Urine CartiLaps® EIA

For the quantification of degradation products of C-terminal telopeptides of type II collagen (CTX-II) in urine.

immunodiagnosticsystems

Intended Use / Abstract*

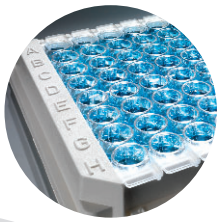
The Urine CartiLaps® EIA detects degradation products of C-terminal telopeptides of type II collagen. It is intended for *in vitro* diagnostic use as an indication of degradation of cartilage and may be used as an aid for:

- Quantitative assessment of disease activity (structural damage of articular cartilage) in patients with RA and OA.
- Prognosis of disease activity in patients with RA and OA.
- Early assessment of long-term effect of therapy in patients with RA.

Physiology

Disruption of the structural integrity of cartilage is the major histological finding in osteoarthritis and rheumatoid arthritis. Type II collagen is the major organic constituent of cartilage and fragments of type II collagen (CTX-II) are being released into the circulation and subsequently secreted into urine following degradation of cartilage. In urine, the CTX-II fragments can be quantified by Urine CartiLaps® EIA.

The Urine CartiLaps® EIA has been reported to be useful in the prediction of progression of osteoarthritis (Reijman (2003), Garnero (2003)), rheumatoid arthritis (Garnero (2002) and in other clinical and pre-clinical investigations (please refer to References).



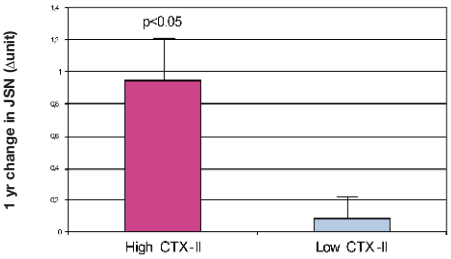
Clinical Application*

Clinical Studies

- Quantitative assessment of cartilage degradation in rheumatoid arthritis and osteoarthritis.
- Monitoring therapeutic effect on cartilage degradation.
- Predicting disease progression in arthritis patients.

The Urine CartiLaps® ELISA is used for quantitative assessment of cartilage degradation. The assay detects C-telopeptide fragments of collagen type II (CTX-II) generated during cartilage erosion.

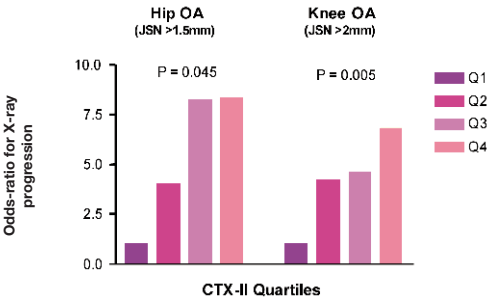
Predicting disease progression in rheumatoid arthritis:



Garnero et al. Arthritis Rheum 2002 Jan; 46(1):21-30

Baseline levels of CTX-II correlated with the changes over 1 year in the total sharp score (JSN and bone erosion).

Predicting disease progression in osteoarthritis:

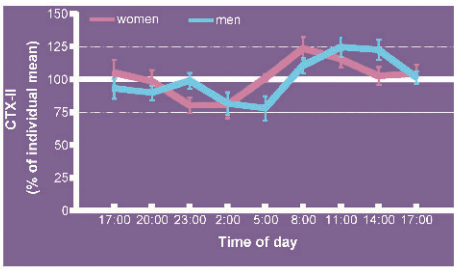


M. Reijman et al. Arthritis Rheum 8: 2471-2478 (2004).

Baseline CTX-II is predictive of hip OA progression in 1235 study participants followed for 6.6 years.

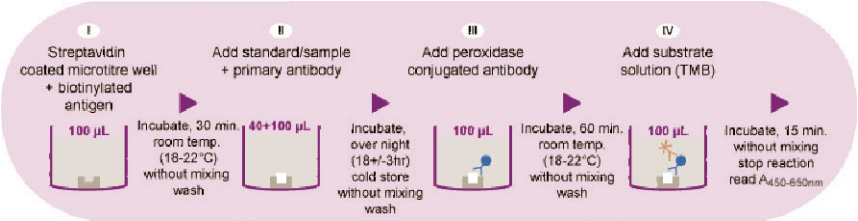
Circadian variation of Cartilage Markers

Collection time should be consistent



Christgau et al. Bone; 29 (3): 209-215 (2001)

Assay Protocol / Workflow



Assay Details

Code:	AC-10F1
Intended Use:	For IVD use
Format:	96 Wells
Methodology:	Competitive ELISA
Number of Tests per Kit:	40 determinations in duplicate
Standards:	6
Controls:	2
Specimen Type:	Urine
Specimen Volume:	40 µL
Sample Extraction:	No
Min. Det. Concentration:	0.20 ng/mL
Specificity:	Human
Assay Range:	0-10 ng/mL
Precision	
CV's within run:	< 6%
CV's between runs:	< 10%
Total Assay Time:	Overnight
Hands-on Time:	60 minutes
Data reduction:	4-parametric curve fit

Sampling

It is recommended to use second morning void urine specimens, but any spot urine sample may be used. Urine samples are stable for 24 hours at 4°C and should be stored frozen (<-18°C) for longer storage. Urine samples are stable for at least 10 freeze-thaw cycles. Prior to use, urine specimens should be shaken and sedimentation allowed for a minimum of 30 minutes.

