

In this lecture there will be some differences between males & females' slides:

- Only in females' slides is in **PINK**
- Only in males' slides is in **light BLUE**

BIOCHEMICAL MARKERS FOR DIAGNOSIS OF DISEASES AND FOLLOW UP



Color Index:

- **Original slides.**
- **Important.**
- 436 Notes
- **438 notes**
- **Extra information**

رابط التعديل:

<https://docs.google.com/document/d/1WvdeC1atp7J-ZKWOUSukSLsEcosjZ0AqV4z2VcH2TA0/edit?usp=sharing>



Biochemistry team 438

Objectives:

- Define biomarkers and its criteria
- Comprehend the importance and diagnostic qualities of various biomarkers
- Understand the importance of different biomarkers in the diagnosis, treatment and follow up of a disease. (their clinical application)
- Recognize the types of biomarkers and their use in specific diseases such as heart, cancer, liver, kidney and pancreatic diseases



What is a biomarker?

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

(أي شيء تلقاه بالجسم سواء بالسوائل او بالأنسجة غريب على الجسم او شيء موجود ولكن بنسبة غير طبيعية)

-A biomarker is measured to follow up a disease or treatment

مثال: لو شفت واحد الجلوكوز بدمه عالي تعطيه انسولين *الجلوكوز هنا هو البايوماركر*

Diagnosis vs prognosis

Diagnosis

Identification of a disease from its signs and symptoms

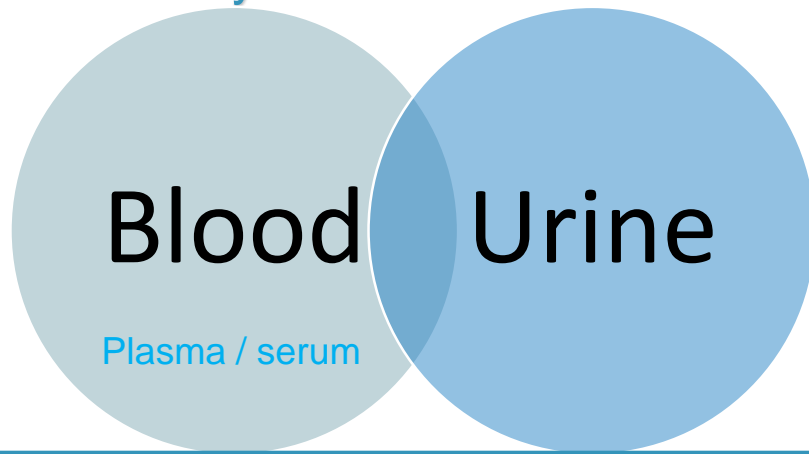
Prognosis

The future outcome of a disease

بعد ماتعطي العلاج لازم تتأكد ان فيه تأثير عالبايوماركر



Most common body fluids for measurement of biomarkers are:



What is the difference between Serum and Plasma ?
They are the same , but plasma has coagulation factors and serum has no coagulation factors.

biomarkers are either:

Plasma-specific biomarkers

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

- **Examples:**

- blood clotting enzymes (thrombin)
- cholinesterase, etc.

Tissue-specific biomarkers:

- Present inside the cell
 - Conc. is lower in plasma
- can be detected due to cellular turnover
- if Released into the body fluids in high conc.

Its due to:

- cell damage
- defective cell membrane

- **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 →
↑ **plasma [Troponin]** in myocardial infarction

ALT*: alanine aminotransferase



- Intracellular enzymes are present only In their cells of origin
- Some are secretory enzymes that are secreted by salivary glands, gastric mucosa and pancreas
- In disease, plasma levels of secretory enzymes increase when their cells are damaged
- The diagnosis of organ disease is done by measurement of enzymes of that tissue



Factors affecting serum biomarker levels:

- Cell damage
- Rate of biomarker synthesis and clearance
- Enzyme inhibitors
- Glucose deficiency
- Localized hypoxia (less oxygen)
- Ischemia (obstruction of blood vessels)
- Necrosis
- Tissue infarction due to ischemic necrosis
- Myocardial infarction



Qualities of a good biomarker assay

(الاجتبار اللي نقيس به البايوماركر = assay)

