PLASMA YKL-40: A NEW POTENTIAL SIEROLOGICAL BIOMARKER IN ANAL CANCER

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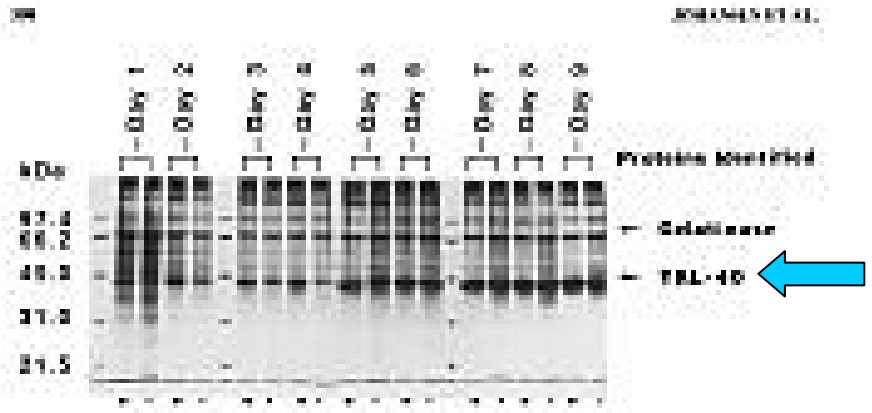
BACKGROUND

J Bone Miner Res. 1992 May;7(5):501-12.

Identification of proteins secreted by human osteoblastic cells in culture.

Johansen JS[1], Williamson MK, Rice JS, Price PA.

. The major proteins secreted by MG-63 cells were identified by N-terminal sequencing to be gelatinase, a novel 40 kD human bone protein we termed YKL-40, TIMP-1, the recently discovered TIMP-2, and beta 2-microglobulin. Further studies revealed that YKL-40 is the only protein detectable by Coomassie staining of SDS gels of MG-63 media proteins that is induced by extended time at confluence or by treatment with 1,25-(OH)2D3.



BACKGROUND

YKL-40

J Biol Chem. 1993 Dec 5;268(34):25803-10.

Human cartilage gp-39, a major secretory product of articular chondrocytes and synovial cells, is a mammalian member of a chitinase protein family.

Hakala BE[1], White C, Recklies AD.

J Biol Chem. 1995 Jun 2;270(22):13076-83.

Identification of a 38-kDa heparin-binding glycoprotein (gp38k) in differentiating vascular smooth muscle cells as a member of a group of proteins associated with tissue remodeling.

Shackelton LM[1], Mann DM, Millis AJ.

Genomics. 1997 Jul 15;43(2):221-5.

Molecular characterization of the gene for human cartilage gp-39 (CHI3L1), a member of the chitinase protein family and marker for late stages of macrophage differentiation.

Rehli M[1], Krause SW, Andreesen R.

Clin Chem. 1998 Mar;44(3):509-16.

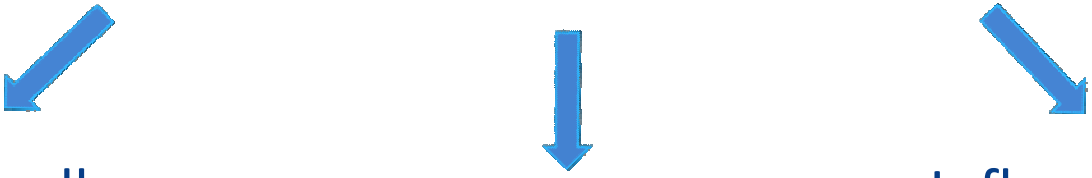
Chondrex: new marker of joint disease.

Harvey S[1], Weisman M, O'Dell J, Scott T, Krusemeier M, Visor J, Swindlehurst C.

BACKGROUND

YKL-40

Secreted glycoprotein



Cancer cells

Stem cells

Inflammatory cells

BACKGROUND

Serum YKL-40, A New Prognostic Biomarker in Cancer Patients?

Cancer Epidemiol Biomarkers Prev 2006;15(2). February 2006

and Paul A. Price[3]

Departments of [1]Rheumatology and [2]Oncology, Herlev University Hospital, Herlev, Denmark; and [3]Department of Biology, University of California San Diego, La Jolla, California

Roles of YKL-40

- Inflammation
- Cell proliferation
- Cell differentiation
- Protection against apoptosis
- Stimulation of angiogenesis
- Regulation of extracellular tissue remodeling

BACKGROUND

Cancers (Basel). 2010 Jul 12;2(3):1453-91. doi: 10.3390/cancers2031453.