Do not add HCl to urine samples.

Analyte Stability

	Urine
RT	8 hours
4-8°C	7 days
-20°C	>36 months
-80°C	>36 months

Expected Values

It is advisable for each laboratory to establish its own range of healthy and pathological CTX-II values. As an example, the geometric mean values and 95% confidence interval (CI) for various populations are given in the table below. For further information, please refer to the reference list at the end of these instructions.

Expected values

Populations	Number of subjects	Age (Years)	Mean CTX-II (ng/mmol)	95% CI (ng/mmol)
All women	459	20-85	299	79-1137
Pre 20-30 yrs	38	20-30	464	103-2086
Pre 30-60 yrs	165	30-59	200	65-618
Post	256	46-85	363	112-1172
Pre 48-53 yrs	28	48-53	164	66-410
Post 48-53 yrs	38	48-53	318	89-1132
All male	247	22-87	278	87-895
Male 20-30 yrs	27	20-30	501	214-1171
Male 30-60 yrs	141	30-60	236	89-628
Male > 60 yrs	79	60-87	305	85-1096

The CTX-II value determined should be corrected with creatinine concentration. Determine the concentration of creatinine (mmol/L) in the sample using an enzymatic colorimetric routine method for clinical chemistry analysers and perform the correction using the equation:

$$\text{Corrected CTX-II Value (ng/mmol)} = \frac{1000 \times \text{Urine CartiLaps } (\mu g/L)}{\text{Creatinine (mmol/L)}}$$

Assay Features

- Easy to perform.
- All values should be corrected for creatinine.
- Overnight incubation.
- 2 kit controls supplied with the kit.
- Analyte is very stable.