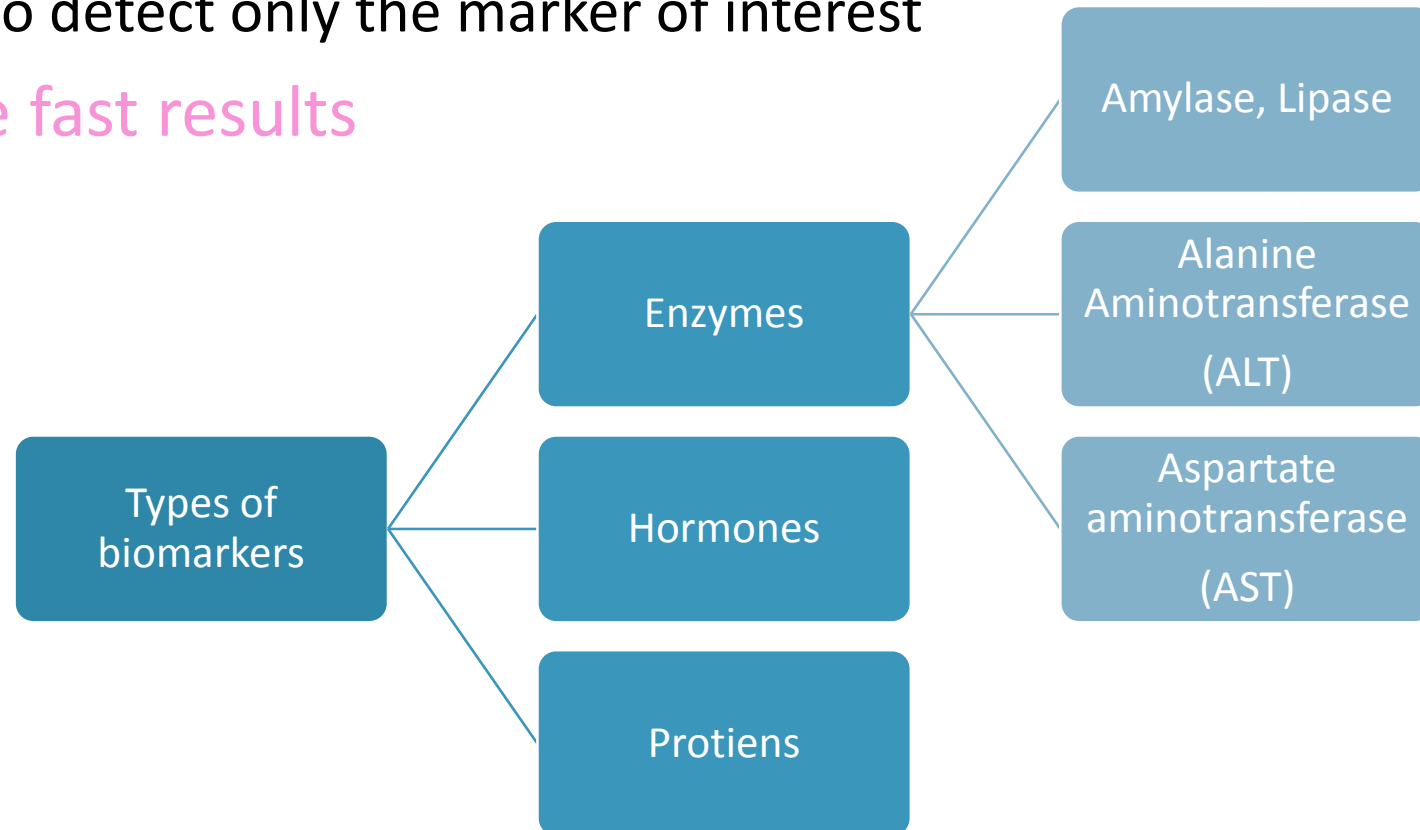
- **Sensitive**

Ability of an assay to detect small quantities of a marker

- **Specific**

Ability of an assay to detect only the marker of interest

- **Robust to produce fast results**



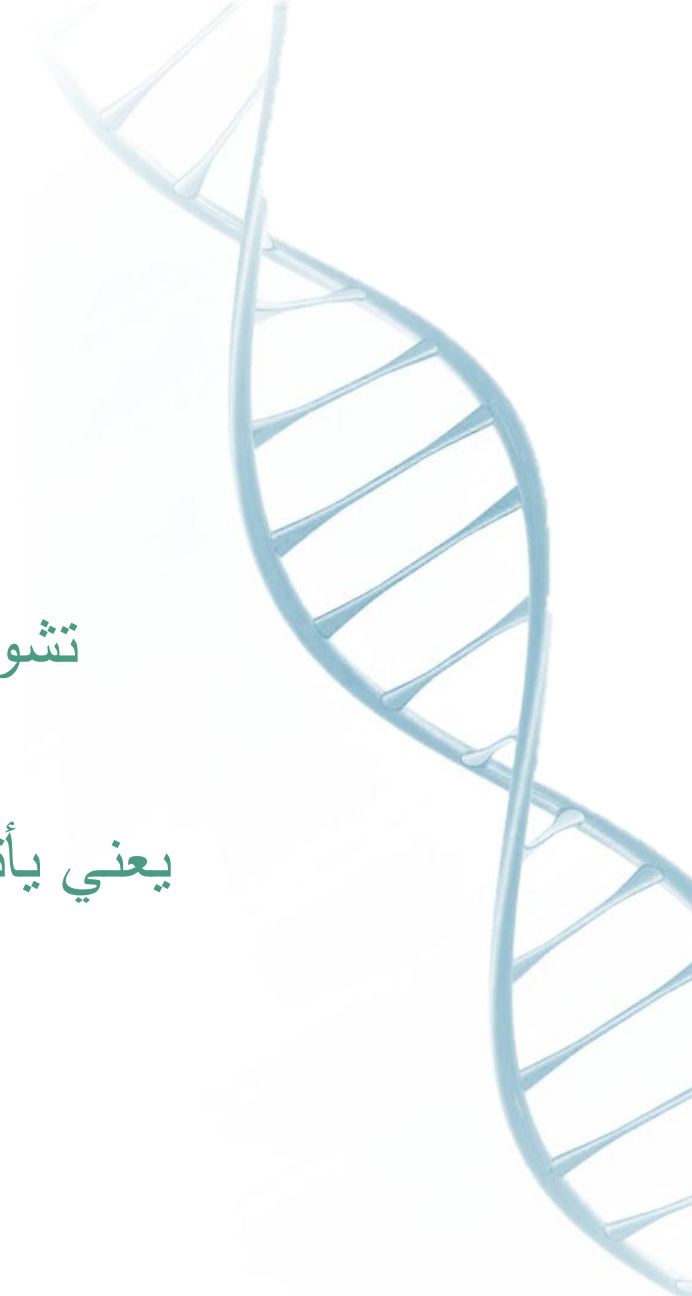
Qualities of a good biomarker

- Able to accurately diagnose a disease
- Able to accurately predict prognosis of a disease

تشوف اذا ماتغير تركيزه مع العلاج فيعني ان المريض مراح يتحس بالعلاج ذا

- Compliant with treatment follow up يعني يآثر فيه العلاج يغير تركيزه

- Easily obtainable from blood, urine, etc.



Amylase vs lipase

