14-3-3eta for Rheumatoid Arthritis

Enabling earlier diagnosis, prognosis, and ongoing monitoring

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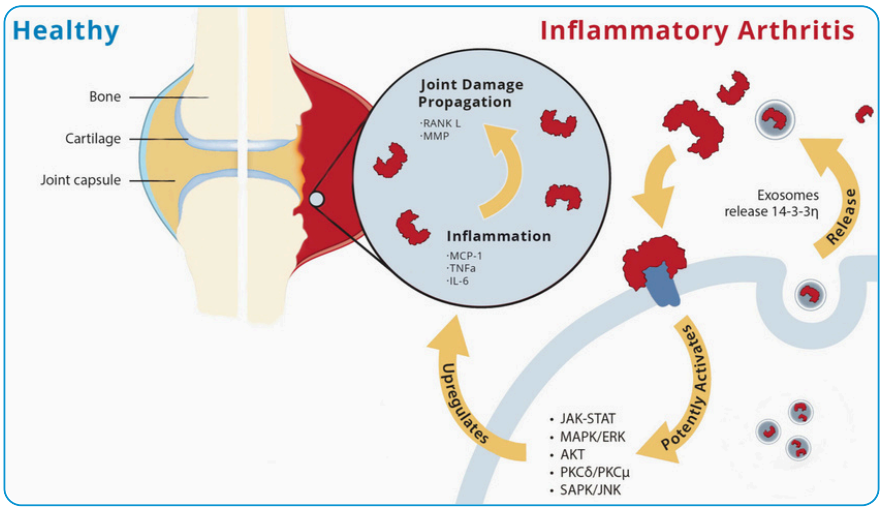
Mechanism

Early and accurate diagnosis

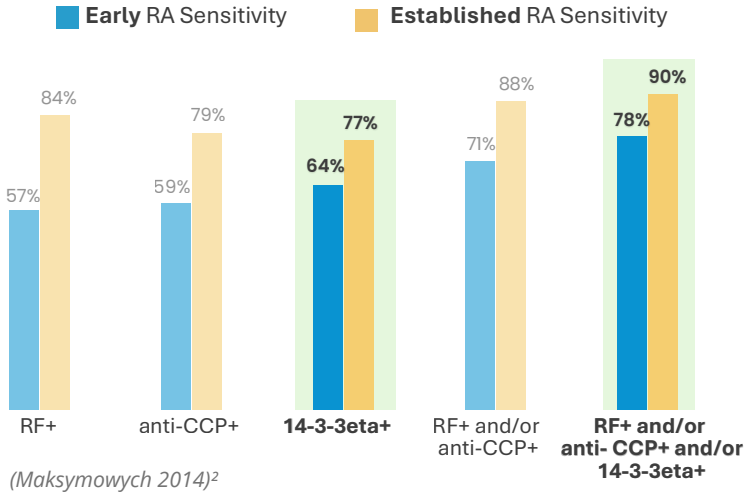
14-3-3eta is a joint-specific RA biomarker

The 14-3-3η (eta) protein is a joint-derived, pro-inflammatory mediator that is implicated in the joint erosion process and pathogenesis of rheumatoid arthritis (RA):[1]

- **Function**: 14-3-3eta is an intracellular chaperone and signal transduction protein.
- **Propagation of RA pathology**: During joint inflammation, 14-3-3eta is released into synovial fluid and serum, acting as a pro-inflammatory ligand and driving joint damage.
- **Specificity**: Elevated levels of 14-3-3eta in serum and synovial fluid are highly specific to RA, distinguishing it from other inflammatory arthritides and from healthy individuals.
- **Joint inflammation**: The presence of 14-3-3eta in serum indicates ongoing joint inflammation and damage risk.



14-3-3eta complements RF and anti-CCP, enabling earlier and more accurate diagnosis of RA



(Maksymowych 2014)[2]

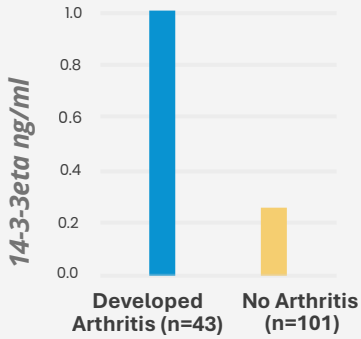
Pooled sensitivity

Pooled specificity

Based on a 16-report meta-analysis
(Abdelhafiz, 2021)[4]

- **High Sensitivity and Specificity**: 14-3-3eta is highly sensitive and specific for diagnosing early and established RA.
- **Seronegative RA**: 14-3-3eta is valuable in detecting RA in RF/anti-CCP seronegative patients.
- **Complements existing markers**: When combined with RF and anti-CCP, 14-3-3eta improves diagnostic accuracy.
- **Predictive Value**: Elevated 14-3-3eta levels are associated with joint damage risk and flares.

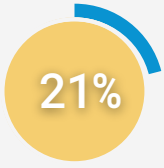
Identify at-risk patients, years before clinical onset



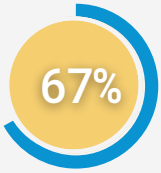
- 14-3-3eta is detectable prior to onset of arthritis in patients who are positive for anti-CCP and/or RF.
- Arthralgia patients who develop clinical arthritis have 3.4x higher levels of 14-3-3eta up to 5 years before onset.