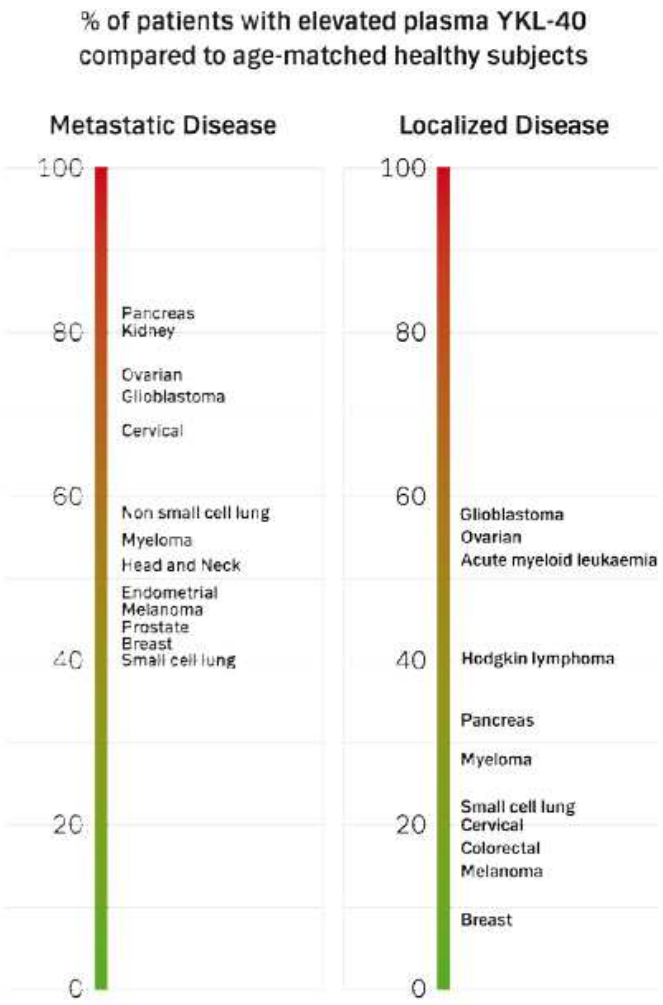
YKL-40-A Protein in the Field of Translational Medicine: A Role as a Biomarker in Cancer Patients?

Schultz NA[1], Johansen JS.

YKL-40 in Healthy Subjects

- Correlation with age
- No difference between gender
- No association with BMI
- No association with CRP-levels

BACKGROUND



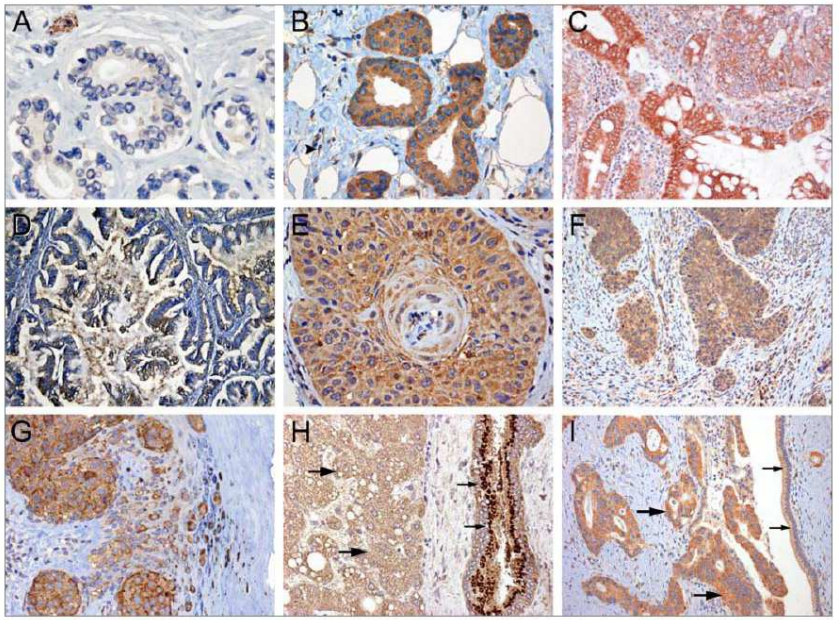
Elevated YKL-40

Higher than the age-adjusted 95th percentile of plasma YKL-40 in healthy subjects

