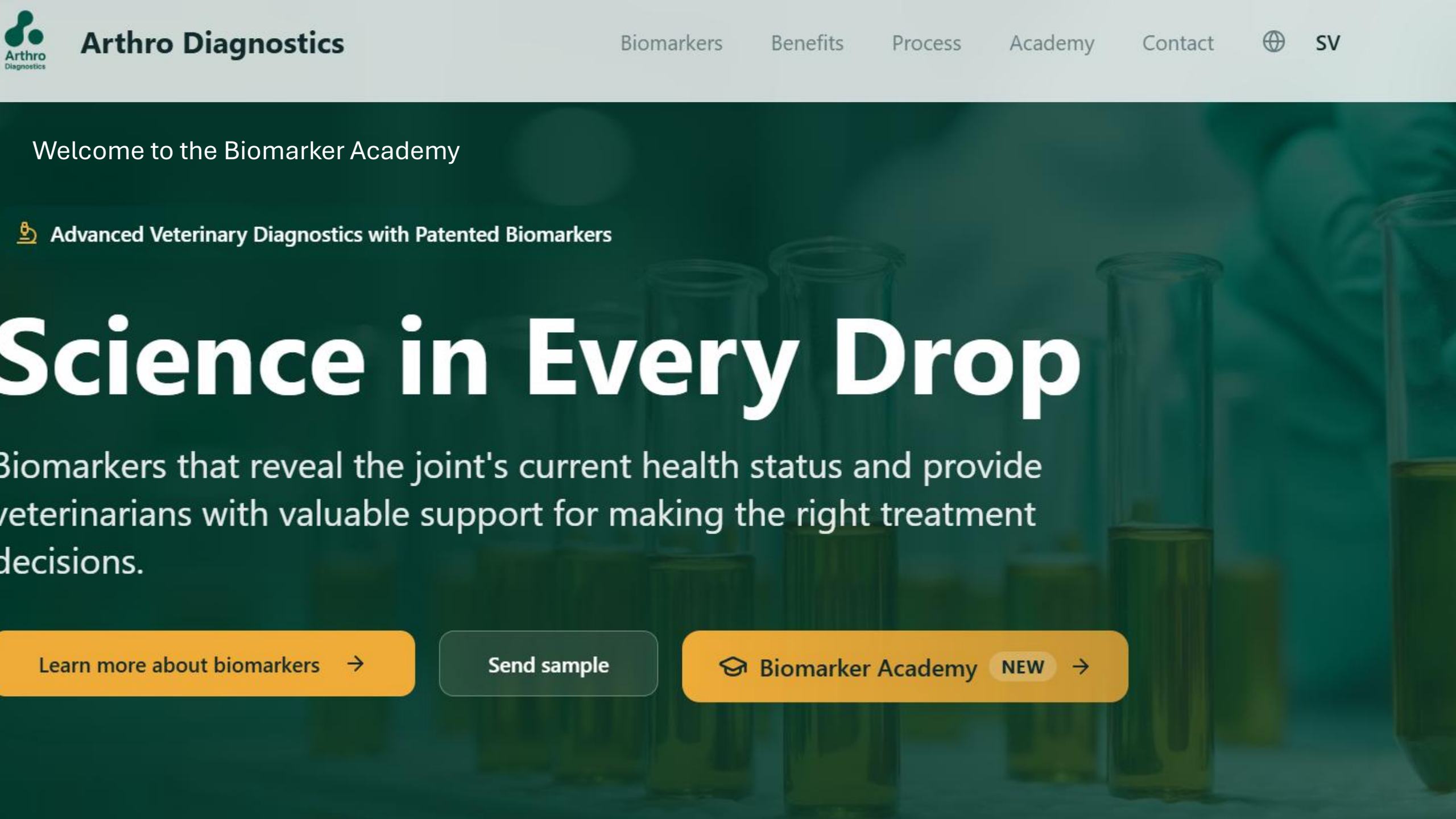
Arthro Diagnostics
Biomarkers
Benefits
Process
Academy
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Welcome to the Biomarker Academy
Advanced Veterinary Diagnostics with Patented Biomarkers
Science in Every Drop
Biomarkers that reveal the joint's current health status and provide
veterinarians with valuable support for making the right treatment
decisions.
Learn more about biomarkers
Send sample
Biomarker Academy
NEW

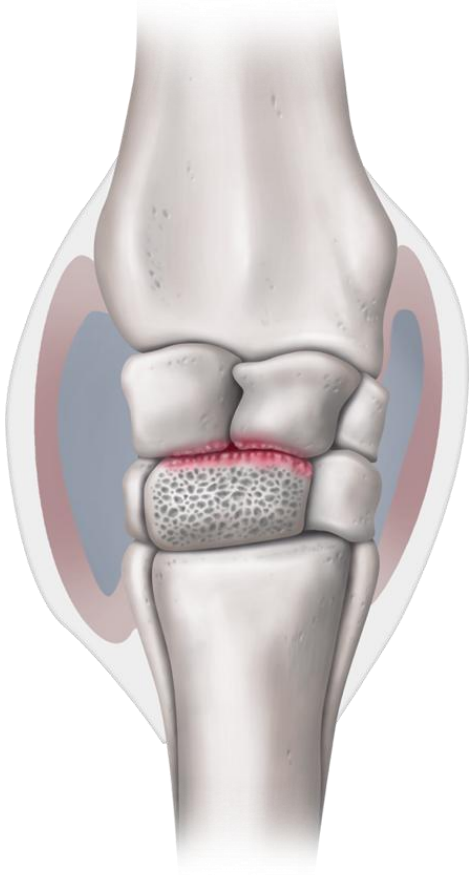
Todays academy

- Osteoarthritic progression- the timeline, what is happening with the cells, inflammation and tissue destruction?
- Clinical phenotype- we need to know the molecular endotype
- Pain and tissue destruction- not always parallel processes
- Treatment efficay , treatment failures and side effects
- The lab in Mölndal ArthroDiagnostics

What is osteoarthritis? - A disorder of the whole joint (organ)

The most common cause for lameness in the horse

- Not wear and tear
- **Chronic low grade inflammatory disease**



- Arthritis/-os
- Joint inflammation
- Degenerative joint disease
- **Osteoarthritis**
- **often treatment failures**

Timeline of osteoarthritis



OA starts



Clinical symptoms



End stage

Reversible stages of OA

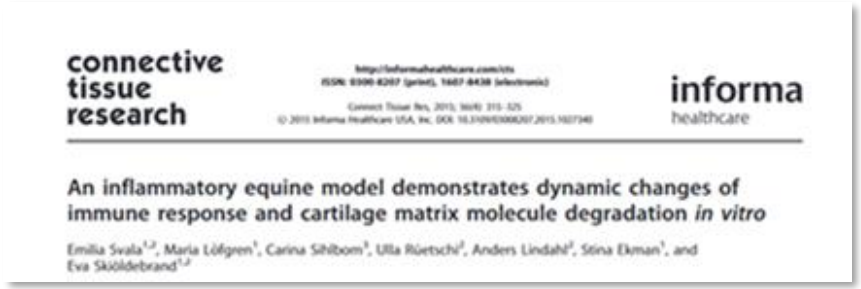
- Early biochemical degradation
- Healing is possible

Irreversible stages of OA

- Too late detection of OA with todays diagnostics
- No DMOAD
- FDA, EMEA new claims

