From Metabolomics to Theragnostic: Advancing Personalized Care in Musculoskeletal Disorders

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English Man in New York

Q1#: Description of **Theragostics.**

- Theragnostics combines diagnostics and therapy to tailor treatments based on individual biological markers, enabling personalized and timely medical interventions.
- Theragnostics = diagnosis + therapy, personalized for each patient.

Q2#: What can an Analytical Chemist do about **Theragnostics?**

- An analytical chemist plays a central role in advancing theragnostics, especially by enabling precise, **molecular-level** understanding of disease and treatment response.

Q3: What is metabolomics?

- Just as genomics is the study of DNA and genetic information within a cell, and transcriptomics is the study of RNA and differences in mRNA expression; metabolomics is the study of substrates and products of metabolism, which are influenced by both genetic and other factors (Figure 1).
- Metabolomics is a powerful approach because metabolites and their concentrations, unlike other "omics" measures, directly reflect the underlying biochemical activity and state of cells / tissues. Thus, metabolomics best represents the molecular phenotype.

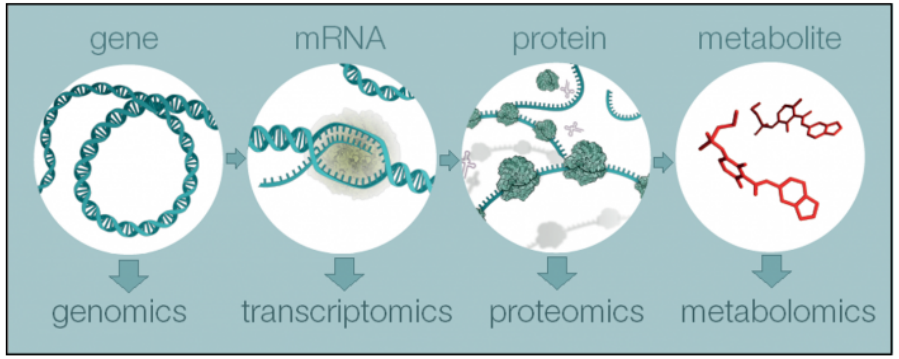
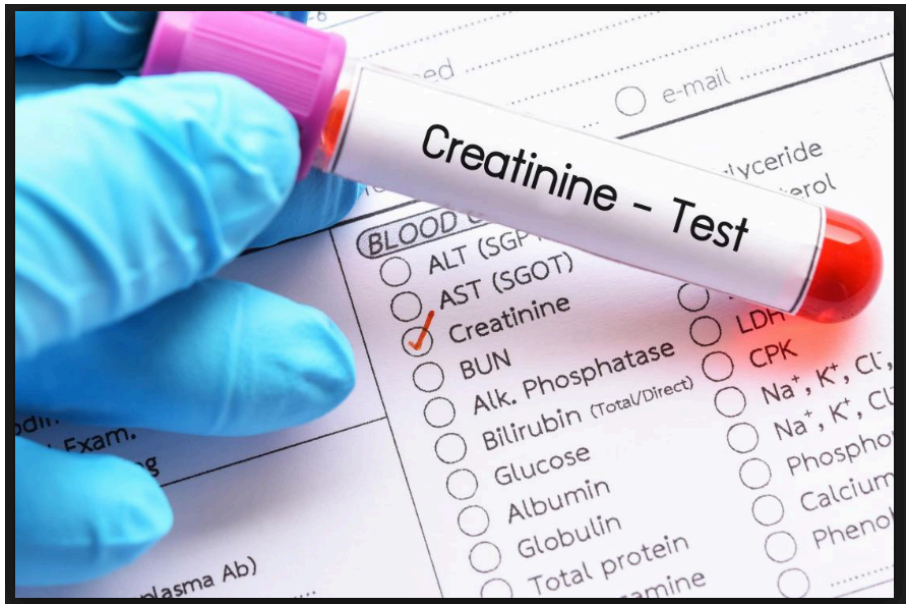
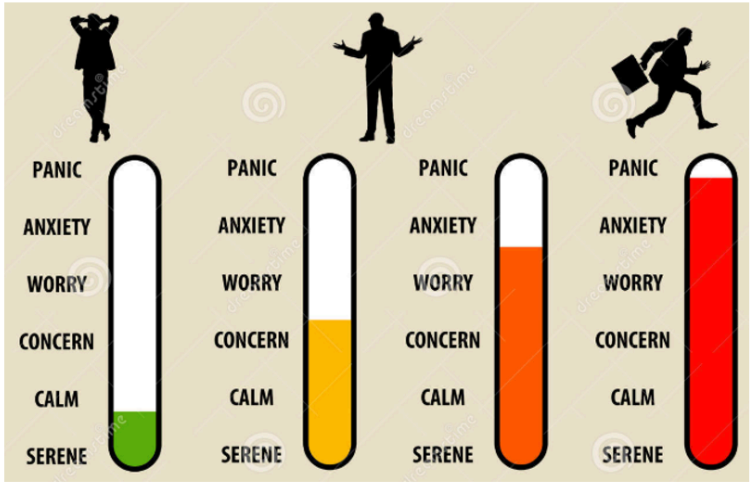


