

LEARNING OBJECTIVES



By the end of this presentation, students will be able to:

1. UNDERSTAND THE FUNDAMENTALS OF NANOBIO TECHNOLOGY AND ITS RELEVANCE TO DRUG DELIVERY.
2. EXPLORE VARIOUS NANOCARRIERS USED IN DRUG DELIVERY SYSTEMS.
3. ANALYZE CASE STUDIES OF NANOBIO TECHNOLOGY APPLICATIONS IN MEDICINE.

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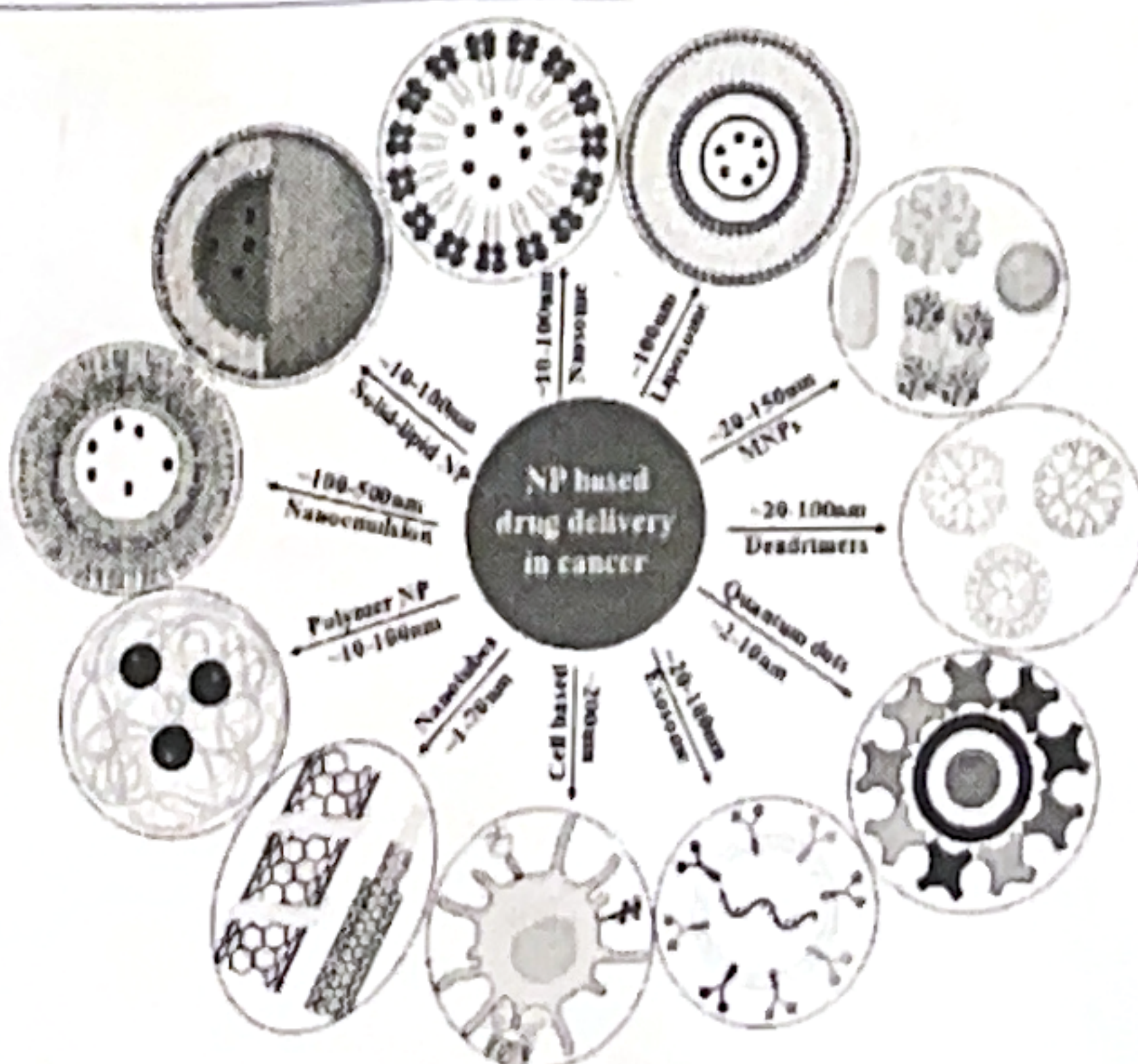
INTRODUCTION



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- **Nanobiotechnology** in drug delivery systems is transforming pharmaceutical sciences, from improving the bioavailability of life-saving drugs to enabling targeted treatments for complex diseases.



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- A drug delivery system (DDS) is defined as a formulation or a device that enables a therapeutic substance to selectively reach its site of action without reaching the nontarget cells, organs, or tissues.
- Traditional drug delivery systems: Pills, injections, and topical treatments.
- Main purpose of DDSs:** Enhance therapeutic efficacy and reduce side effects of drugs.
- Challenges in conventional drug delivery (e.g., low bioavailability, off-target (side) effects).
- How **Nanotechnology** addresses these issues?

