

Biochemical Markers For Diagnosis & Follow Up Of Diseases

Editing File

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Objectives

- Define Biomarkers and its criteria.
- Recognize different types of biochemical markers
- Demonstrate the clinical applications of biomarkers in diagnosis of various diseases

Introduction

What is a Biomarker?

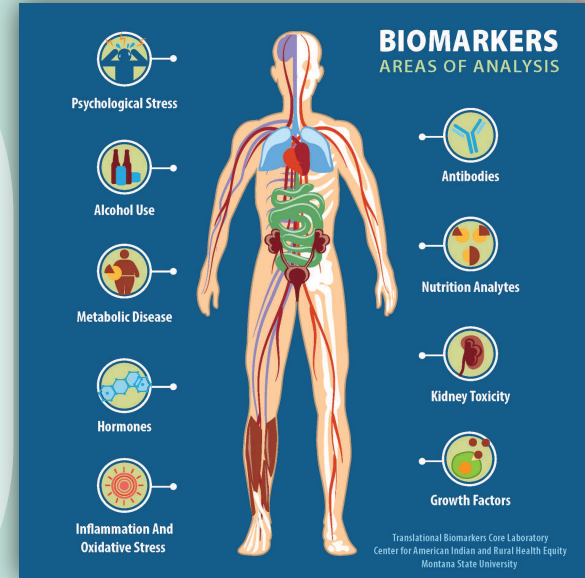
It is a biological molecule that is found in blood, other body fluids, or tissues that **indicates a normal or abnormal process** such as a disease or a condition.

Most common body fluids for the measurement of biomarkers are?

Blood
Urine

Biomarkers are either:

Plasma-specific
Tissue-specific



Types of Biomarkers:

Plasma-Specific

- Normally present in plasma
- Perform their functions in blood
- **High level of activity in plasma than in tissue cells**

Tissue-Specific

- Present **inside the cell**
- A low concentration can be detected in plasma due to cellular turnover
- If higher concentration is detected in plasma, it indicates **cell damage**

Biomarker enters circulation

Cell Damage

Cell damage can be due to:

1- **Tissue inflammation**, example:

-**ALT*** in liver disease (e.g., acute hepatitis)

-Amylase in acute pancreatitis

2- **Ischemia/hypoxia/infarction** (Closing of the artery)

Increase Plasma [Troponin] in **myocardial infarction**

(Troponin in a healthy person supposed to be zero)

ALT*: Alanine aminotransferase

Diagnosis and Prognosis

Diagnosis: Identification of a disease from its signs and symptoms

Prognosis: The future outcome of a disease

Ideal marker should be both high specificity and sensitivity %50 of sensitivity or specificity is not considered high (not good enough)
It is possible to combine markers
-one with high specificity but low sensitivity
-and the other with high sensitivity but low specificity

Criteria of a good biomarker assay

Assay is the technology used to detect biomarkers

Sensitive

01

Sensitivity is the ability of an assay to detect small quantities of a marker

How easy it is to detect the biomarker (high sensitivity is good)

Specific

02

Specificity is the ability of an assay to detect only the marker of interest

The less markers it detects, the better

Troponin is specific for heart

Robust

03

To produce fast results

Increase sensitivity which increase specificity

بالعربي: لو عندنا مركب معين نبي نقيسه بالدم وفي فحصين:

1) specific:

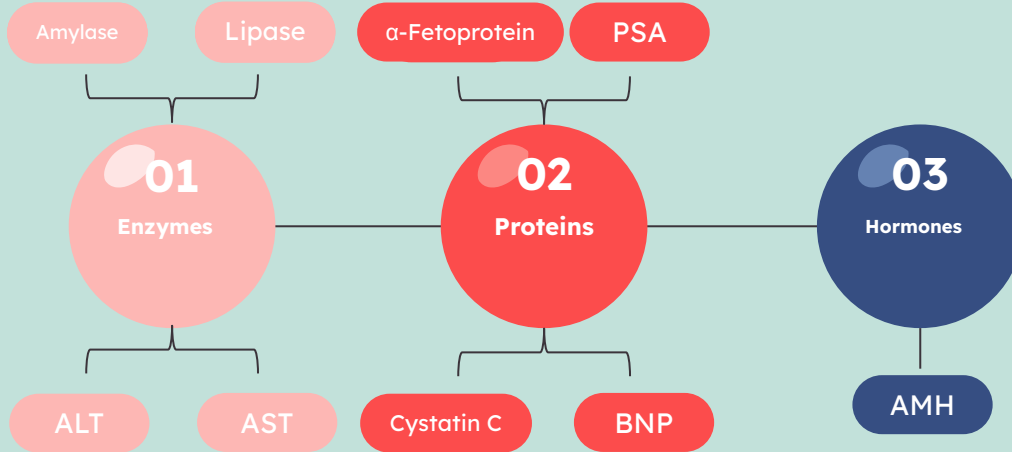
يكون دقيق بحيث ما يتعرف الا على المركب الي نبيه مو غيره بس بسبب دقته، قد يكون المركب موجود بس ما يتعرف عليه (يعني اذا قالك موجود) (المركب فانه موجود)