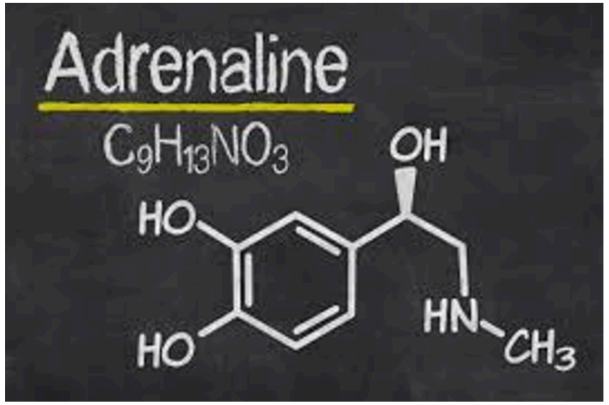
Figure 1 An overview of the four major "omics" fields, from genomics to metabolomics.

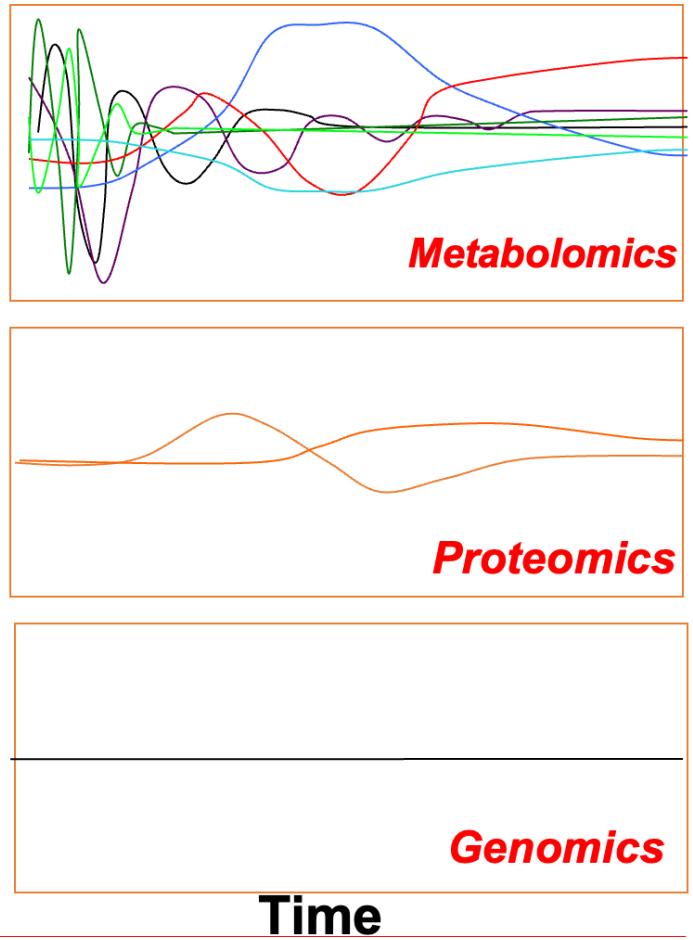
Q4: Why metabolomics?

Your DNA never changes. Your proteins change slowly. But your metabolites? They scream what's happening right now!