Unusable horse

New tools: Biomarkers



connective tissue research

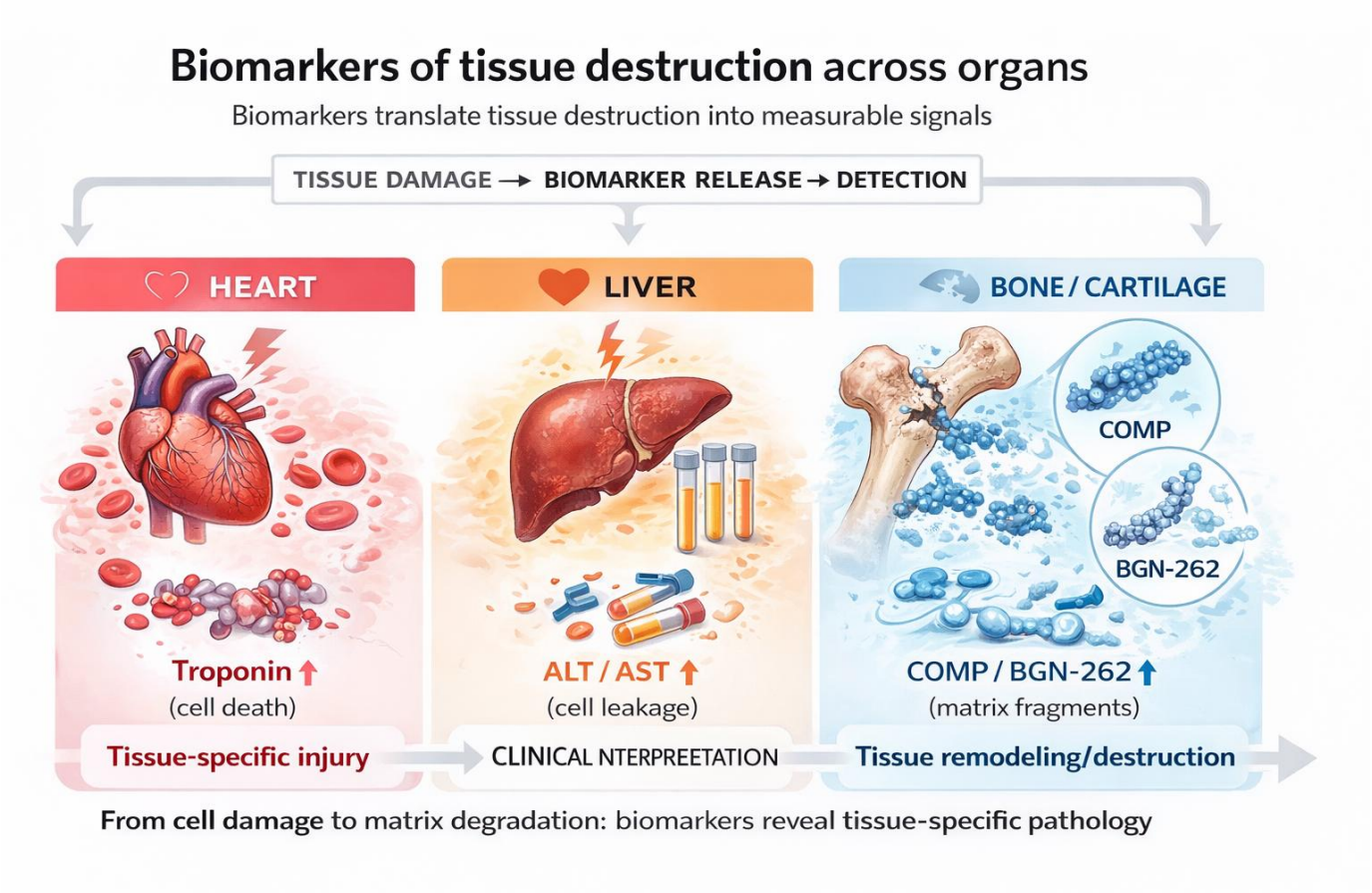
informa healthcare

An inflammatory equine model demonstrates dynamic changes of immune response and cartilage matrix molecule degradation *in vitro*

Emilia Svala, Maria Löfgren, Carina Sihlbom, Ulla Rüetschi, Anders Lindahl, Stina Ekman, and Eva Skiöldebrand

Why biomarkers?

Biomarkers provide real-time insight into what is happening within the joint tissues such as bone and cartilage



Biomarkers reflect ongoing biological activity, whereas imaging reflects accumulated structural changes.

Biomarkers

- Detect **active processes:**
  - inflammation
  - tissue degradation

  Provide:
  - real-time information
  - dynamic changes

- **Can detect disease:**
- before structural damage is visible

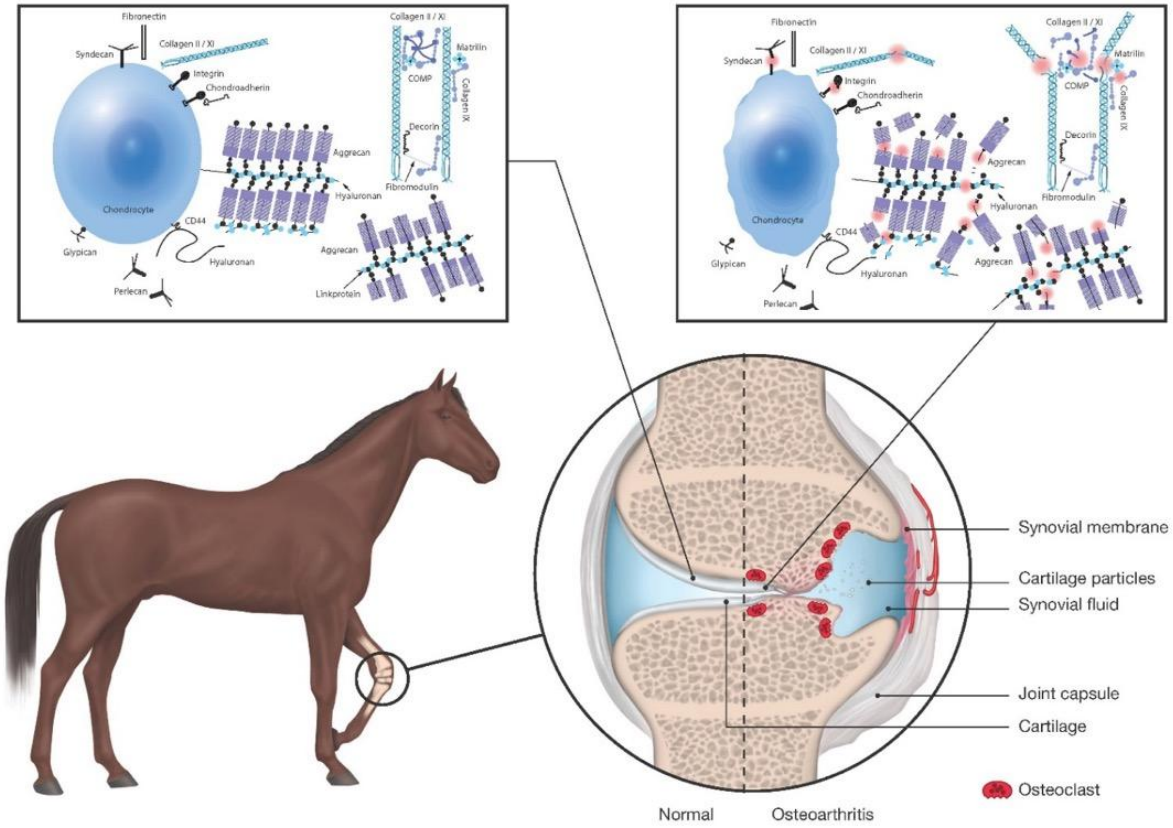
Imaging (CT, MRI, X-ray)