2) sensitive:

يكون جدا حساس بحيث ما يفوت المركب ويتعرف عليه على طول لكن بسبب الحساسية العالية هذي، قد انه يتعرف على اشياء ثانية ماهي المركب (يعني اذا قالك مو موجود) (معناته مو موجود)

Examples of Biomarkers

Biomarkers can either be:



will be explained in details on the coming slides

Enzymes as Biomarkers:

Examples Include:

1. Amylase, Lipase
2. Alanine Aminotransferase (ALT)
3. Aspartate Aminotransferase (AST)

Enzymes as Biomarkers

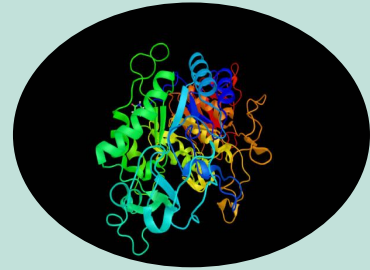
Amylase:

Elevated serum amylase level is a diagnostic indicator of acute pancreatitis

Amylase level greater than **10 times** the upper limit indicates **acute pancreatitis**

The test has **low specificity** because elevated amylase level is also present in other diseases Like salivary gland

Amylase **appears in the serum within 2-12 hours after abdominal pain**, and returns to normal in 3-5 days



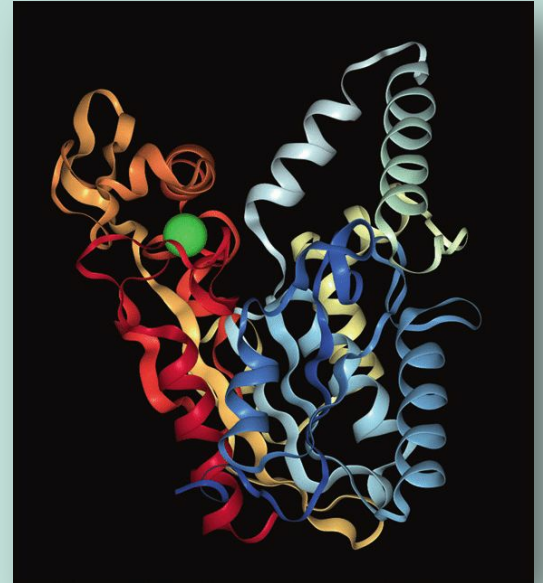
Enzymes as Biomarkers:

Lipase:

Serum lipase has higher **specificity** than serum amylase (**elevated only in acute pancreatitis**) Highly specific

It appears in plasma within **4-8 hours** and remains 8-14 days

Amylase and Lipase both are enzymes that diagnose **acute pancreatitis**, but **Lipase is more specific** than Amylase



AST and ALT

AST:

- Aspartate aminotransferase.

- **Produced by:**

1. liver
2. Heart
3. Skeletal muscles
4. Erythrocytes
5. kidney

- **Elevated in:**

1. Liver disease
2. Heart disease
3. Skeletal muscle disease
4. hemolysis

ALT:

- Alanine aminotransferase.

- **Produced by:**

Liver

- **Elevated in:**

Liver disease

ALT is more specific than AST because it is only found in the liver.

Case example:

A GP was called to see 21-year-old female student who had been complaining a flu-like illness for two days, with symptoms of fever, vomiting and abdominal tenderness in the right upper quadrant. On examination, she was jaundiced, moreover; the liver was enlarged and tender. A blood sample was taken for liver function tests which showed elevated ALT (Alanine aminotransferase) and AST (Aspartate aminotransferase). What is the most likely diagnosis?