(van Beers-Tas 2016)[3]

14-3-3eta identifies patients that are RF and anti-CCP seronegative:



of patients who have **early** RA



of patients who have **established** RA

(Naides 2015)[5]

Monitor joint damage risk

Continuum of care

Ongoing Management

Monitor response to therapy and disease progression

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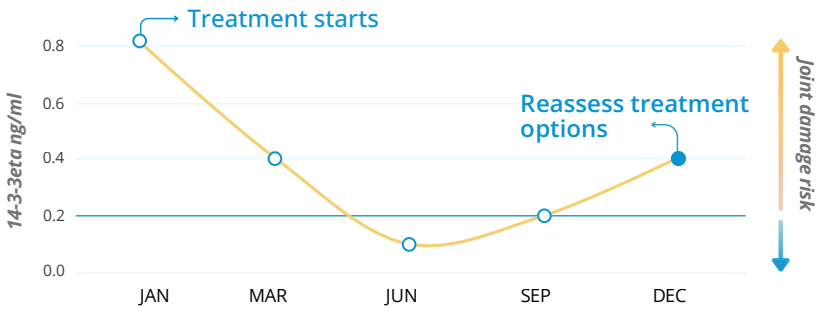
14-3-3eta is modifiable and an independent predictor of radiographic progression. Closely monitor your patient's response to therapy by serial testing of 14-3-3eta:

- Decreases in 14-3-3eta levels in response to therapy are associated with better clinical outcomes.[6,8]
- Increases or sustained 14-3-3eta levels are associated with a worse prognosis. [7,9,10]
- Levels of 14-3-3eta ≥ 0.50 ng/mL indicate significant joint damage risk. [9,10]

Combining the modifiable 14-3-3eta and CRP markers results in better prediction of joint damage than either marker alone, and assists with tight-control RA treatment strategies.

- 14-3-3eta and CRP do not correlate and represent independent predictors of joint damage progression.[9,10]
- High CRP (>8.0 mg/L) and 14-3-3eta protein (≥0.50 ng/mL) represent an adverse prognostic signature.[9,10]

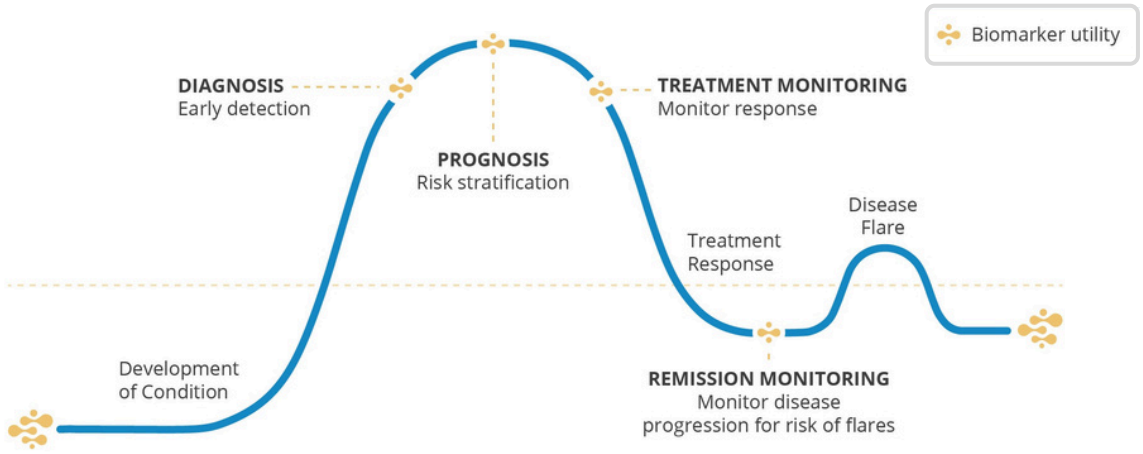
Example of serial testing of 14-3-3eta every 3 months



Uncouple joint damage and inflammation

Combine 14-3-3eta and CRP testing (every 3-6 months) to monitor joint damage risk and assist with tight treatment control strategies in RA.

14-3-3eta is a mechanistic and modifiable biomarker, providing clinical utility from early diagnosis to remission



Decreasing levels	→	Better outcomes[6,7,8]
≥ 0.5 ng/ml	Persistently high (≥0.5 ng/ml)	→	Increased risk of joint damage and flares[9,10,11]
Increasing levels	→	Worsening disease progression[7,9,10]
+CRP	Combined with CRP	→	Enhanced treatment decisions[9,10]

Confidently maintain patients in remission

Guidance for Remission Maintenance

Monitoring 14-3-3eta and CRP can help identify patients at higher risk of radiographic progression, aiding in more informed decisions on dose tapering and remission maintenance.[9,10]

Predictive Value for Flare Risk

Higher 14-3-3eta levels at baseline, especially when combined with low CRP, are strong predictors of flare risk in patients discontinuing biologic therapy.[11]

14-3-3eta ASRs are available as an LDT at the following labs:

Quest Diagnostics	
Test Name	**Test Code**
14-3-3eta Protein	91455

Labcorp	
Test Name	**Test Code**
14-3-3eta Protein	504550
RheumAssure® (14-3-3eta, RF, anti-CCP)	504509

ARUP Laboratories	
Test Name	**Test Code**
14-3-3eta Protein	3017890
Early and Established Rheumatoid Arthritis (RA) Panel (14-3-3eta, RF, anti-CCP)	3017891

COMING SOON

Sonic Healthcare USA	
Divisions	**Test Code**
Clinical Pathology Laboratories	2871
Sonic Reference Laboratory	F679
Sunrise Medical Laboratories	Coming soon
East Side Clinical Laboratory	Coming soon
American Esoteric Laboratories	Coming soon
Pathology Laboratories	Coming soon
Clinical Labs of Hawaii	Coming soon

References

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