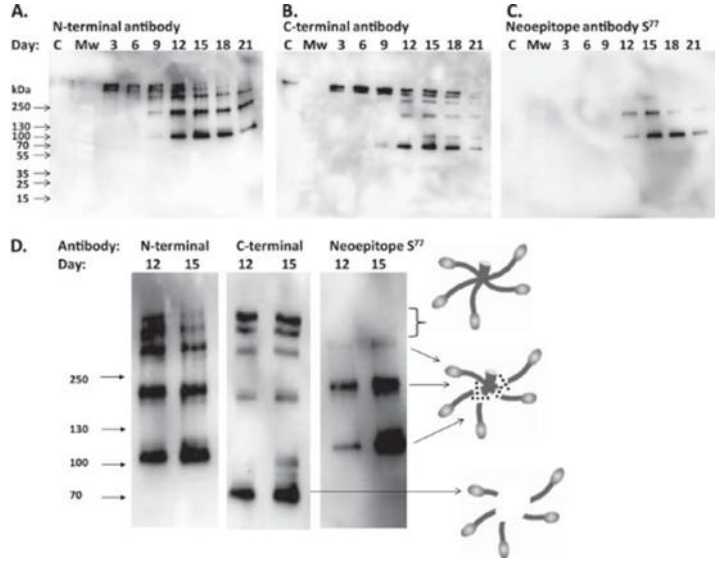
Detect **structural changes**
osteophytes
cartilage loss
bone sclerosis
edema (MRI)

Provide:
anatomical information
static snapshots

Reflect:
what has already happened

Joint inflammation induce fragmentation of the native proteins creates neo-epitope specific peptides (biomarkers)






ELSEVIER
Journal of Orthopaedic Research 23 (2005) 156–163
Journal of Orthopaedic Research
www.elsevier.com/locate/orthres

Enhanced concentration of COMP (cartilage oligomeric matrix protein) in osteochondral fractures from racing Thoroughbreds

E. Skiöldebrand [a,*], D. Heinegård [b], M.-L. Eloranta [c], G. Nilsson [d], J. Dudhia [e], B. Sandgren [f], S. Ekman [a]

The inflammation is creating the biomarkers

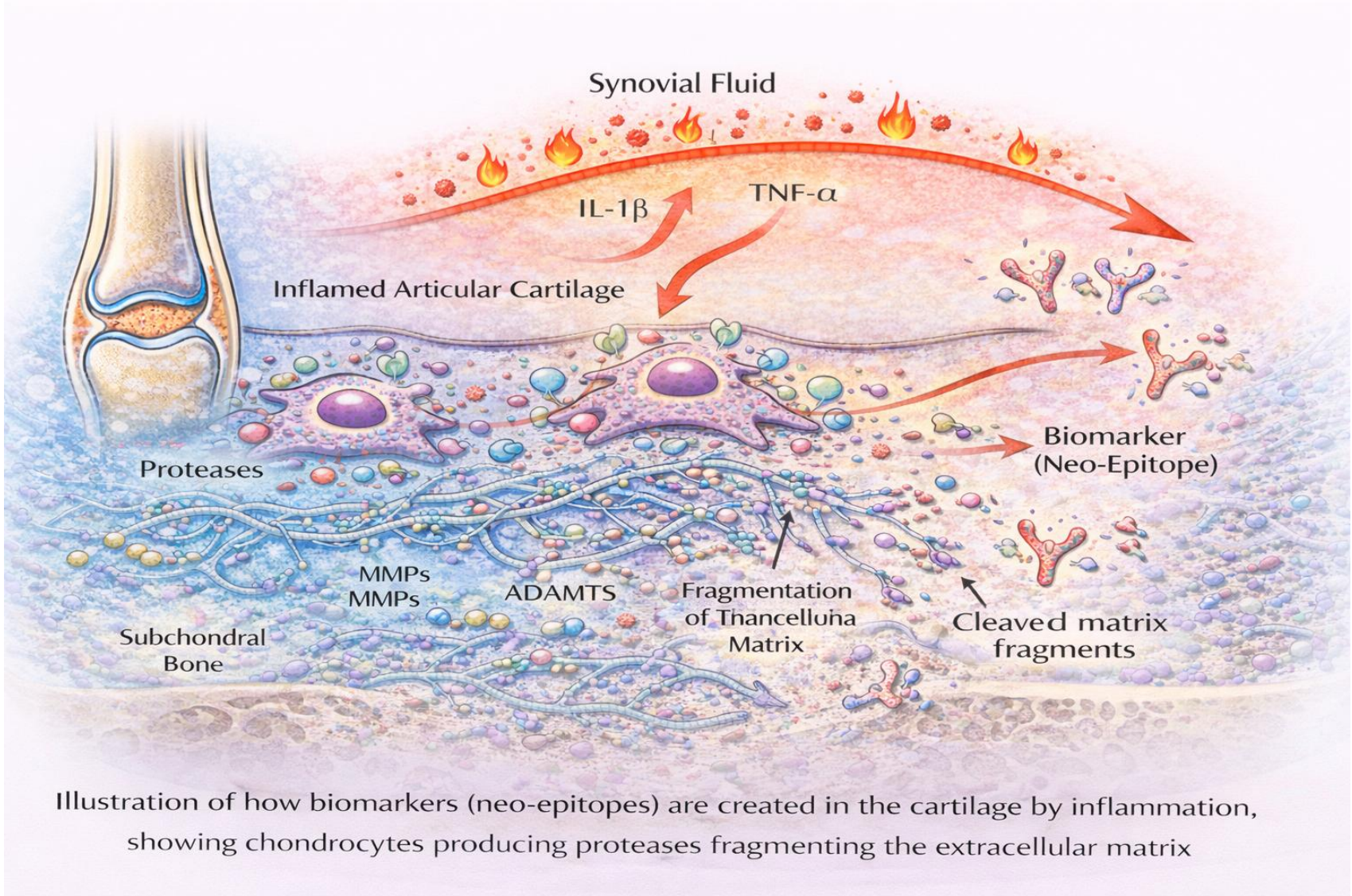
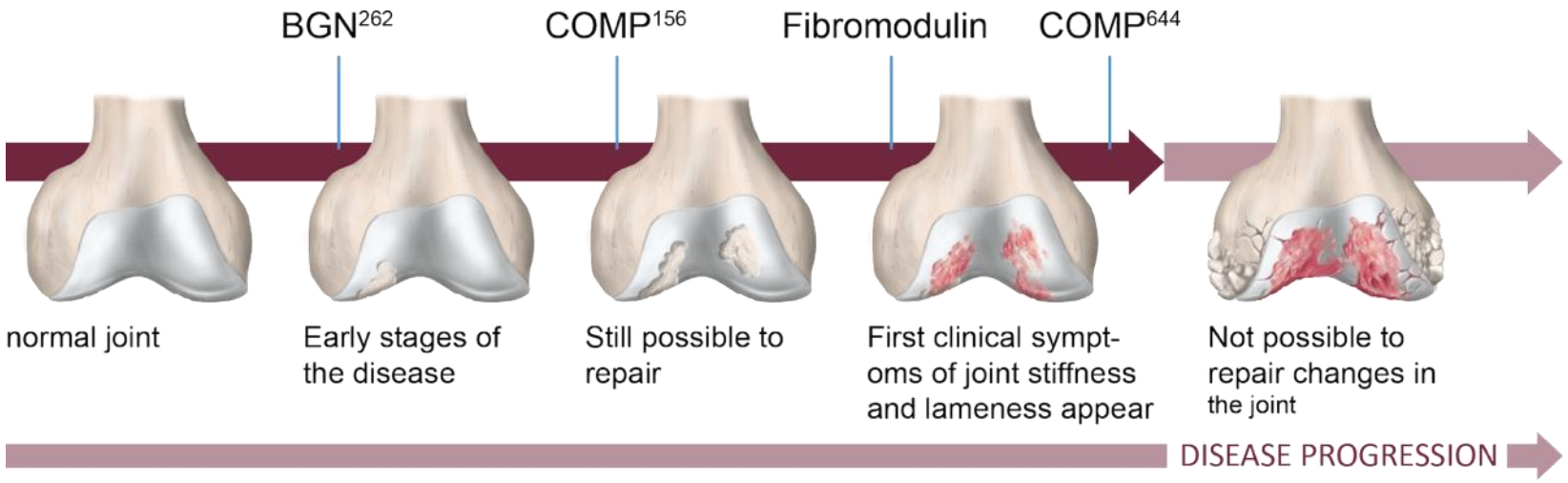