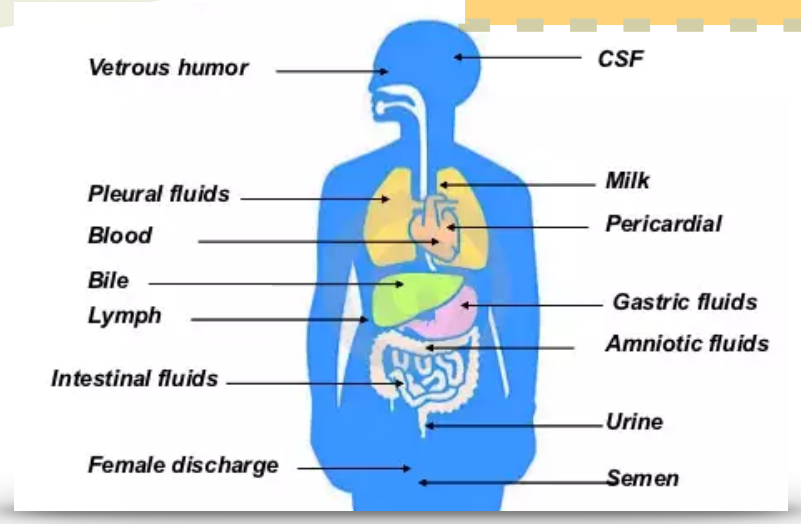


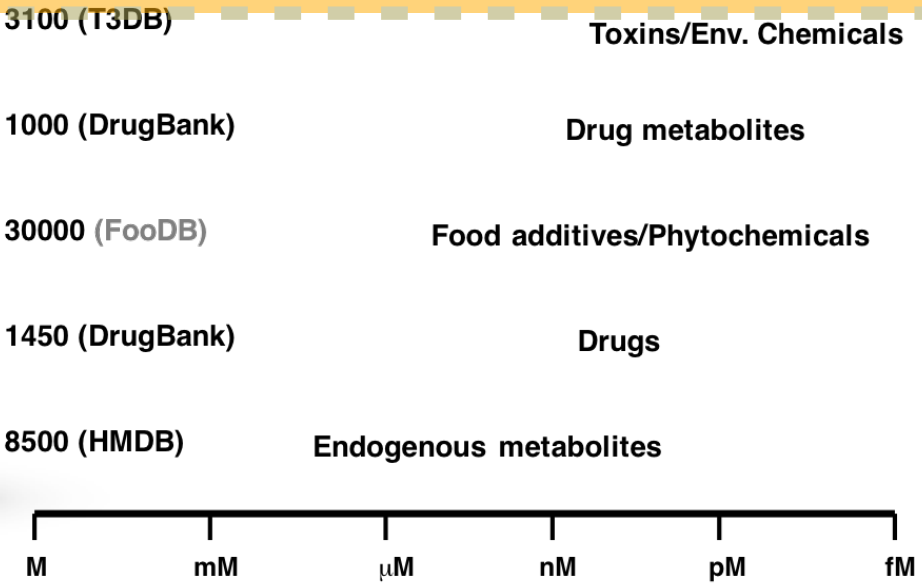






Q5: From Metabolomics to Theragnostics?





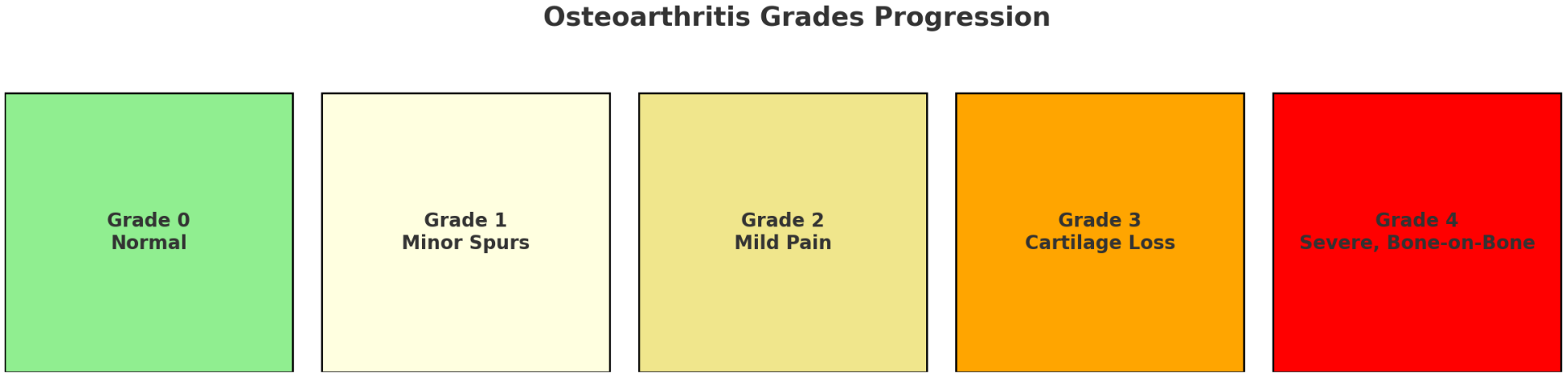
🗣️ “Every drop of fluid in the human body—from blood to bile, urine to amniotic fluid—is a window into our metabolic state. And metabolomics? It reads these windows like a language.”