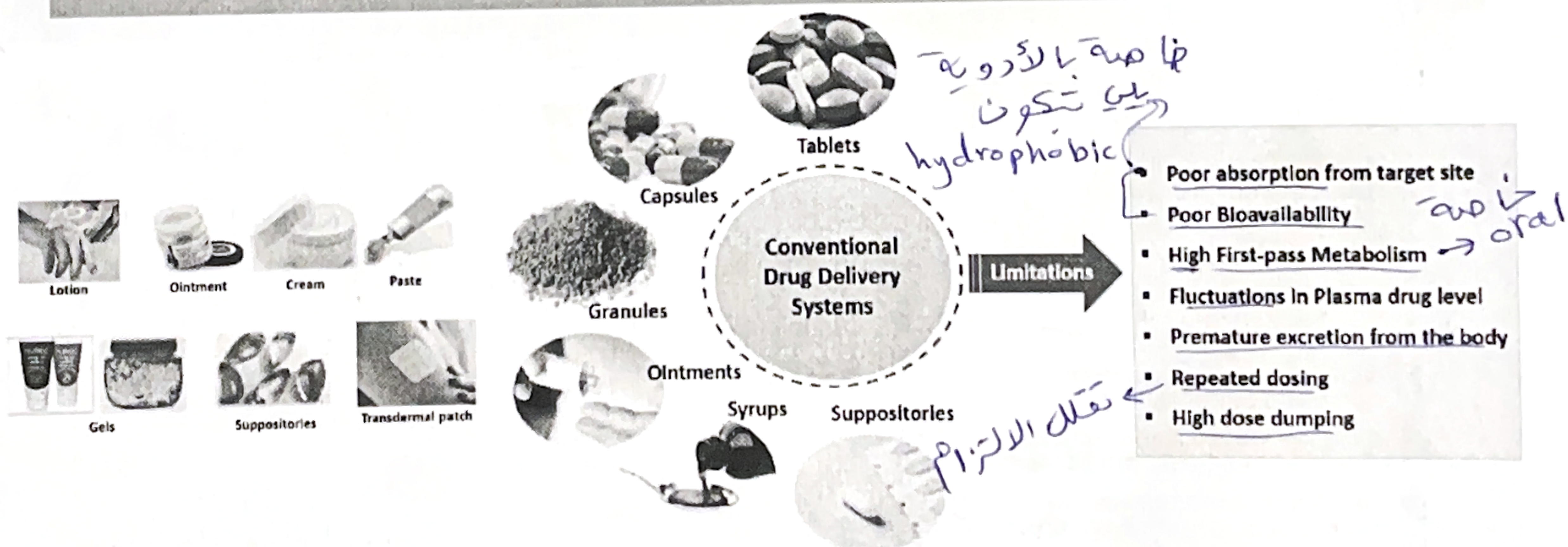
كيف حل هذه التحديات
بواسطة الـ DDS
Conventional

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Limitations Of Conventional Drug Delivery Systems



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ROUTES OF DRUG DELIVERY



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+ parenteral
routes
(injection)

كيفية
مقارنة الجزيئات البيولوجية
Common biological molecules

NANOMEDICINE



▪ Nanotechnology is the use and application of materials with sizes in the nanometre range.

▪ Nanomedicine is simply the application of nanotechnologies in a healthcare setting to improve the behaviour of drug substances.