BACKGROUND

YKL-40 in Different Types of Cancer

A. Normal breast epithelium
B. Invasive ductal carcinoma of the breast
C. Colorectal carcinoma
D. Ovarian carcinoma
E. Squamous cell carcinoma of the head and neck
F. Squamous cell carcinoma of the cervix
G. Melanoma
H. Hepatocellular carcinoma
I. Pancreatic carcinoma



Cancers (Basel). 2010 Jul 12;2(3):1453-91. doi: 10.3390/cancers2031453.

YKL-40-A Protein in the Field of Translational Medicine: A Role as a Biomarker in Cancer Patients?

Schultz NA[1], Johansen JS.

BACKGROUND

Table 1. Serum levels of YKL-40 (μg/L) in patients with cancer and the percentage of patients with elevated serum YKL-40

Diagnosis	*n*	Serum YKL-40	High YKL-40 (%)*	Reference
Primary breast cancer †	271	57*** (22-688)	19	Johansen et al. (91)
Metastatic breast cancer, all ‡	54	80*** (20-560)	41	Johansen et al. (83)
Soft tissue	10	59 (29-433)	20	
Bone	25	75*** (21-560)	35	
Viscera	19	157*** (20-468)	61	
Metastatic breast cancer, all ‡	100	65*** (20-430)	31	Jensen et al. (90)
Nodes and skin only	36	51 (20-267)	9	
Bone	28	61*** (24-310)	24	
Viscera	36	110*** (21-430)	57	
Colorectal cancer, ‡ all †	603	86*** (27-1,298)	26	Cintin et al. (84)
Dukes A	58	73** (27-295)	16	
Dukes B	223	86*** (27-604)	26	
Dukes C	175	77*** (27-582)	19	
Dukes D	147	119*** (27-1,298)	39	
Glioblastoma multiforme	45	130*** (38-654)	72	Tanwar et al. (31)
Lower grade gliomas	20	101*** (50-225)	57	
Ovarian cancer, all †	50	94*** (20-517)	72	Dupont et al. (81)
Ovarian cancer, stages I-II †	31	75*** (20-517)	65	Dupont et al. (81)
Ovarian cancer, stage III †	47	168*** (32-1,808)	74	Høgdall et al. (89)
Ovarian cancer, relapse	73	94*** (20-1,970)	55	Dehn et al. (87)
Small cell lung cancer, all ‡	131	82*** (23-1,188)	32	Johansen et al. (92)
Local disease	59	71* (23-417)	22	
Extensive disease	72	101*** (27-1,188)	40	
Metastatic renal cell cancer	58	235*** (45-1,896)	83	Geertsen et al. (88)
Metastatic prostate cancer	153	112*** (20-2,080)	43	Brasso et al. (86)
Metastatic malignant melanoma	110	95*** (20-1,262)	45	Schmidt et al. (93)

Elevated YKL-40 plasma levels are seen in patients with primary or advanced cancer, but also in patients with other diseases.

Is it a potential neoplastic marker in patients affected by anal cancer?

BACKGROUND

Histopathology. 2009 Aug;55(2):238-40. doi: 10.1111/j.1365-2559.2009.03364.x.

YKL-40 expression in anal carcinoma predicts shorter overall and disease-free survival.

Castellano I, Mistrangelo M, Crudo V, Chiusa L, Lupo R, Ricardi U, Morino M, Mussa A, Cassoni P.