👉 “With over 15,000 endogenous metabolites—and even more from diet, drugs, and toxins—metabolomics doesn’t just detect disease; it tells us which patient, which pathway, and what treatment. That’s the essence of theragnostics.”

Q6: Can we use metabolomics to guide personalized treatment decisions in osteoarthritis?

Osteoarthritis is a well-known progressive joint disorder marked by cartilage degradation, inflammation, and structural bone changes, ultimately causing pain, stiffness, and reduced mobility.

Grade 0: Normal joint, no damage.
Grade 1: Minor bone spurs, no symptoms.
Grade 2: Mild OA, visible spurs, occasional pain.
Grade 3: Moderate OA, cartilage loss, frequent pain.
Grade 4: Severe OA, bone-on-bone, constant pain, limited mobility.



Q7: So… Where is the problem?

Eurythmics
Here comes the rain again!
Falling on my head like a memory
Falling on my head like a new emotion

Theragnostics
Here comes the pain again!
Falling on my joints like a tragedy…
So what can we actually do about it?

Can we finally listen to what the metabolites are trying to say?

Q8: Can metabolomics tell us when to suppress inflammation and when to start regeneration in osteoarthritis?

Grade 1 – Moderate OA

Best window for detecting and suppressing early inflammation

Why?

Minor osteophyte (bone spur) formation begins, but cartilage is still intact.
No pain or only mild, activity-related discomfort.
Inflammation may already be present at the molecular level (e.g., synovial irritation, NO, cytokines).
This stage is often silent but biochemically active.

Goal: Identify and control subclinical inflammation to prevent structural damage.

Grade 3 – Moderate OA
Best window for regenerative therapy

Why?

Cartilage loss has begun but joint structure is still partly preserved.
Inflammation may still be modifiable.
Treatments like PRP, stem cell injections, and hyaluronic acid can support cartilage repair and reduce symptoms.

Goal: Delay or prevent progression to irreversible damage.

Q9:
What if a simple blood test could tell us who needs anti-inflammatory therapy—right now?

🟥 Arginine

Arginine is converted into nitric oxide (NO) by immune cells during inflammation.
NO is a powerful inflammatory mediator, especially active in infections and tissue damage.

🟥 Arachidonic Acid

Released from cell membranes when the body senses injury.
It is the main source of several inflammatory molecules.

🟥 Prostaglandins

Produced from arachidonic acid by the COX enzymes.
They cause pain, fever, and swelling — the classic signs of inflammation.
Drugs like ibuprofen work by blocking prostaglandin production.

🟥 Leukotrienes

Also made from arachidonic acid, but through a different pathway (5-LOX).
They cause bronchoconstriction, attract immune cells, and worsen allergic or autoimmune reactions.

Q10: How do we know when to stop fighting inflammation and start repairing the joint?