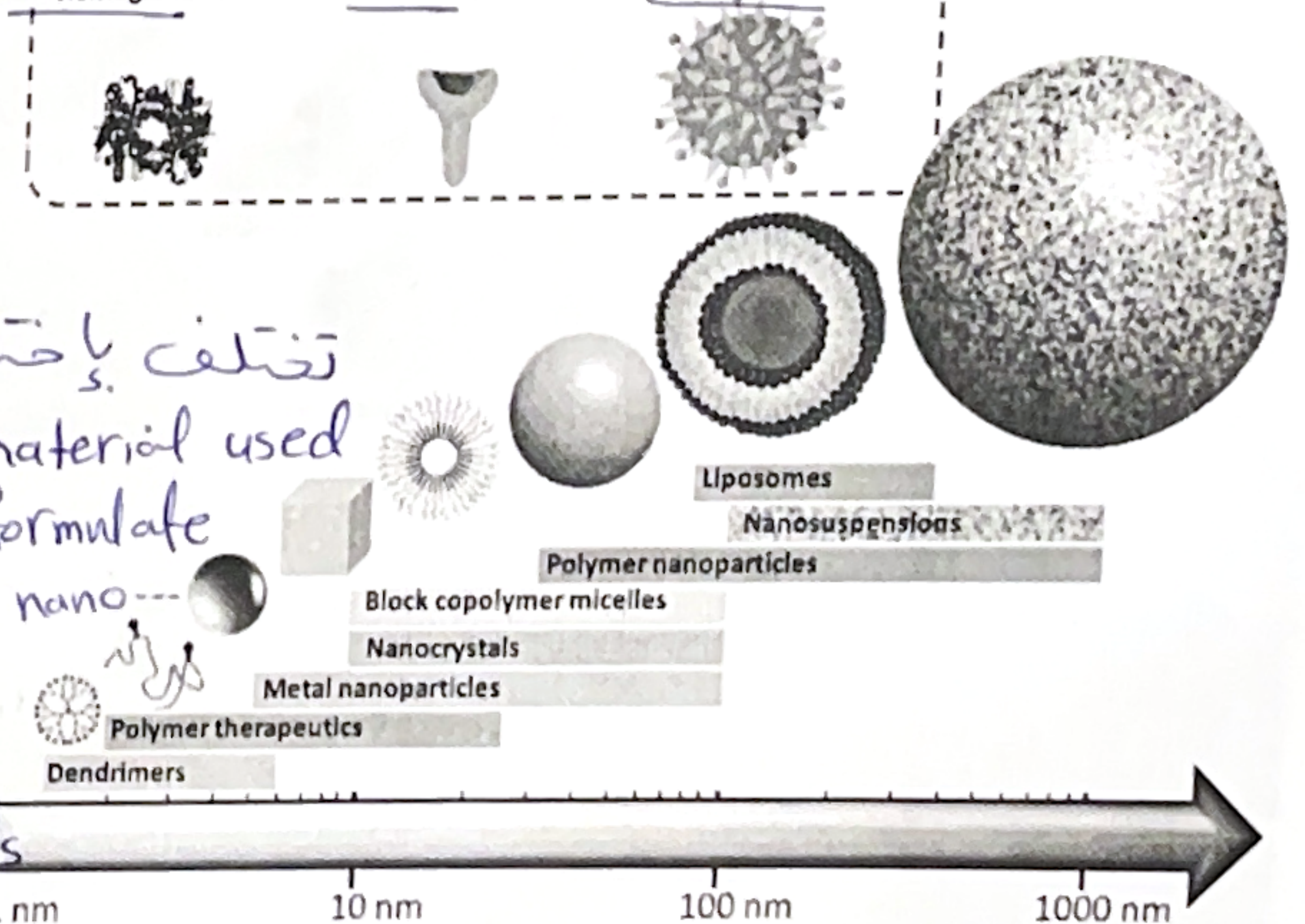
▪ **Nanocarriers in Drug Delivery**

* **Types of Nanocarriers:**

- ① **Lipid-Based Nanocarriers:** Liposomes, solid lipid nanoparticles.
- ② **Polymer-Based Nanocarriers:** Polymeric micelles, dendrimers.
- ③ **Inorganic Nanocarriers:** Gold nanoparticles, quantum dots.
- ④ **Biological Nanocarriers:** Exosomes, viral nanoparticles.

تختلف باختلاف
المواد المستخدمة
لصنع هذه النانو-
حجمها
+ أشكالها

Hemoglobin- 6.5 nm Antibody- 12 nm Influenza virus- 130 nm



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- Nanomedicines key advantages over conventional DDS:

- ① ▪ Increased bioavailability - Nanomedicines enhance the solubility of poorly water-soluble drugs, ensuring more efficient absorption and therapeutic efficacy..
- ② ▪ Targeted delivery - Site-specific delivery minimizes off-target effects and toxicity while maximizing therapeutic impact..
- ③ ▪ Controlled release mechanisms - Nanocarriers provide sustained and controlled drug release, reducing dosing frequency and improving patient compliance..

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3) pH sensitive nano drug release
stimuli مثل تغيرات pH , certain enzymes , Tem
tumor , acidic pH , other tissues .
drug releases tumor

Enhanced Permeability and Retention (EPR) Eff

Enhanced Permeability and Retention (EPR) Effect:

- Accumulation in tumor tissues via leaky vasculature.

Ligand-Targeted Delivery:

- Functionalized nanoparticles bind to specific receptors on cells.

Stimuli-Responsive Systems:

- Drug release triggered by pH, temperature, or enzymes.

2] جُزْءٌ عَامِلٌ
functional group
(ligand)
↓
than can

بيت طبيعة الأوعية الدموية هناك (leaky)
(تنتقل nano tumor من خلال هذه vessels بكل سهولة)
و يتجمع هناك (retention)

specifically bind to the receptor on cells of interest

TARGETED DRUG DELIVERY



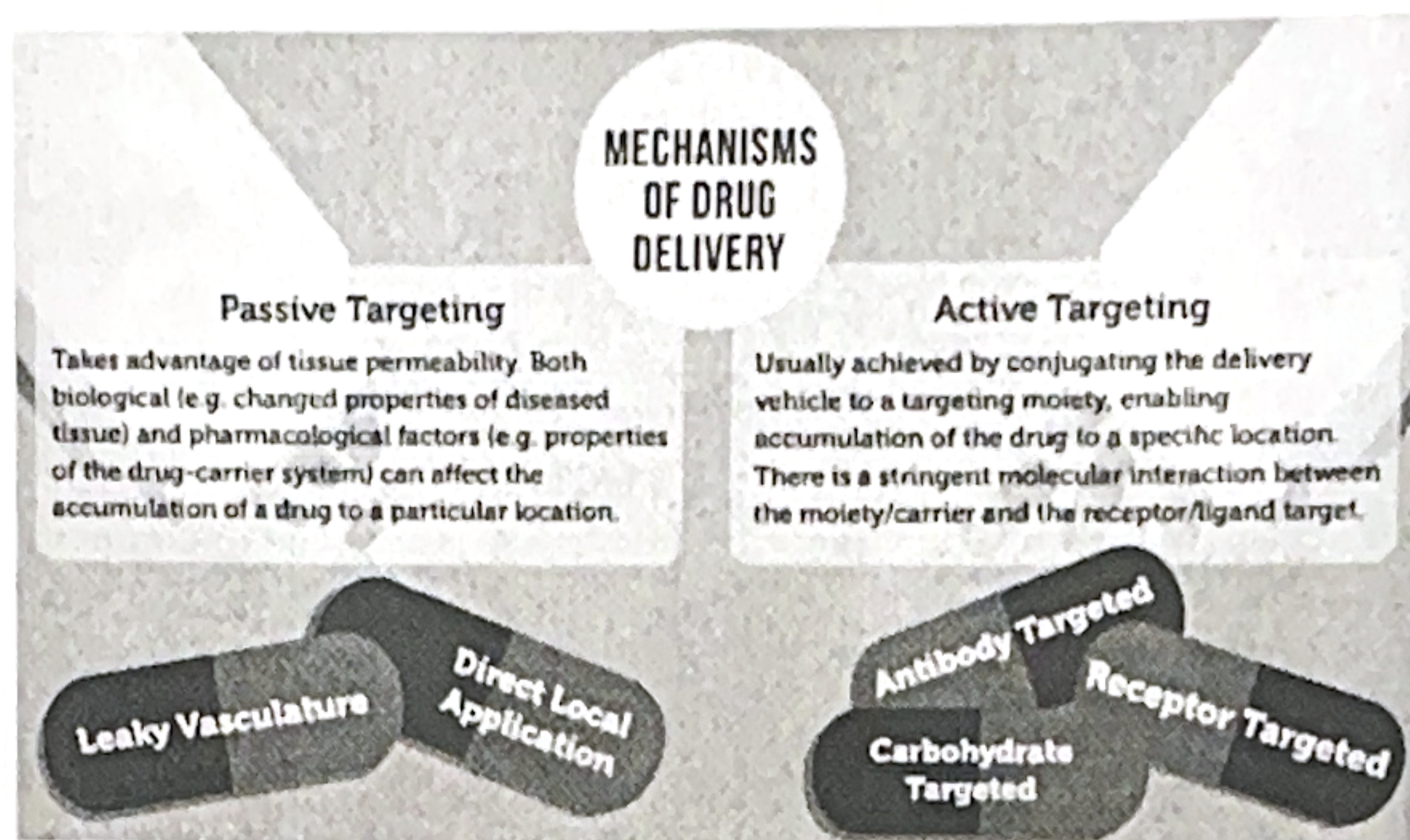
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بما nano
عن conventional