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 serum amylase level is also present in other diseases
- Amylase appears in the serum within **2-12 hours** after abdominal pain **and returns to normal in 3-5 days**
- Free amylase (unbound form) is rapidly cleared by the kidneys

Lipase

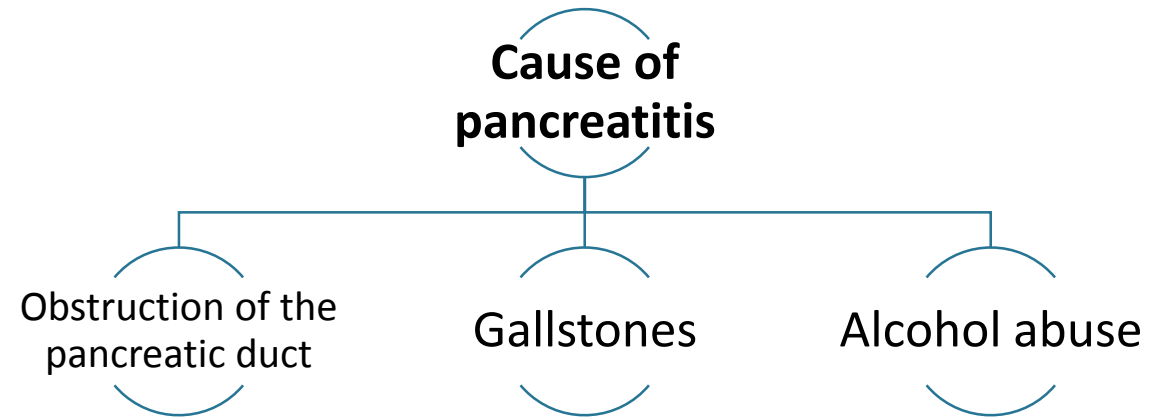
- Serum lipase **has higher specificity than serum amylase (elevated only in acute pancreatitis)**
- It appears in plasma within 4-8 hours and remains for **8-14 days**
- Measurement of amylase and lipase give 90-95% accuracy in the diagnosis of acute pancreatitis and abdominal pain