Key Points:

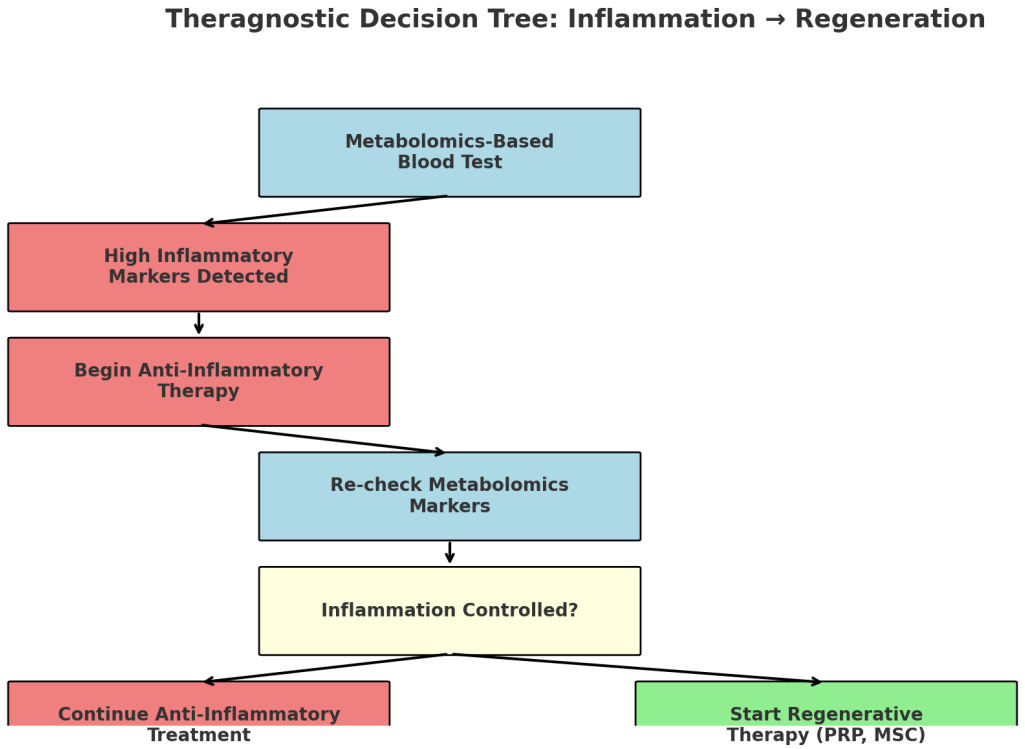
Metabolomics can guide both diagnosis and timing.

It tells us not just what's wrong, but also when to act. Anti-inflammatory therapy is the first step, but it shouldn't continue indefinitely.

Persistent inflammation means regeneration won't succeed.

Re-checking metabolomic markers allows us to monitor therapy effectiveness — not just symptom relief.

Once inflammatory markers normalize, it's the optimal window to begin regenerative treatments like PRP or stem cells.



Q11: What if theragnostics in OA isn't science fiction… but just science we haven't applied yet?

JOURNAL ARTICLE

Metabolomics of osteoarthritis: emerging novel markers and their potential clinical utility

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Abstract

OA is a multifactorial and progressive disease with no cure yet. Substantial efforts have been made and several biochemical and genetic markers have been reported, but neither alone nor in combination is adequate to identify early OA changes or determine disease progression with sufficient predictive values. Recent advances in metabolomics and its application to the study of OA have led to elucidation of involvement of several metabolic pathways and new specific metabolic markers for OA. Some of these metabolic pathways affect amino acid metabolism, including branched chain amino acids and arginine, and phospholipid metabolism involving conversion of phosphatidylcholine to lysophosphatidylcholine. These metabolic markers appear to be clinically actionable and may potentially improve the clinical management of OA patients. In this article, we review the recent studies of metabolomics of OA, discuss those novel metabolic markers and their potential clinical utility, and indicate future research directions in the field.

Application of Metabolomics to Osteoarthritis: from Basic Science to the Clinical Approach