Targeted drug delivery is a means of delivering a drug in a way that considerably enhances the concentration of that drug in particular parts of the body relative to others.

- The mechanism by which a drug is targeted can be broadly divided into two types;
 - a) passive targeting,
 - b) active targeting



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اما هون يكون عنا leaky vasculature, بالتالي nano وهو ما سيقا
في blood stream راح تتجمع عن tumor (cells infiltrated by the vasculature)

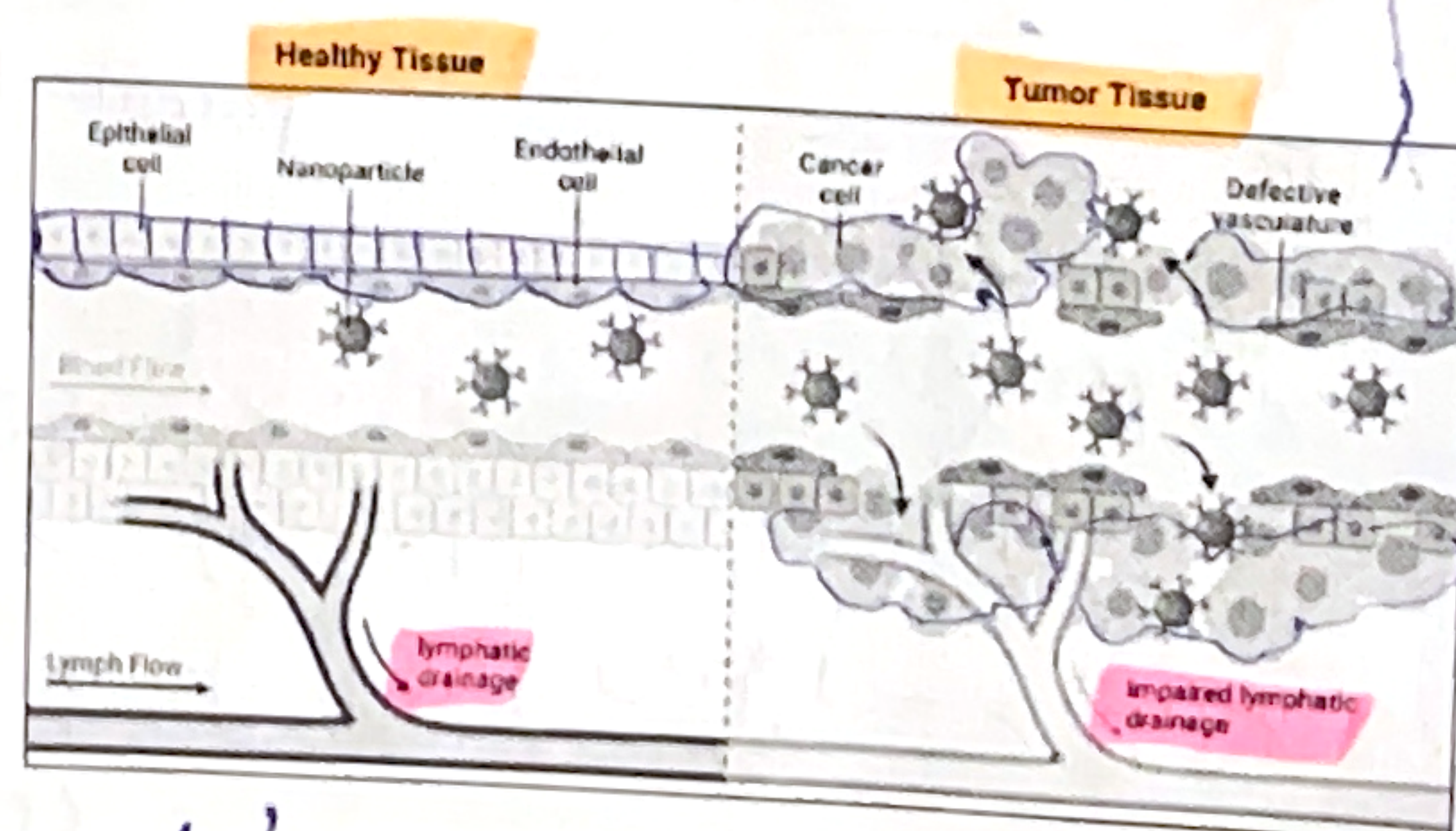
فهو blood vessel يكون طبيعي
لازم يمر من خلاله tumor عن طريق
blood vessels