Acute pancreatitis

the inflammation of pancreas

There is abnormal release and premature activation of pancreatic enzymes (for example amylase, lipase)

Diagnosis conducted by **measuring** pancreatic enzymes



Serum enzymes used in the assessment of liver function:

- Markers used in hepatocellular necrosis
 - Alanine aminotransferases
 - Aspartate aminotransferases

Case:

A GP was called to see a 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 was taken for liver function tests which **showed elevated ALT** (alanine aminotransferase) **and AST** (aspartate aminotransferase)

What is the most likely diagnosis?

Acute Hepatitis



Aspartate aminotransferase (AST) & Alanine aminotransferase (ALT):

	AST	ALT
Produced by:	heart, liver, skeletal muscle, kidney, erythrocytes	liver
Elevated in:	Liver disease, heart disease, skeletal muscle disease, hemolysis	Liver disease



Alanine aminotransferase (ALT)

- **Mostly** present in **liver**
- **Small** amounts in **heart**
- **More specific for liver disease than AST**
- Major diagnosis: **liver disease**

Aspartate aminotransferase (AST)

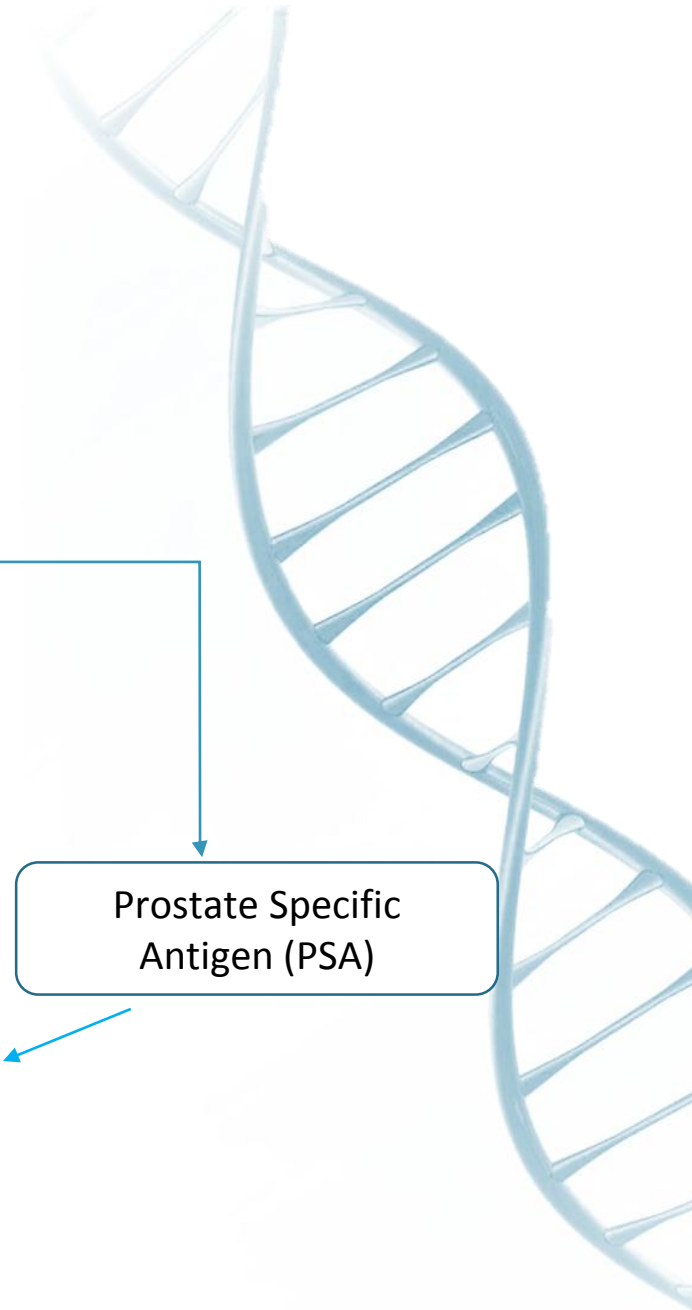
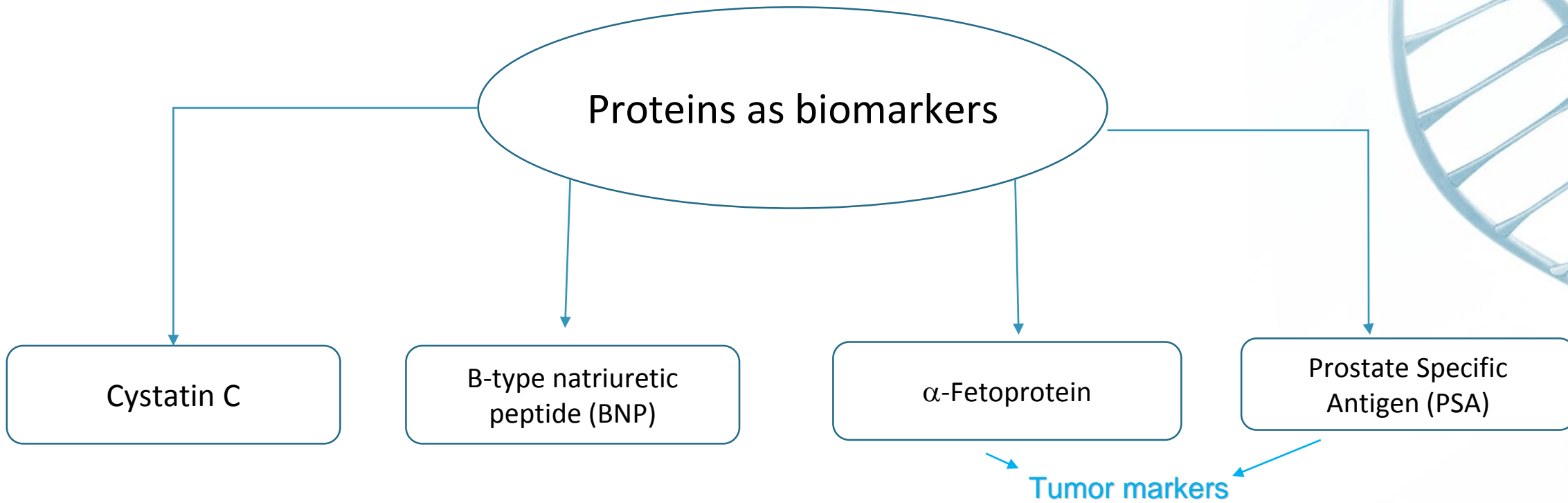
- Widely distributed in **heart, liver, skeletal muscle, kidney**
- Small amounts in erythrocytes
- High serum activity of AST found in:
 - Liver disease, heart disease, skeletal muscle disease, hemolysis
- Major diagnosis: liver and muscle diseases