Illustration of how biomarkers (neo-epitopes) are created in the cartilage by inflammation, showing chondrocytes producing proteases fragmenting the extracellular matrix

Biomarker identification:
A time-depent degradation of the joint



- Healthy cartilage from horse
- Inflammatory model
- Specific neo-epitope fragments for different stages
- The biomarkers are conserved between species: horse, man, dog, cat, sheep, cattle

connective tissue research

http://informahealthcare.com/cts
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Connect Tissue Res, 2015; 56(4): 315–325
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informa healthcare

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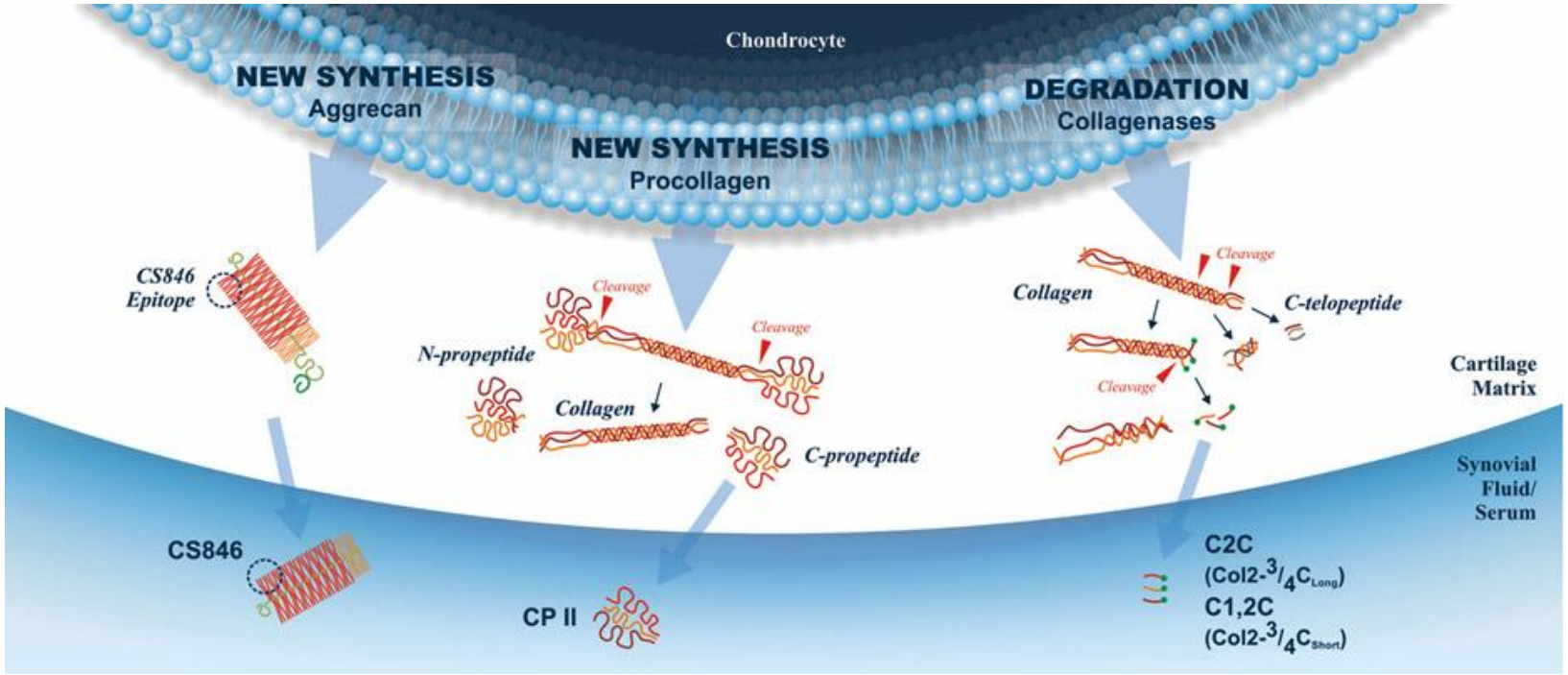
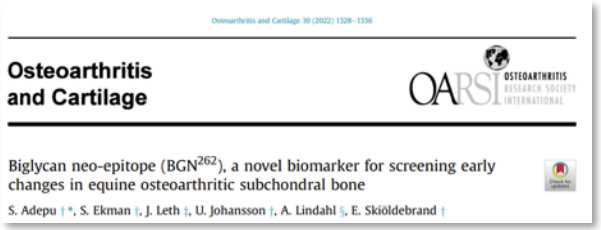
Emilia Svala[1,2], Maria Löfgren[1], Carina Sihlbom[3], Ulla Rüetschi[2], Anders Lindahl[2], Stina Ekman[1], and Eva Skiöldebrand[1,2]

Neo-epitope specific biomarkers in synovial fluid, blood and saliva




Osteoarthritis and Cartilage

Biglycan neo-epitope (BGN^{262}), a novel biomarker for screening early changes in equine osteoarthritic subchondral bone

S. Adepu † *, S. Ekman †, J. Leth †, U. Johansson †, A. Lindahl §, E. Skiöldebrand †


Osteoarthritis and Cartilage Open

Salivary biglycan-neo-epitope-BGN^{262}: A novel surrogate biomarker for equine osteoarthritic sub-chondral bone sclerosis and to monitor the effect of short-term training and surface arena

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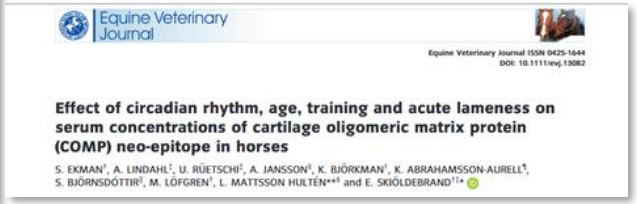
Equine Veterinary Journal

