations often precede obvious clinical progression, however, due to other possible causes of elevations in H3.1 it is recommended to have 2 consecutive elevations before altering the treatment or staging protocol in canine cancer patients.