High serum ALT and AST levels in liver diseases are due to:

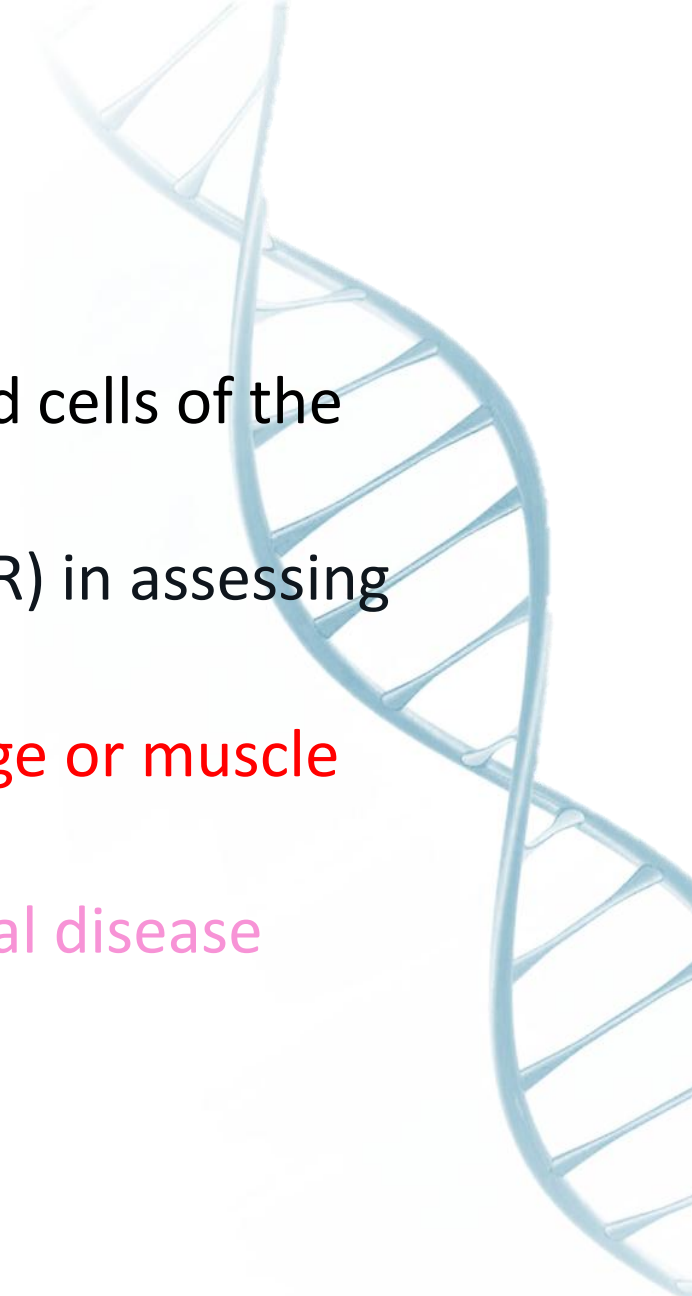
- Alcohol abuse
- Medication
- Chronic hepatitis B and C
- Steatosis and steatohepatitis
- Autoimmune hepatitis
- Wilson's disease
- α_1 -antitrypsin deficiency
- Malignancy
- Poisons and infectious agents