Bibliography / References

References

1. Christgau S. et al., Cartilage Degradation In Glucosamine Sulphate Treated Knee Osteoarthritis Patients With Elevated Levels Of Urinary Collagen Type II C-Telopeptide Fragments. *Clin Exp Rheumatol. (2004) 22(1):36-42.*
2. Christgau S. et al., Collagen type II degradation products in urine as an index of cartilage degradation. *Bone (2001); 29: 209-215.*
3. Garnero P. et al., Association of 10 molecular markers of bone, cartilage and synovium with disease activity and joint damage in hip osteoarthritis patients: the ECHODIAH cohort. *ACR 2003.*
4. Garnero P. et al., Association of baseline levels of markers of bone and cartilage degradation with long-term progression of joint damage in patients with early rheumatoid arthritis: the COBRA Study. *Arthritis & Rheum (2002); 46:2847-2856.*
5. Garnero P. et al., Uncoupling of type II collagen synthesis and degradation predicts progression of joint damage in patients with knee osteoarthritis. *Arthritis & Rheum (2002); 46:2613-2624.*
6. Garnero P. et al., Association of baseline levels of urinary glucosyl-galactosyl pyridinoline and type II collagen C-telopeptide with progression of joint destruction in patients with early rheumatoid arthritis. *Arthritis & Rheum (2002); 46: 21-30.*
7. Garnero P. et al., Cross sectional evaluation of biochemical markers of bone, cartilage, and synovial tissue metabolism in patients with knee osteoarthritis: relations with disease activity and joint damage. *Ann Rheum Dis (2001); 60: 619-26.*
8. Jung M. et al., Elevated urinary concentration of collagen type II C-telopeptide fragments in patients with osteoarthritis. *Pathobiology. (2004); 71(2): 70-6.*
9. Lehmann HJ. et al., The effects of bisphosphonates on CartiLaps: A new marker for cartilage degradation. *Ann Rheum Dis (2002); 61:530-533.*
10. Mazières B. et al., Molecular markers of cartilage breakdown and synovitis are strong independent predictors of structural progression of hip osteoarthritis (OA). the ECHODIAH cohort. *ACR 2003.*
11. Mouritzen U. et al., CartiLaps: A novel marker of Cartilage Degradation. The influence of age, gender, menopause, hormone replacement therapy and bone mass index. *Annals Rheum Dis. (2003); 62: 332-336.*
12. Alexandersen P, Karsdal MA, Qvist P, Reginster JY, Christiansen C.: Strontium ranelate reduces the urinary level of cartilage degradation biomarker CTX-II in postmenopausal women. *Bone. 2007 Jan;40(1):218-22.*
13. Manicourt DH, Azria M, Mindeholm L, Thonar EJ, Devogelaer JP.: Oral salmon calcitonin reduces Lequesne's algofunctional index scores and decreases urinary and serum levels of biomarkers of joint metabolism in knee osteoarthritis. *Arthritis Rheum. 2006 Oct;54(10):3205-11.*
14. Garnero P, Charni N, Juillet F, Conrozier T, Vignon E.: Increased urinary type II collagen helical and C telopeptide levels are independently associated with a rapidly destructive hip. osteoarthritis. *Ann Rheum Dis. 2006 Dec;65(12):1639-44*
15. Bruyere O, Collette J, Kothari M, Zaim S, White D, Genant H, Peterfy C, Burlet N, Ethgen D, Montague T, Dabrowski C, Reginster JY.: Osteoarthritis, magnetic resonance imaging, and biochemical markers: a one year prospective study. *Ann Rheum Dis. 2006 Aug;65(8):1050-4.*
16. Manicourt DH, Bevilacqua M, Righini V, Famaey JP, Devogelaer JP.: Comparative effect of nimesulide and ibuprofen on the urinary levels of collagen type II C-telopeptide degradation products and on the serum levels of hyaluronan and matrix metalloproteinases-3 and -13 in patients with flare-up of osteoarthritis. *Drugs R D. 2005;6(5):261-71.*
17. Garnero P, Mazières B, Guéguen A, Abbal M, Berdah L, Lequesne M, Nguyen M, Salles JP, Vignon E, Dougados M.: Cross-sectional association of 10 molecular markers of bone, cartilage, and synovium with disease activity and radiological joint damage in patients with hip osteoarthritis: the ECHODIAH cohort. *J Rheumatol. 2005 Apr;32(4):697-703.*
18. Reijman M, Hazes JM, Bierma-Zeinstra SM, Koes BW, Christgau S, Christiansen C, Uitterlinden AG, Pols HA.: A new marker for osteoarthritis: cross-sectional and longitudinal approach. *Arthritis Rheum. 2004 Aug;50(8):2471-8.*
19. Landewé R, Geusens P, Boers M, van der Heijde D, Lems W, te Koppele J, van der Linden S, Garnero P.: Markers for type II collagen breakdown predict the effect of disease-modifying treatment on long-term radiographic progression in patients with rheumatoid arthritis. *Arthritis Rheum. 2004 May;50(5):1390-9.*
20. Garnero P, Conrozier T, Christgau S, Mathieu P, Delmas PD, Vignon E.: Urinary type II collagen C-telopeptide levels are increased in patients with rapidly destructive hip osteoarthritis. *Ann Rheum Dis. 2003 Oct;62(10):939-43.*
21. Landewé RB, Geusens P, van der Heijde DM, Boers M, van der Linden SJ, Garnero P.: Arthritis instantaneously causes collagen type I and type II degradation in patients with early rheumatoid arthritis: a longitudinal analysis. *Ann Rheum Dis. 2006 Jan;65(1):40-4. Epub 2005 Aug 26.*
22. Meulenbelt I, Kloppenburg M, Kroon HM, Houwing-Duistermaat JJ, Garnero P, Hellio Le Graverand MP, Degroot J, Slagboom PE.: Urinary CTX-II levels are associated with radiographic subtypes of osteoarthritis in hip, knee, hand, and facet joints in subject with familial osteoarthritis at multiple sites: the GARP study. *Ann Rheum Dis. 2006 Mar;65(3):360-5.*
23. Bagger YZ, Tankó LB, Alexandersen P, Karsdal MA, Olson M, Mindeholm L, Azria M, Christiansen C.: Oral salmon calcitonin induced suppression of urinary collagen type II degradation in postmenopausal women: a new potential treatment of osteoarthritis. *Bone. 2005 Sep;37(3):425-30.*

Visit **www.idsplc.com** for an extended range of products

Contact Details

United Kingdom:
Immunodiagnostic Systems Limited (IDS Ltd)
10 Didcot Way, Boldon Business Park,
Boldon, Tyne & Wear, NE35 9PD, UK
Tel: +44 (0) 191 519 0660 Fax: +44 (0) 191 519 0760
Email: info.uk@idsplc.com www.idsplc.com

United States of America:
Immunodiagnostic Systems Inc.
8425 N. 90th Street, Suite 8, Scottsdale, AZ 85258
Tel: 480.278.8333 Fax: 480.836.7437
Email: info.us@idsplc.com www.idsplc.com

Germany:
Immunodiagnostic Systems GmbH (IDS GmbH)
Mainzer Landstrasse 49, 60329, Frankfurt am Main, Germany
Tel: +49 (0) 69 3085 5025 Fax: +49 (0) 69 3085 5125
Email: info.de@idsplc.com www.idsplc.com

France:
Immunodiagnostic Systems (IDS)
153 Avenue D'Italie, 75013 Paris, France
T: 01 40 77 04 50 F: 01 40 77 04 55
Email: info.fr@idsplc.com www.idsplc.com

Scandinavia:
Immunodiagnostic Systems Nordic a/s (IDS Nordic a/s)
Marielundvej 30, 2. Sal, 2730 Herlev, Denmark
Tel: +45 44 84 0091
Email: info.nordic@idsplc.com www.idsplc.com

AC-10FL
Issue:2
04.09.09

* USA: For research use only, not for diagnostic purposes.

Visit **www.idsplc.com** for a list of world-wide distributors