Effect of circadian rhythm, age, training and acute lameness on serum concentrations of cartilage oligomeric matrix protein (COMP) neo-epitope in horses

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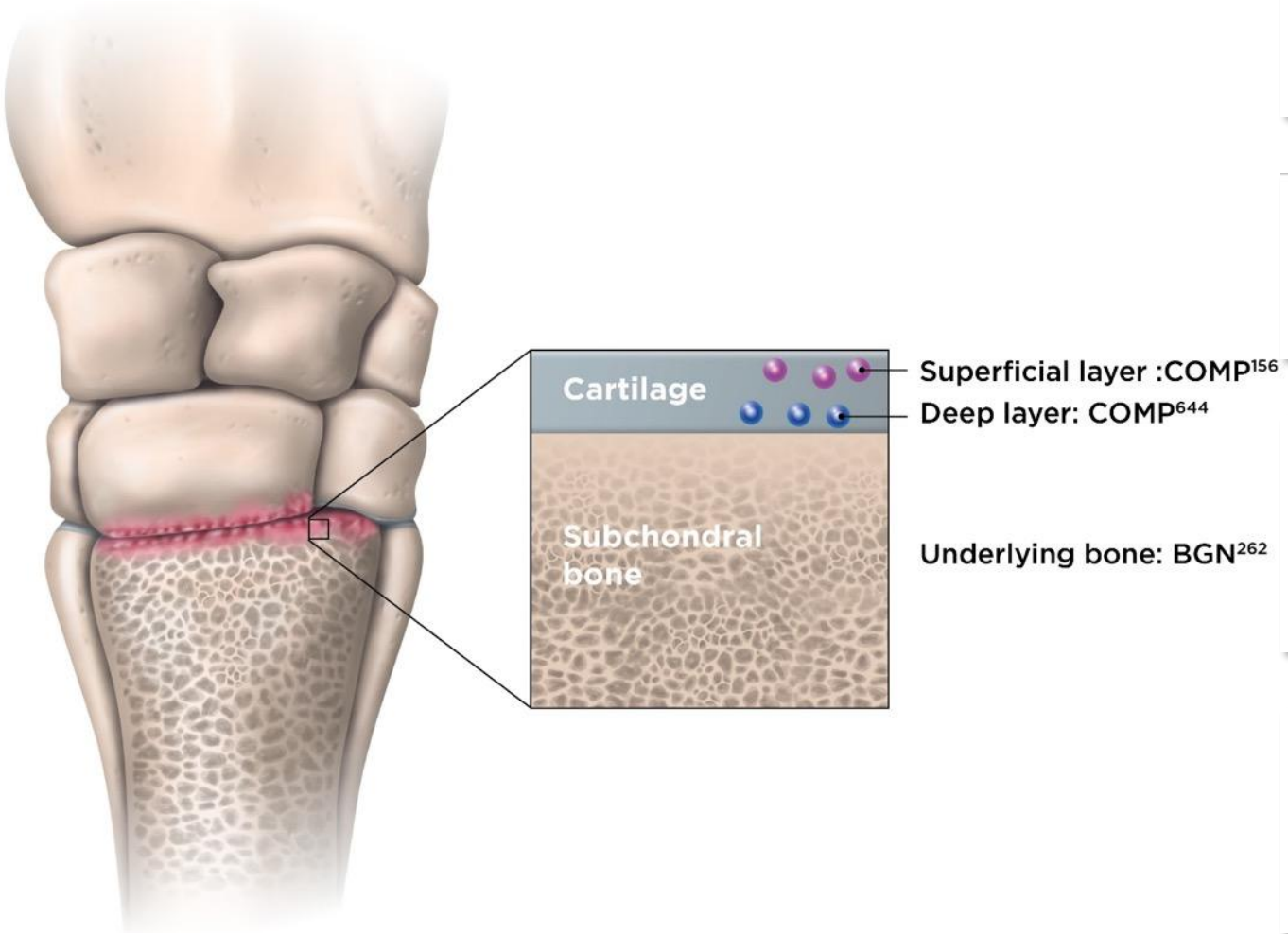
Three biomarkers from different joint compartments

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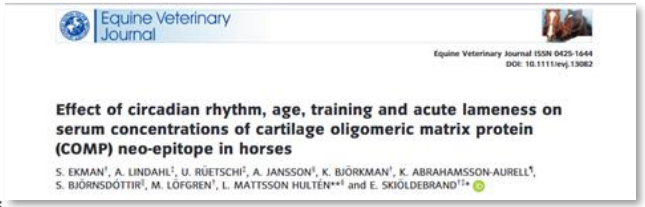
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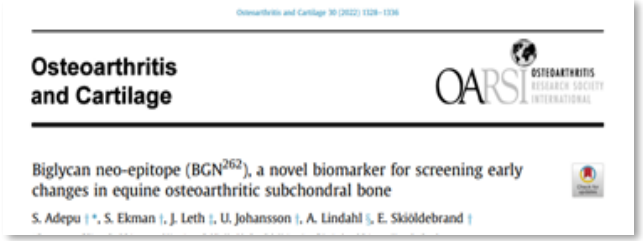
Osteoarthritis and Cartilage

OARSI OSTEOARTHRITIS RESEARCH SOCIETY INTERNATIONAL

Biglycan neo-epitope (BGN^{262}), a novel biomarker for screening early changes in equine osteoarthritic subchondral bone

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Biomarkers in synovial fluid by ArthroDiagnostics

Tissue destruction of cartilage

Quantification of COMP[156] (ng/ml)

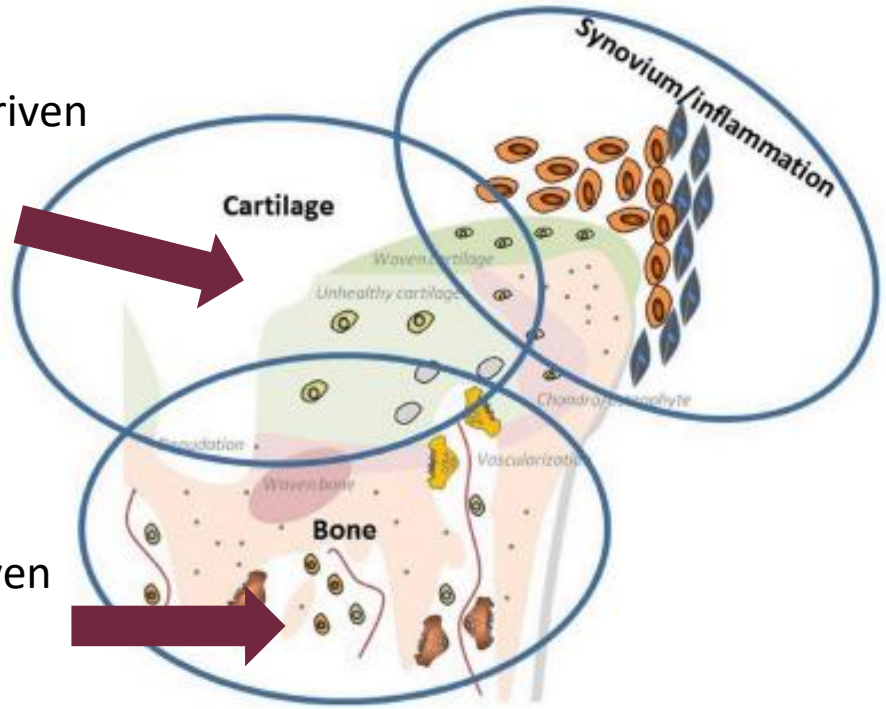
- Cut off values 500 ng/ml

- Tissue destruction of subchondral bone
- Quantification of BGN[262] (ng/ml)

Cut off values 2000 ng/ml

Our biomarkers fulfills the defintion of molecular endotypes differ from clinical phenotype

Cartilage driven
COMP[156]
COMP[644]



Bone driven
BGN[262]

Figure 1. The three endotypes of OA: (1) bone-driven endotype, (2) synovitis-driven endotype and (3) cartilage-driven endotype.