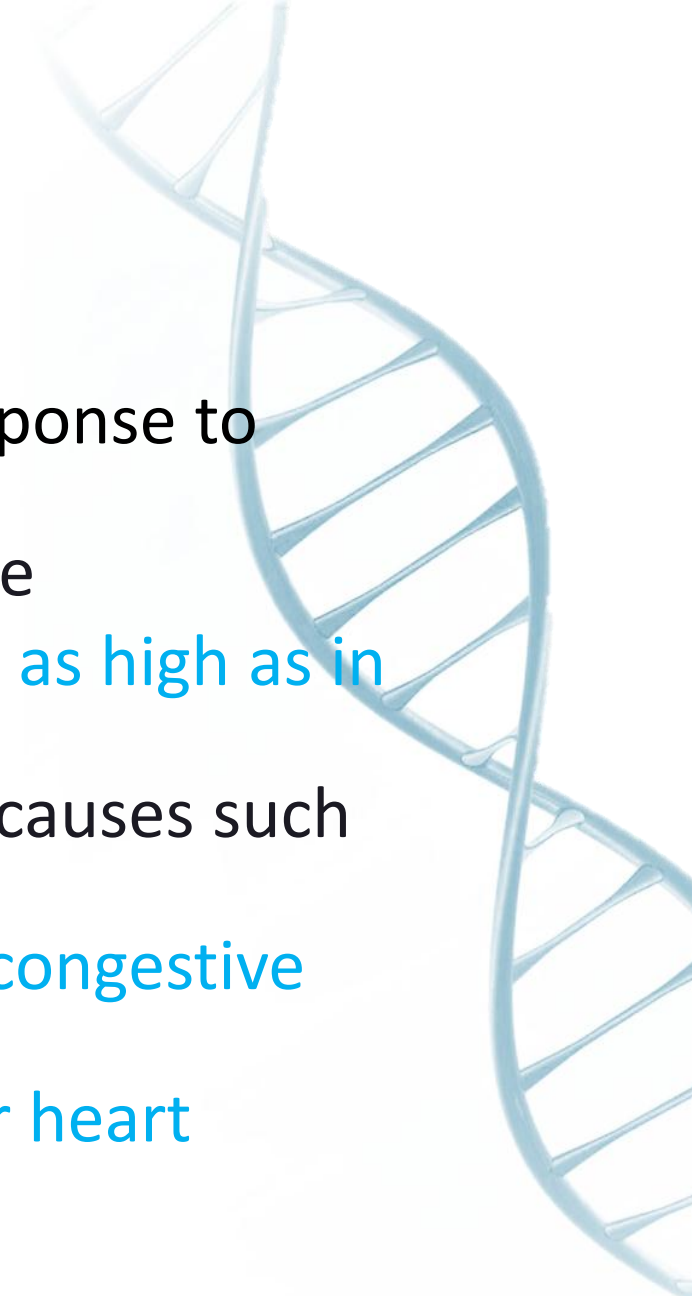
Cystatin C

- A cysteine protease inhibitor mainly produced by all nucleated cells of the body
- Useful biomarker for measuring glomerular filtration rate (GFR) in assessing kidney function and failure
- Unlike creatinine, its serum conc. is independent of gender, age or muscle mass
- Abnormally high serum levels of cystatin C indicates early renal disease “kidney failure”
- Clinically useful marker for detecting:
 - early kidney disease
 - monitoring kidney transplantation and acute kidney injury