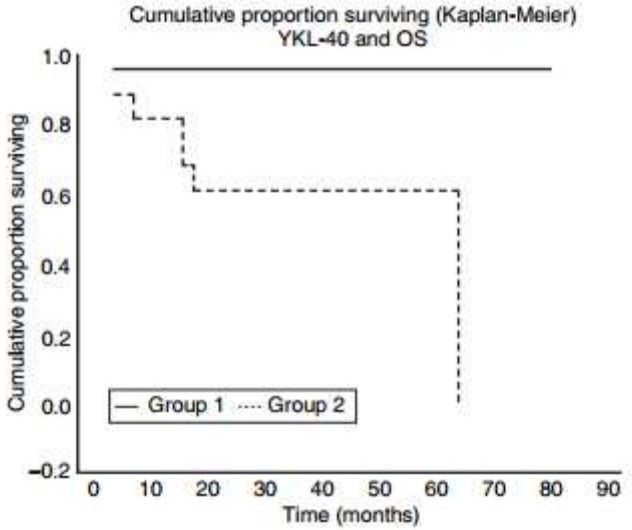


Figure 1. YKL-40 expression and overall survival. Group 1: YKL-40 negative cases. Group 2: YKL-40 positive cases. Time units are given in months.

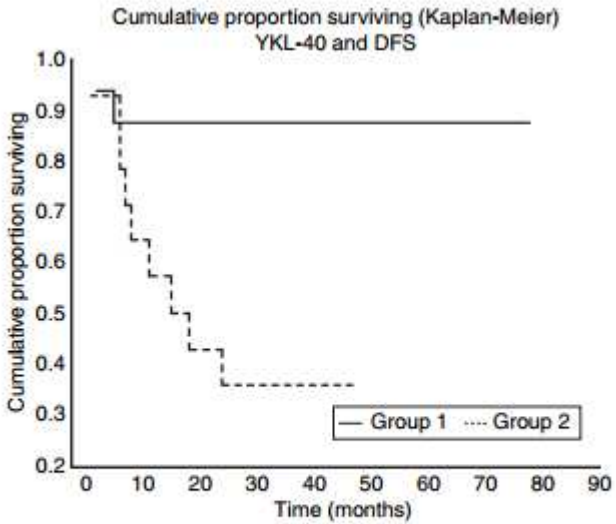


Figure 2. YKL-40 expression and disease-free survival. Group 1: YKL-40 negative cases. Group 2: YKL-40 positive cases. Time units are given in months.

MATERIAL & METHODS

Plasma YKL-40: a new potential sierological biomarker in anal cancer

M. Mistrangelo[1], E. Ugliono[1], V. Testa[1], P. Cassoni[2], T. Manetta[3], L. Idda[1], M. Goia[2] & G. Mengozzi[3] & M. Morino[1]

- YKL-40 serum level
- Preoperative values in patients affected by:
  - Benign diseases - [21 cases]
  - Anal cancer - [17 cases]
  - Colorectal neoplasms - [17 cases]

RESULTS

	N	YKL-40 neg	YKL-40 pos
Benign disease	21	12 [57.1%]	9 [42.9%]
Anal cancer	17	3 [17,7%]	14 [82,3 %]
Colorectal cancer	17	9 [52.9%]	8 [47.1%]

RESULTS

	Anal Cancer vs Healthy Patients	Colo-Rectal Cancer vs Healthy Patients
Sensitivity	82,3%	41,2%
Specificity	57,1%	57,1%
VPP	60,9%	41,1%
VPN	80%	57.1%

RESULTS

Follow-up

- 20 patients [16 F and 4 M] were submitted to follow up with YKL-40 serum dosage every 3 months
- 10 had higher YKL-40 serum levels:
  - ✓ 6 anal recurrences confirmed by biopsy
  - ✓ 1 case of pulmonary metastases from anal cancer
  - × 3 cases were FP (all active smokers)

RESULTS

Follow-up

Follow-up in Anal Cancer	
Sensitivity	87.5%
Specificity	75%
VPP	70%
VPN	90%

CONCLUSIONS

Neoplasm markers

	YKL-40 in Anal Cancer	CEA in Colorectal Cancer
Sensitivity	87.5%	~80% *[17–89%]*
Specificity	75%	~70% *[34–91%]*

CONCLUSIONS

- ✓ Pre and post-treatment serum YKL-40 levels could be considered as a new neoplastic marker in anal cancer
- ✗ Sensitivity is high, but specificity is low, especially when compared with patients affected by colorectal cancer

CONCLUSIONS

New studies needed:

- ✓ Confirm these preliminary results
- ✓ Investigate the utility of serum YKL-40 dosage in
  - Diagnosis
  - Follow up
- ✓ Determine its role as a prognostic biomarker in patients affected by HPV-related cancer

THANK YOU