Oo WM, Hunter DJ. Ther Adv Musculoskelet Dis. 2022

Definition:
Molecular endotypes should pertain to the molecular drivers of disease pathogenesis via cellular, molecular and biomechanical signalling pathways and is irrespective of its clinical manifestations

Definition: Clinical phenotyp

- Lameness
- Stiffness
- Pain: joint flexion
- Joint pathology:
- Performance decline:
- Reduced willingness or ability to perform discipline-specific tasks
- Chronicity: Long-term disease course with episodic exacerbations

Questions to be answered with the biomarkers



Prognosis

Is it likely that the horse will develop OA?

Early diagnosis

Which joint?
Cartilage?
Bone

Treatments

Use of the most appropriate pharmaceutical
Dose?
Side effects?

Rehabilitation

When can the horse starts to train?

Preventive

Training
Footings
Shoeing
Barefot

Clinical trial in 20 Swedish trotters with lameness associated with OA

Use of the most appropriate pharmaceutical Dose?
Side effects?



New drug combination CARTAOS



Control group Celestone® bifas®

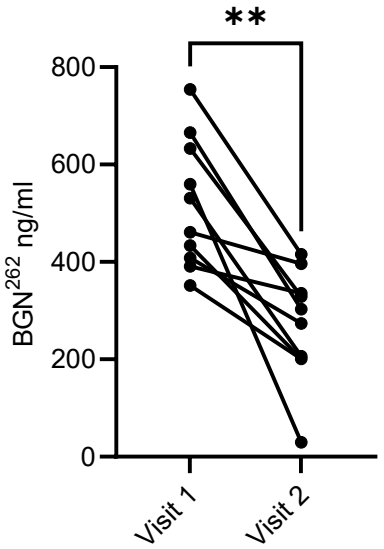
bethametason

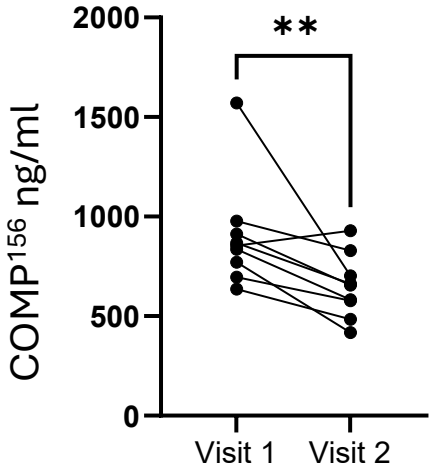
Disease modifying drug

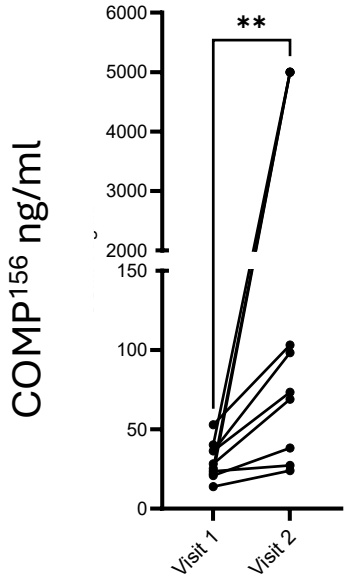
Severe side effect

Bone and cartilage biomarkers are **reduced** after treatment





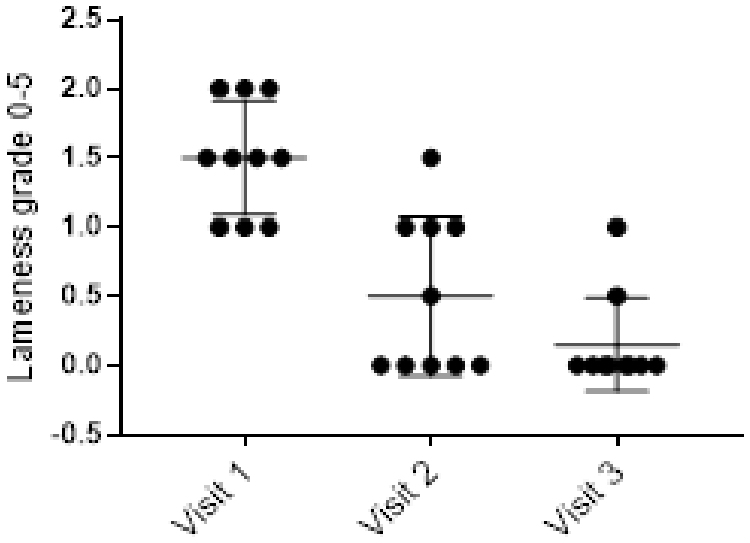




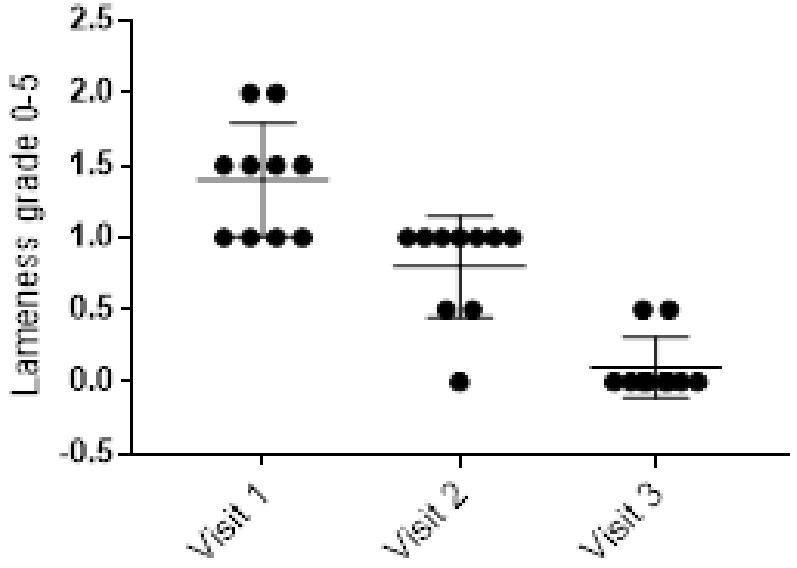
Bone and cartilage biomarkers are **increased** after treatment

Lameness improvement similar in both groups

CARTAOS



Celeston Bifas



Clinical lameness after flexion test at visit 1, 2 and 3 for horses treated with CARTAOS compared to Celeston® bifas®. The faster decline in lameness for CARTAOS group was found to be statistically significant (*P = 0.033)*.

Many drugs on the market today-only proven to have symptom inhibiting (SIOAD) but could they also be DMOADs?