PASSIVE TARGETING
نفس الفكرة بين مكنياها عن mechanism

(enhance permeability and retention)

- In passive targeting, macromolecules including **nanoparticles** accumulate preferentially in the neoplastic tissues as a result of the enhanced permeability and retention (EPR) phenomenon, first described by Maeda and Matsumura.
- The EPR is based on:
 - the nanometer size range of the nanoparticles (which typically falls between **10 to 200 nm**), and
 - two fundamental characteristics of the neoplastic tissues, namely:
 - the leaky vasculature (Tumor blood vessels have enhanced permeability with gaps ranging from **200 to 800 nm**, allowing nanoparticles in the 10–200 nm range to **passively** accumulate at tumor sites)
 - and impaired lymphatic drainage.

Passive Targeting of Nanoparticles to Cancer Cells



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vasculature يكون كبير مرتبة
بكونو قريبا بين على بعض ومرتبين بشكل
ما يسمح بسهولة لـ nano اني موجوده بالدم
to cross the blood vessels
in a tight way, الكلا

Ideal Size Range Of Nanoparticles ? (For clinical Translation)



For Avoiding Clearance:

- Nanoparticles smaller than 10 nm are rapidly cleared by renal filtration.
- Particles larger than 200 nm are likely to be cleared by the Reticuloendothelial System (RES) or trapped in the spleen.
- Liver:** Kupffer cells in the liver are the primary components of RES and are highly efficient at clearing nanoparticles from the bloodstream.
- Spleen:** The spleen filters nanoparticles, especially those larger than the size of its interendothelial cell slits (~200 nm).
- Bone Marrow:** Plays a minor role in nanoparticle clearance.
- 50-100 nm:** This size range is often considered optimal for EPR-based delivery as it balances tumor penetration, circulation time, and reduced clearance.

RES

عشان يتجنبو

clearance by renal filtration and RES

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(ideal size)

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Strategies To Minimize RES Uptake:



foreign material

1) Surface Coating:

- Polyethylene glycol (PEG) coating (PEGylation) reduces opsonization (protein adsorption) and recognition by RES.
- Hydrophilic coatings can enhance stealth properties.

2) Size Optimization:

- Keeping nanoparticle sizes within the range of 50-100 nm minimizes RES clearance while optimizing tumor accumulation through the EPR effect.

3) Charge Neutralization: (net charge for the surface)

- Neutral or slightly negative surface charges are less likely to be recognized by RES compared to strongly charged surfaces.

4) Targeting Ligands:

- Functionalizing nanoparticles with specific ligands can redirect them to targeted cells or tissues, bypassing RES.

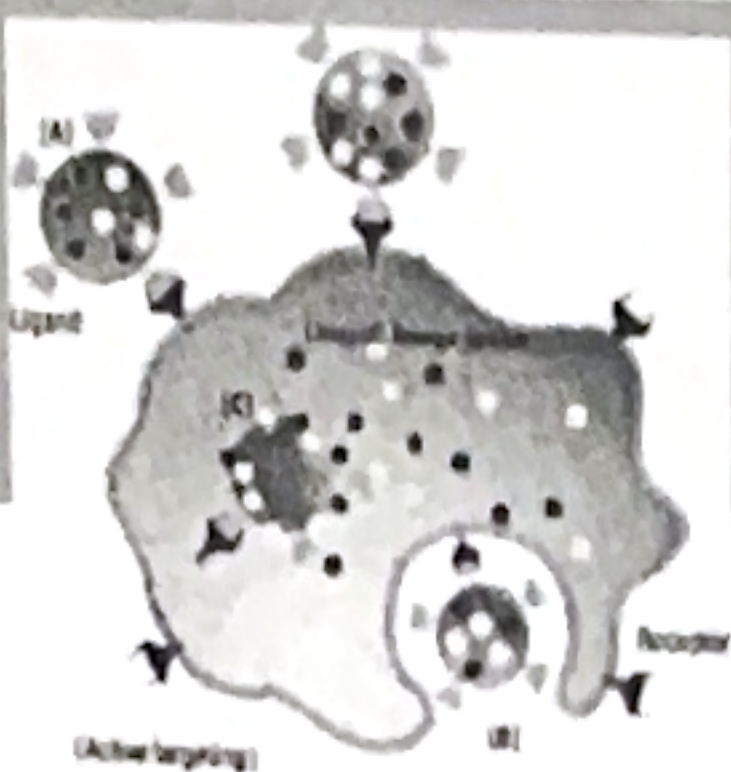
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لانه طبيعة cells و
macro molecules
من جسمنا يكونو غالبهم neutral او slightly -
فعلما ان كل اشي من برا + اشي من جسمنا -
foreign