Osteoarthritis (M Goldring, Section Editor) | Published: 06 May 2019
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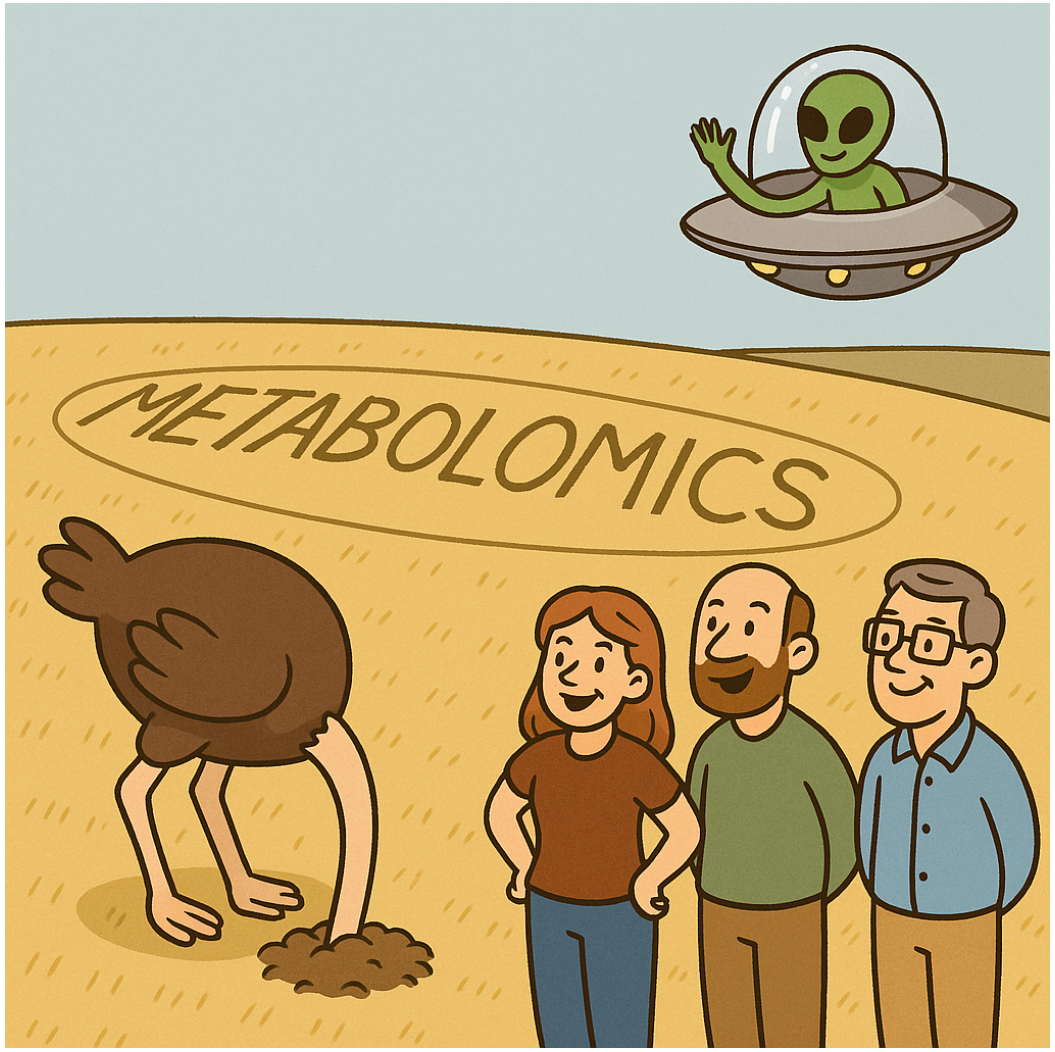
Abstract

Purpose of the Review

Osteoarthritis (OA) is a multifactorial and progressive disease affecting whole synovial joint. The extract pathogenic mechanisms and diagnostic biomarkers of OA remain unclear. In this article, we review the studies related to metabolomics of OA, discuss the biomarkers as a tool for early OA diagnosis. Furthermore, we examine the major studies on the application of metabolomics methodology in the complex context of OA and create a bridge from findings in basic science to their clinical utility.

Q11: What if theragnostics in OA isn't science fiction… but just science we haven't applied yet?