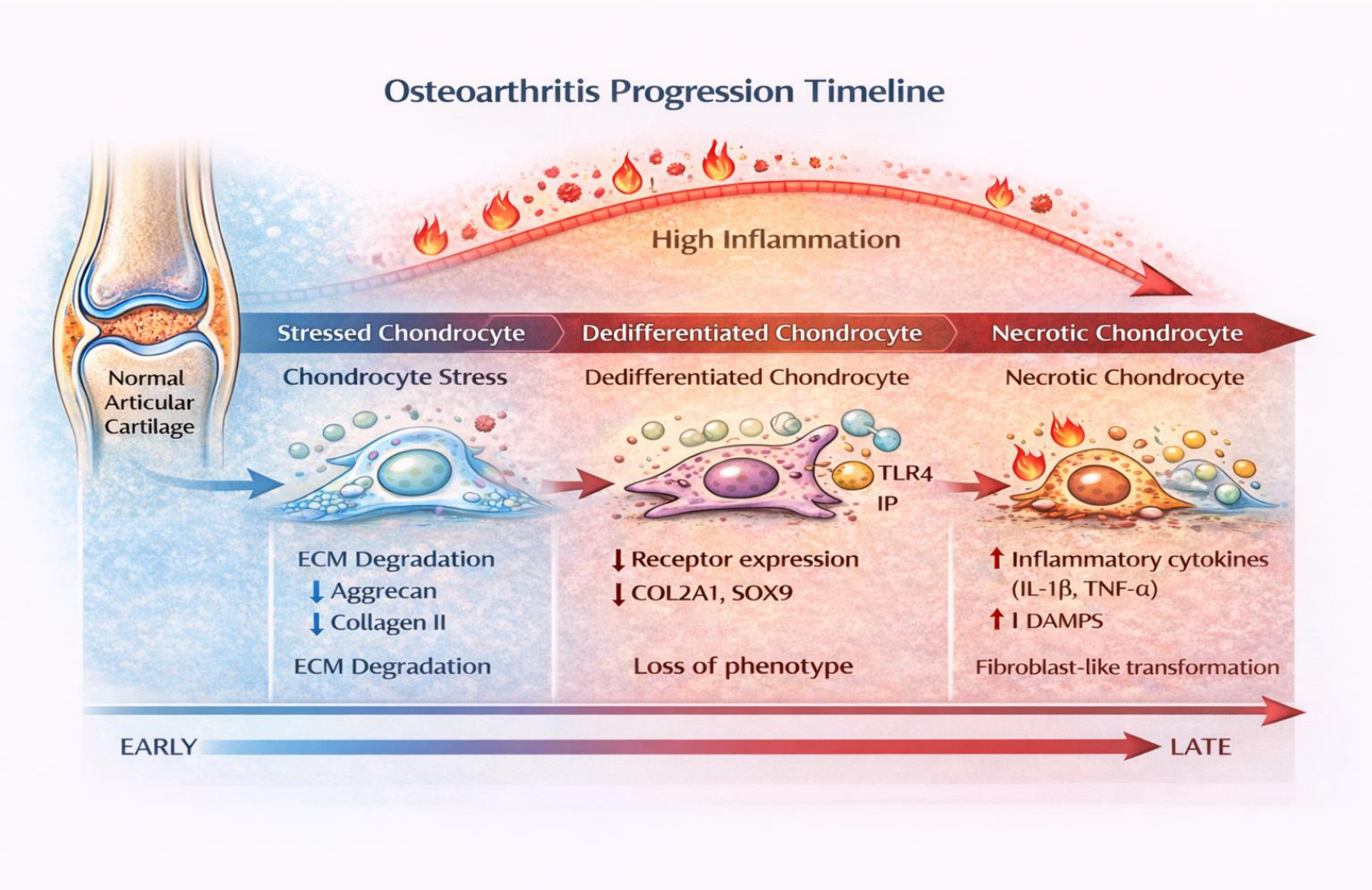
Lameness improvement

- IRAP (Interleukin-1 Receptor Antagonist Protein)
- PRP (Platelet-Rich Plasma) TGF-β, VEGF
- Corticosteroids (inhibition of gene transcription)

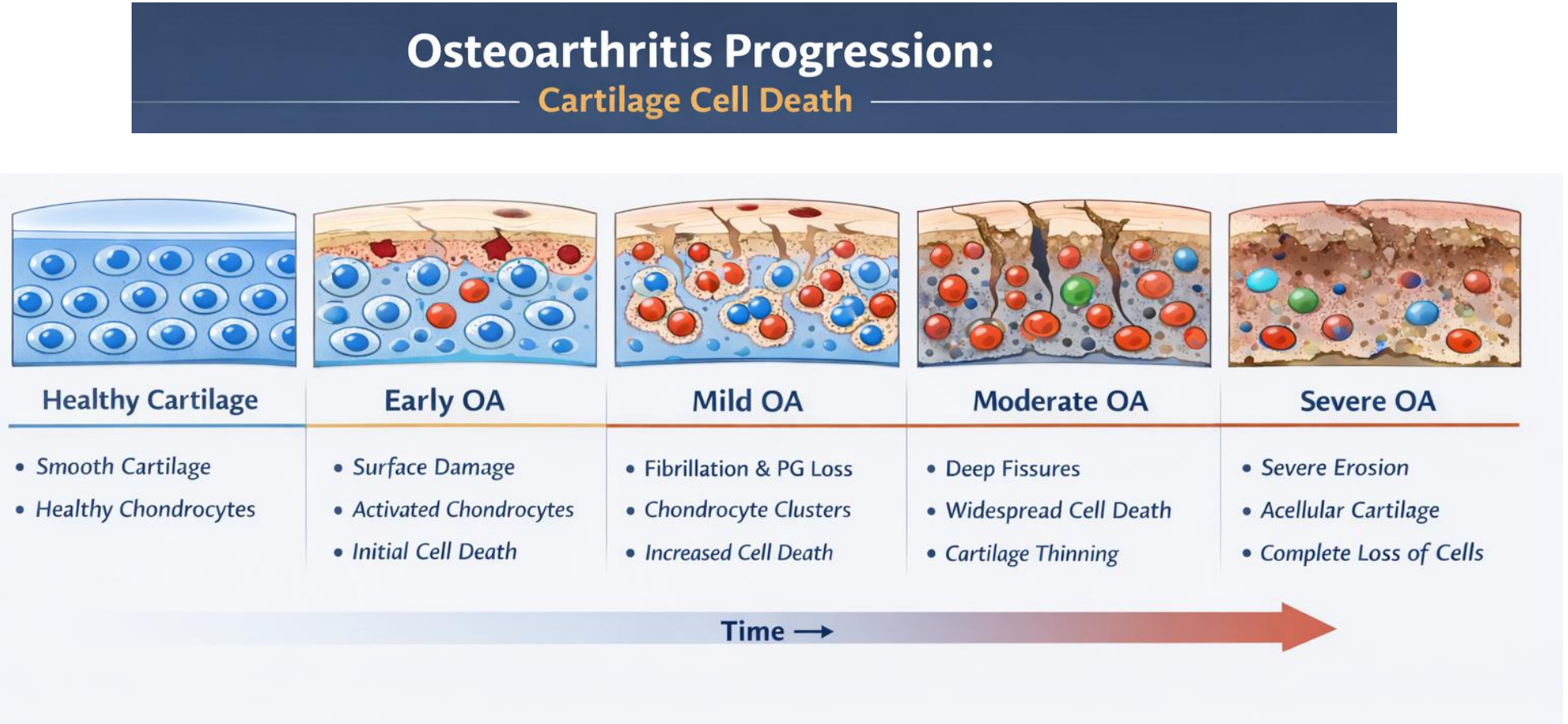
How to prove that a drug has diseasemodifying properties (DMOAD)?