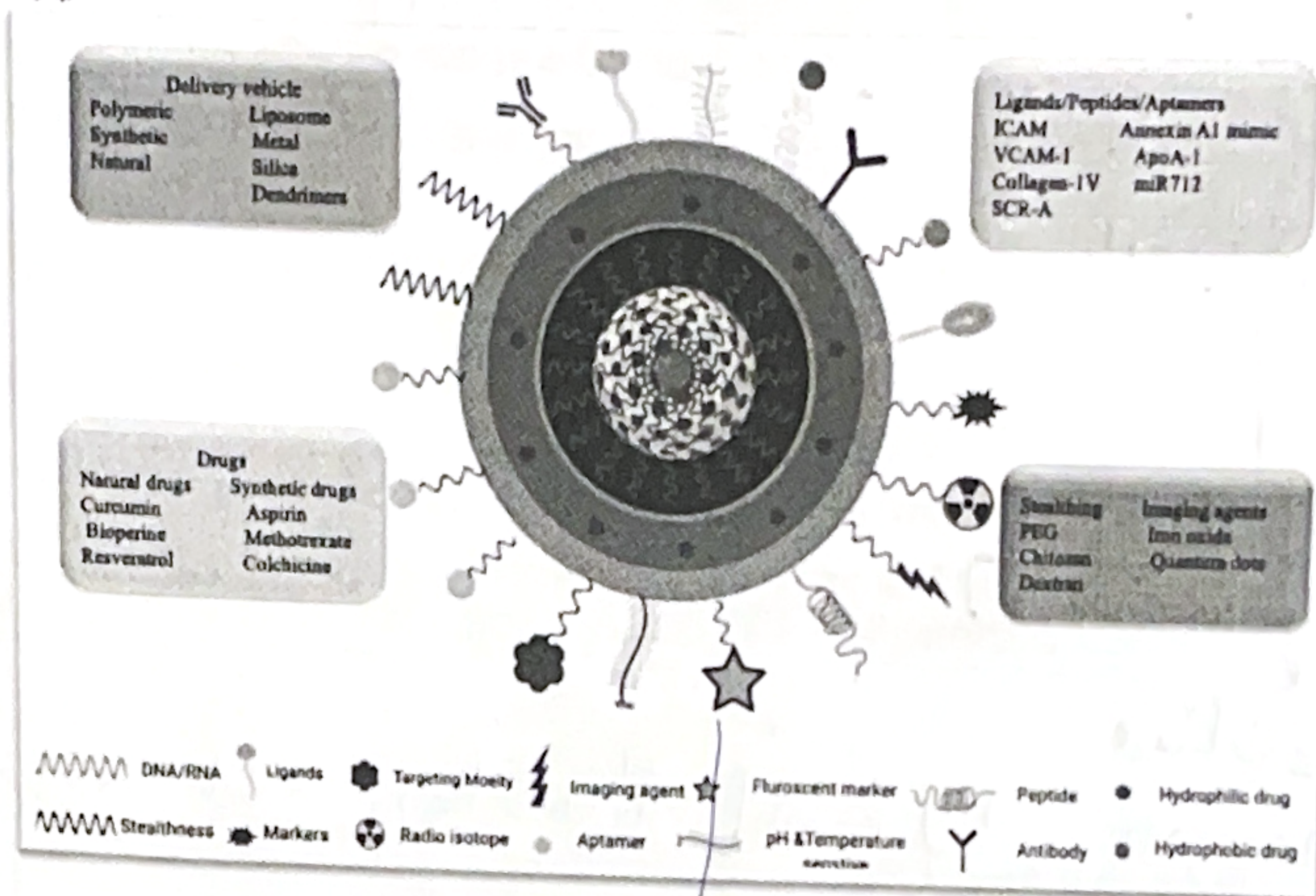
ACTIVE TARGETING



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- Active targeting refers to the functionalization of nanoparticles or drug delivery systems with specific ligands that bind to molecular markers (e.g., proteins, receptors, or antigens) expressed on target cells, tissues, or pathogens. This approach enhances the precision and efficacy of drug delivery by ensuring that the therapeutic agent is delivered directly to the site of interest, minimizing off-target effects and reducing systemic toxicity.



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nano drug delivery system encapsulated with active molecules and surface modified