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
- **In some pulmonary diseases, BNP levels are high but not as high as in heart failure**
- BNP helps differentiate between heart failure and other causes such as pulmonary disease
- **An important marker for the diagnosis and prognosis of congestive heart failure**
- **Currently being investigated as a screening biomarker for heart disease**



Tumor markers

A molecule secreted by a tumor that is measured for diagnosis and management of a tumor

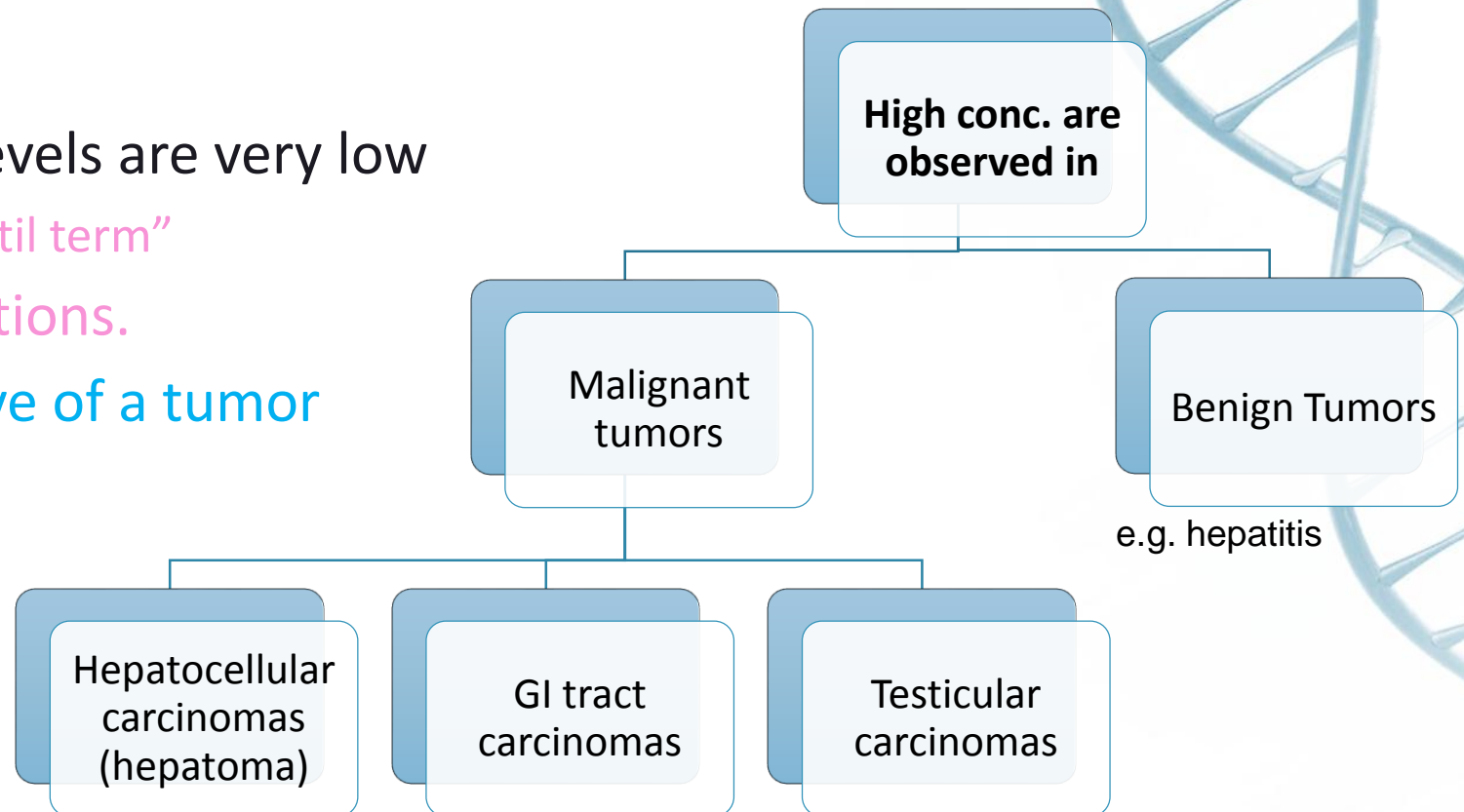
- α -fetoprotein
- Prostate specific antigen (PSA)