Answer: Acute hepatitis

If lipase and amylase are high what disease does the patient have? **Answer: Acute pancreatitis**

Summary for Enzyme biomarkers:

Acute hepatitis	Acute pancreatitis
ALT More specific to <u>L</u> iver diseases	Lipase More specificity / appears within 4-8 hrs, remains up to 8-14 days
AST Low specificity (elevated in other diseases)	amylase Low specificity (present in other diseases) / appears within 2-12 hrs, remains up to 3-5 days/ elevates x10 the upper limit

Proteins as Biomarkers:

1. α -fetoprotein
2. Prostate Specific Antigen (PSA)
3. Cystatin C
4. B-type Natriuretic Peptide (BNP)

α -fetoprotein

- it is produced by: **fetal liver** and falls until term. (α -fetoprotein levels are **very low** in newborns).

- remains **low under normal conditions**

- **non-specific** marker.

- high conc. are found in: Hepatocellular (**hepatoma**), testicular, and gastrointestinal tract **carcinomas**.

Both commonly used as tumor markers

Prostate Specific Antigen (PSA)

- it is produced by: **prostate gland**.

- PSA level is used as a tumor marker to aid diagnosing and monitoring patients with **prostatic cancer**.

-high serum levels are found in:

1. Benign prostatic hyperplasia (BPH)
2. Prostatic inflammation/infection

PSA is specific for the prostate as an organ. however it is not specific to which disease

Protein Biomarkers

Cystatin C

- A cysteine protease inhibitor mainly produced by **all nucleated cells** of the body. (RBCs don't produce it)
- Useful biomarker for measuring glomerular filtration rate (GFR) in assessing **kidney** function and failure. (specific)
- Unlike **Creatinine**, its serum conc. is independent of gender, age, or muscle mass.
- Abnormally high serum levels of Cystatin C indicate early renal disease, so it is used as a marker for:
 1. Detecting early **renal (kidney)** diseases
 2. Monitoring **kidney transplantation** (for donors)

B-type natriuretic peptide (BNP)

- A peptide secreted mainly in the **cardiac ventricles** in response to cardiac expansion and pressure overload
- High serum levels are observed in **congestive heart failure**.
- It can be used to differentiate patients whose symptoms are due to **heart failure** from those whose symptoms are due to **other causes such as pulmonary disease**.

Note:
BNP for heart failure Troponin for myocardial infarction



Hormones Biomarkers

Anti-Mullerian Hormone (AMH)

- In females it is produced by **ovaries**.
- Appears to be best marker for **estimating egg cell reserve in the ovaries** (ovarian reserve testing).
- Only growing follicles produce AMH.
- **Plasma AMH levels strongly correlate with number of growing follicles.**

AMH

Low levels in women
with **ovarian
dysfunction**

e.g., menopause

High levels in women
with **polycystic
ovarian syndrome
(PCOS)**



Take Home Messages

- Biochemical markers are essential for accurate and non-invasive laboratory tools offering the treating physician fast means for better management.
- They could be proteins, enzymes, or hormones.
- Biomarkers are used for diagnosis, prognosis and follow up of diseases.
- A biomarker exhibit good diagnostic and prognostic values.
- Examples of biomarkers used in different diseases will help understand their qualities and limitations.
- Recent development in medicine provides new biomarkers.

Quiz

1. A biological molecule that can be measured to follow up a disease or a treatment?

A) Biomarker

B) Diagnosis

C) Prognosis

D) Serum

2. A biomarker that is released in myocardial infarction:

A) PSA

B) AMH

C) α -fetoprotein

D) Troponins

3. Which of these biomarkers can be considered as tumor markers?

A) α -fetoprotein

B) PSA

C) Amylase

D) A and B

4. Which of these Biomarkers elevate only in acute pancreatitis?

A) Amylase

B) Lipase

C) AST

D) ALT

5. Which biomarker can be used to differentiate between heart failure and pulmonary diseases?

A) PSA

B) AMH

C) BNP

D) Cystatin C

SAQ

Define the terms
1-diagnosis
2-prognosis:

Slide 5

SAQ

List 3 cases where High concentration of A-fetoprotein is observed:

Slide 11

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