therapeutic

different targeting moieties

diagnostic effect

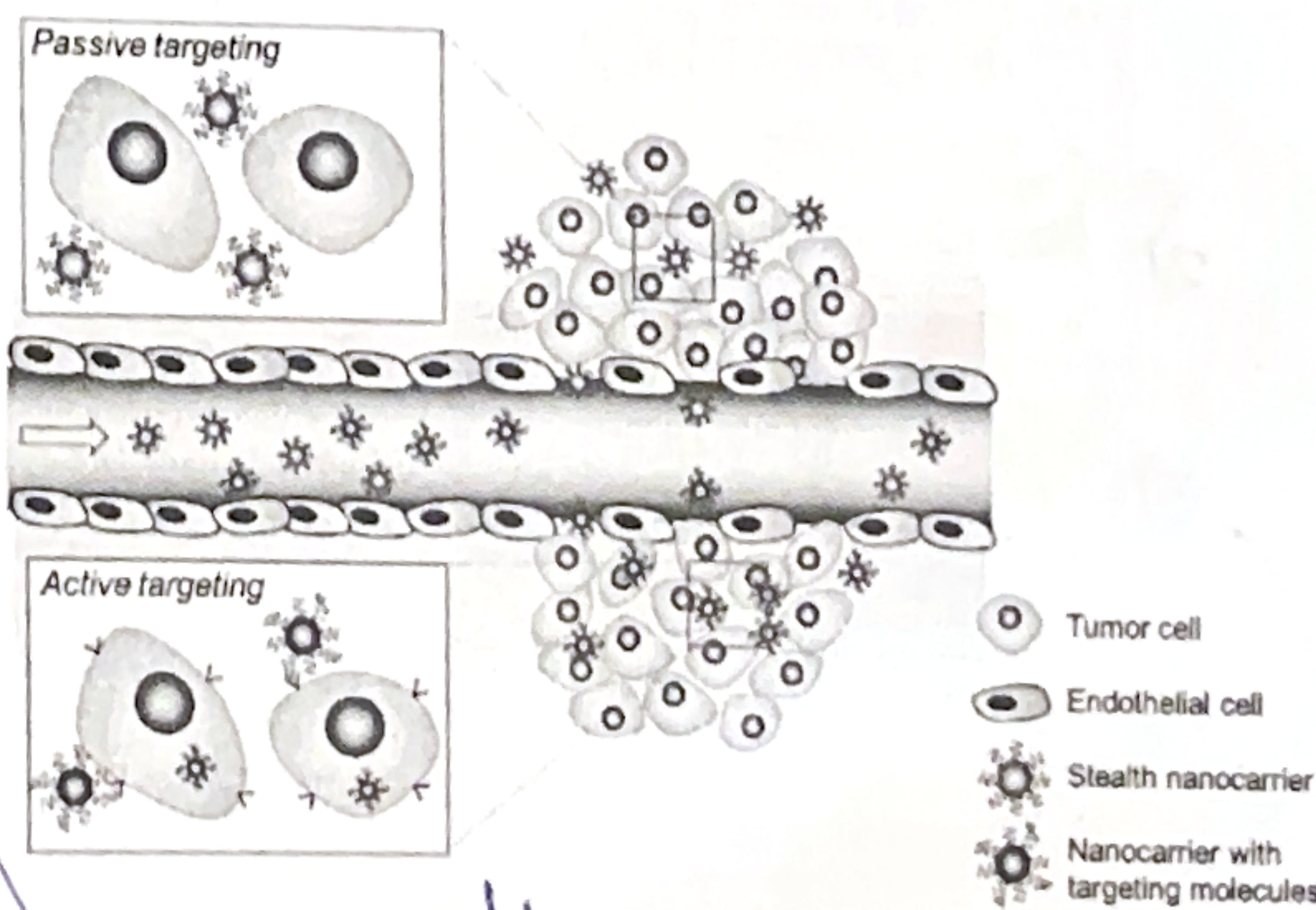
PASSIVE VS. ACTIVE TARGETING



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Feature	Passive Targeting	Active Targeting
Mechanism	Relies on physiological phenomena like the Enhanced Permeability and Retention (EPR) effect.	Uses ligands (e.g., antibodies, peptides) to bind specifically to target cell receptors.
Specificity	Non-specific; exploits leaky vasculature in tumors and poor lymphatic drainage.	Highly specific; binds to molecular markers on diseased cells.
Therapeutic Outcome	Moderate selectivity, with some off-target effects.	Improved selectivity, reducing off-target effects and systemic toxicity.
Examples	- Doxil® (liposomal doxorubicin using EPR for tumors).	- Kadcyla® (trastuzumab-drug conjugate targeting HER2+ cancer).
Complexity	Simpler formulation with no need for targeting ligands.	More complex due to ligand attachment and stability requirements.
Applications	Most effective in solid tumors with accessible leaky vasculature.	Broad potential, including solid tumors, inflammatory sites, and specific molecular targets.



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chemical reaction
ممكن تكون صفة
purification
ممكن تحتاج