α -Fetoprotein

- In **newborn babies** α -fetoprotein levels are very low

“It is produced by the fetal liver, and falls until term”

- It remains low under normal conditions.
- High conc. are not always suggestive of a tumor
- It is a non specific marker



Prostate Specific Antigen (PSA)

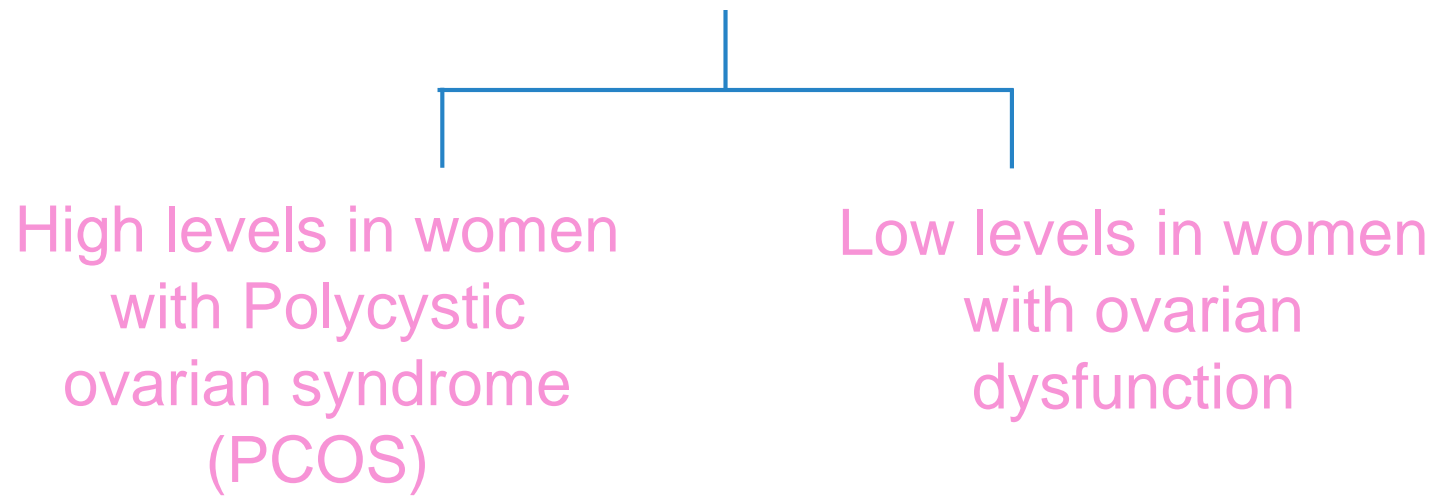
- A serine protease enzyme also called kallikrein III, seminin
- Produced by prostate gland
- Liquefies ejaculate
- PSA level is used as a tumor marker to aid diagnosis and for monitoring in patients with prostatic cancer.
- Less specific in diagnosis
- High serum levels are also observed in
 - benign prostatic hypertrophy (BPH) (enlarged prostate gland)
 - Prostatic inflammation/infection



Hormones as biomarkers: Anti-Mullerian hormone (AMH)



Anti-Mullerian hormone (AMH)



Take-home messages

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



MCQs

Q1; identification of disease from its signs and symptoms is

- A- prognosis
- B- diagnosis
- C-biomarker

Q2; amylase and lipase are biomarkers of

- A- pancreatitis
- B-congestive heart failure
- C-pregnancy

Q3; what do we call the ability of a biomarker assay to detect small quantities of the marker

- A- sensitivity
- B-specificity

Q4; what's the best team ever?

- A- biochemistry 438

Answer key:

- 1)B
- 2)A
- 3)A
- 4)A



❖ Girls team:

- أجدد آل رشود
- الوثن البلوي
- إيلاف المسحل
- جود الخليفة
- جود العتيبي
- ريم القرني
- سارة الهلال
- شهد السلامه
- طيف العتيبي
- عبير الخضير
- غيداء البرين
- لينا العصيمي
- نورة التركي
- نورة المزروع
- نوف الحميضي
- هيفاء الوايلي

❖ Boys team:

- بدر الشهري
- حميد حميد
- سهيل باسهيل
- عمر الغامدي
- مهند القرني
- نايف السبر

❖ Team leaders:

ديما المزيد
رائد العجيري



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➤ Special thanks to:



BIO TEAM



Biochemistry Team⁴³⁵



Biochemistry team 436