- Biomarkers and lameness improvement

Treatment failure;
What is happening to the chondrocytes during the timeline?
Cells will be less responsive to treatments

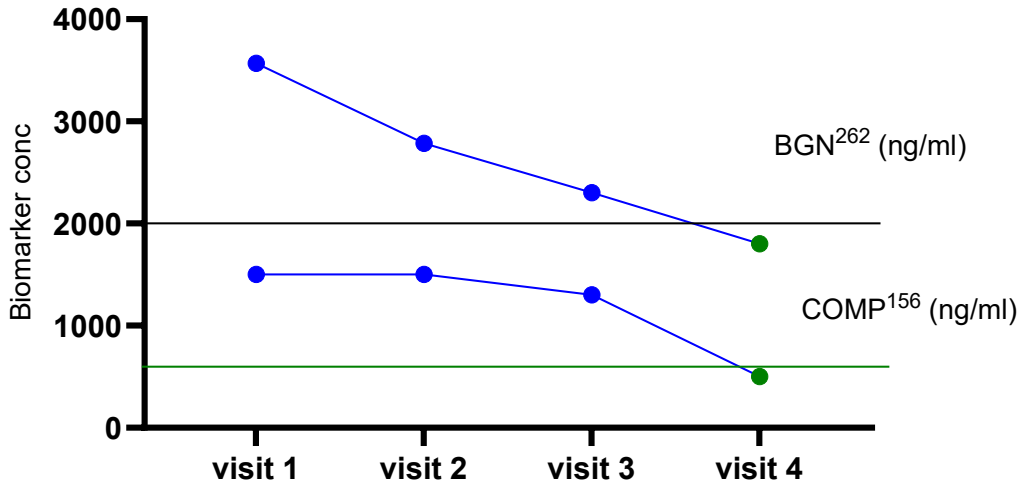


Treatment failure:
Celldeath ongoing (both necrosis and apoptosis)
Less cells left to respond to treatments.



Biomarkers assist in precision diagnosis and evaluation of treatment effects

- 7 year old jumper, gelding ,
- lame from left fetlock , flexion test 2, blocking ++
- no x-ray changes
- treated intra-articular with IRAP at 4 visits

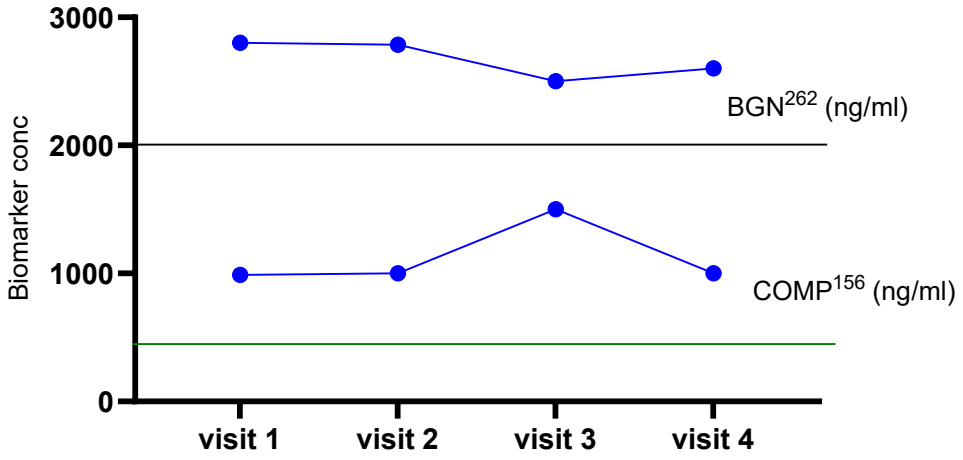


Lameness	2	2	1	0

- Summary
- Efficent treatment both on biomarker levels and lameness
- Biomarker level back to normal
- No xray changes
- Good prognosis

Biomarkers assist in precision diagnosis and evaluation of treatment effects

- 8 year old showjumper, gelding , 1.45m
- lame from right fetlock for 6 month
- No x-ray performed
- treated intra-articular with IRAP at 4 visits



Lameness 1 0.5 1 0

Summary

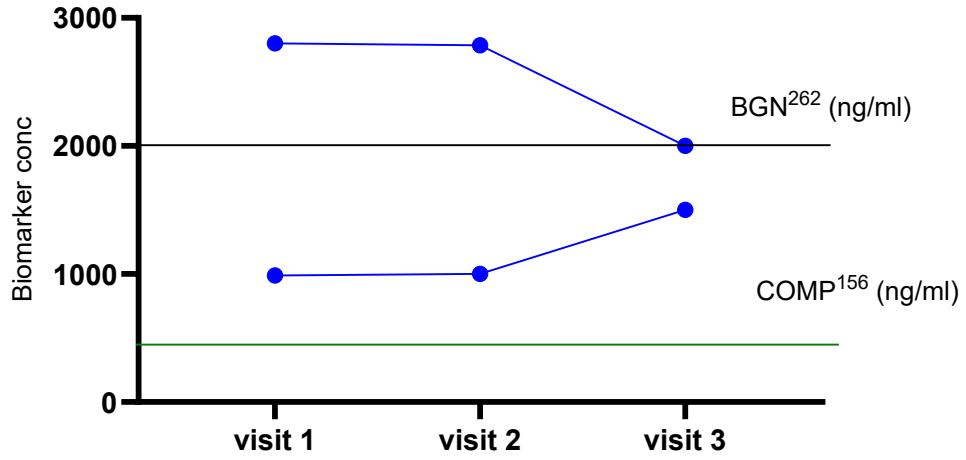
In some horses blocking of IL-1 alone is not sufficient

- TNF-α
- IL-6
- TLR

- Are there other underlying joint pathologies contributing to the elevated biomarker levels? Ligament tear, osteochondrosis?

Biomarkers assist in precision diagnosis and evaluation of treatment effects

- 14 year old SWH, mare , low level of derssage
- lame from right fetlock for 6
- x-ray: mild subchondral bone sclerosis
- treated with PRP 2 times with 1 month in between



- Summary
- Efficent treatment of subchondral bone, iomarker level back to normal
- Still high cartilage biomarkers
- Free of lameness at visit 3

- The horse should be continued treated for high concentration of COMP156
- Vet check again after 6 month

Molecular endotype differ from clinical phenotype

Osteoarthritis is a **complex and heterogeneous disease** involving multiple biological processes, including inflammation, cartilage degradation, and subchondral bone remodeling. Available treatments target different aspects of this disease process, and their efficacy therefore depends on which mechanism predominates in the individual horse.

Biomarkers are critical for monitoring treatment efficacy and enabling individualized therapeutic decisions in the horse

Please welcome to send in synovial fluid samples

Sample collection considerations

Synovial fluid should always be collected prior to intra-articular anesthesia (joint blocking), as anesthetic compounds may interfere with ELISA-based analyses and compromise the accuracy of biomarker measurements.

In addition, contamination of synovial fluid with blood should be avoided, as the presence of blood can interfere with ELISA assays and affect the reliability of the results.




Thanks for listening.....
Do you have any questions?