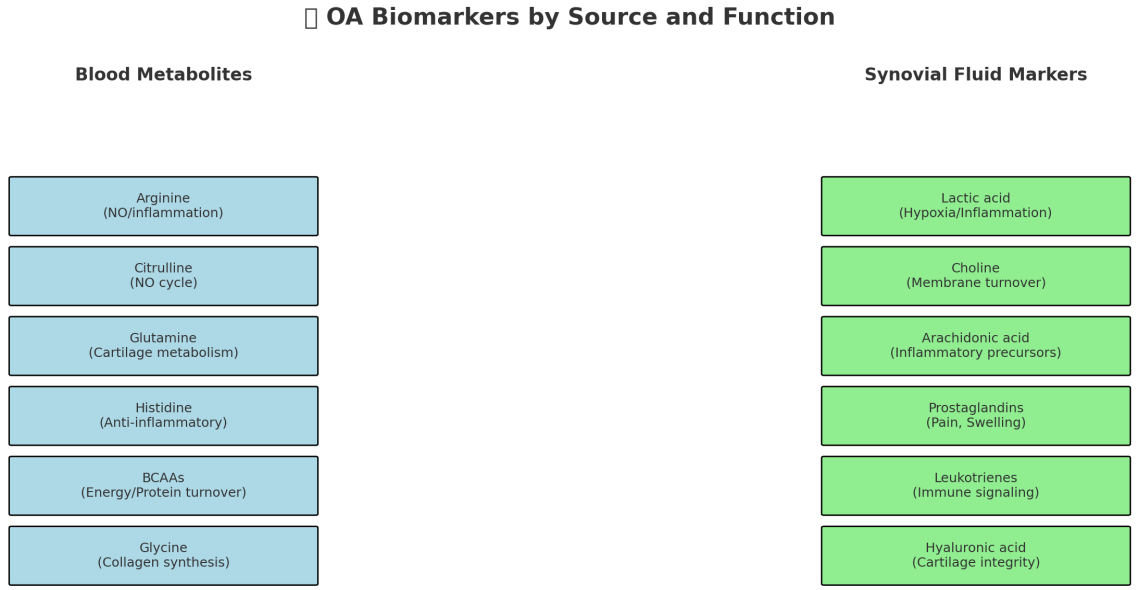


Results

Osteoarthritis Biomarkers

🩸 In Blood:

Arginine – linked to nitric oxide production and inflammation
Citrulline – reflects nitric oxide cycle activity
Glutamine / Glutamate – involved in cartilage matrix metabolism
Histidine – often reduced, anti-inflammatory marker
Branched-chain amino acids (BCAAs) – altered energy and protein turnover
Glycine – related to collagen synthesis



💧 In Synovial Fluid:

Lactic acid – increased, associated with hypoxia and inflammation
Choline / GPC (glycerophosphocholine) – linked to membrane turnover
Arachidonic acid – precursor of pro-inflammatory eicosanoids
Prostaglandins & Leukotrienes – direct markers of inflammatory cascade
Hyaluronic acid – decreased in advanced stages, indicates cartilage degradation

Results

Unpublished Results | Theragnostics in Osteoarthritis

Study 1:

Title: Leukocyte content and storage changes the metabolic profile of platelet rich plasma

Authors: F. Koç, B. Fidan, A. Kaplan, S. Korkusuz, S. Çiftçi, M. Çelebier, F. Korkusuz
Affiliations: Hacettepe University, Faculty of Pharmacy (Analytical Chemistry, Pharmaceutical Biotechnology), and Faculty of Medicine (Orthopedics and Traumatology, Sports Medicine), Ankara, Türkiye.

Objective:

To evaluate how leukocyte content and -20 °C storage alter the metabolic composition of PRP formulations.

Results:

L-PRP is metabolically rich in inflammation-associated compounds (e.g., epinephrine, L-tyrosine).
P-PRP shows enhanced regenerative profiles (e.g., glucuronic acid, citrate).
Storage induces mild but significant shifts in metabolite stability.

Theragnostic Value: Supports metabolomics-guided selection of PRP type based on patient needs (inflammatory vs. regenerative phases).

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Conclusion

Metabolomics-Based Theragnostics in OA

Metabolomics enables real-time insight into inflammation, tissue damage, and regeneration potential—beyond what imaging or symptoms can show.

Theragnostics = Right treatment, right time.

With molecular markers, we can identify when to suppress inflammation and when to promote regeneration.

Osteoarthritis is not one-size-fits-all.

Patient-specific metabolomic signatures can guide personalized therapies like PRP, stem cells, or anti-inflammatories.

Unpublished results from our lab show how leukocyte-rich PRP or specific secretomes can be matched to patient needs—pro-inflammatory vs. regenerative.

Next step: Move from knowing to applying—translate metabolomic data into clinical decision-making.

Thank you for your kind attention!