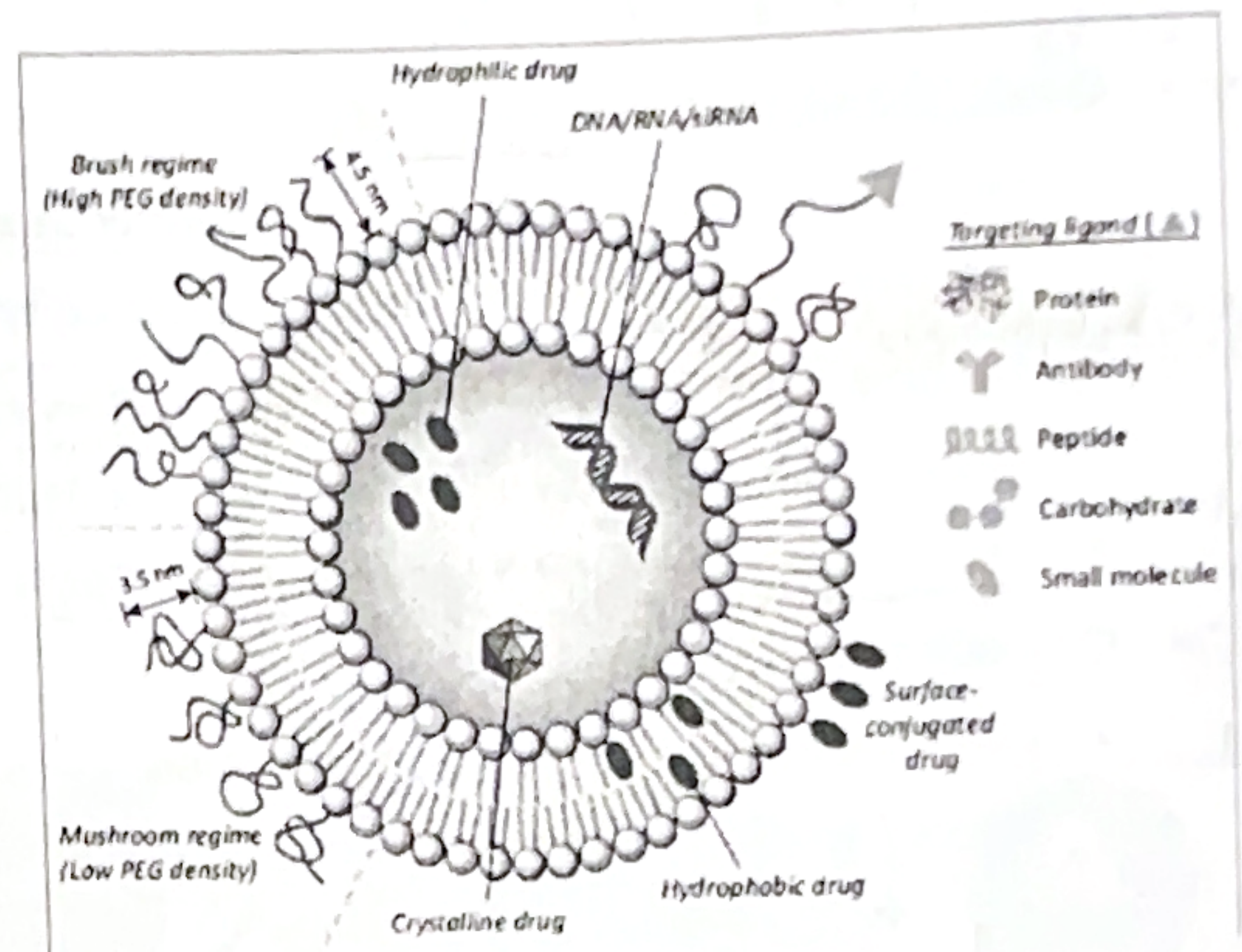
Revolutionizing Medicine: Nanobiotechnology In Drug Delivery Systems



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- Nanobiotechnology : Intersection of nanotechnology and biotechnology.
- Nanobiotechnology integrates nanotechnology with biological systems to create innovative solutions in medicine and healthcare.
- Why it matters?
 - Precision in medicine, reduced side effects, and enhanced efficacy.



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Areas Of Clinical Applications in Nanobiotechnology



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- ① **Cancer Therapy:** e.g. Targeted (chemotherapy) using nanomedicine such as liposomes and polymeric nanoparticles. *(Handwritten: targeted, S.E, not targeted, S.E)*
- ② **Gene Therapy:** e.g. Lipid nanoparticles delivering siRNA or mRNA (e.g., COVID-19 vaccines).
- ③ **Infectious Diseases:** e.g. Nano-antibiotics and antimicrobial nanoparticles.
- ④ **Neurological Disorders:** e.g. Nanocarriers crossing the blood-brain barrier.

Lipid nanoparticle LNP-based
delivery of CRISPR-Cas9

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PHARMACEUTICAL NANOTECHNOLOGY- REAL-WORLD EXAMPLES

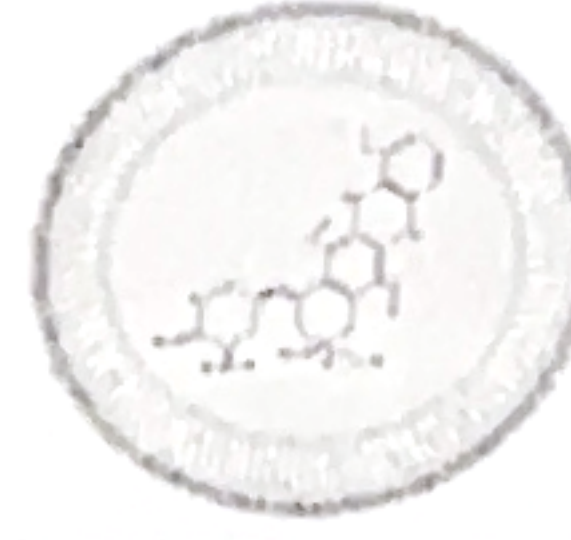


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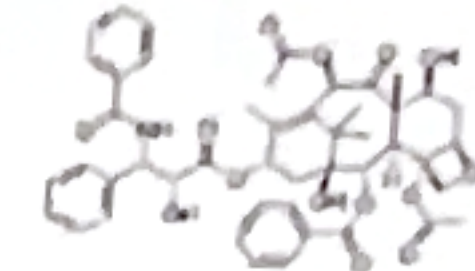


تكون uptake
cells tumor

- ① **Doxil (Doxorubicin liposomal):**
 - First FDA-approved nanodrug for cancer therapy
 - Liposomal formulation reduces cardiotoxicity.
- ② **Abraxane (Paclitaxel albumin-bound):**
 - Albumin nanoparticles for breast cancer treatment.
 - Improved solubility and reduced side effects.
- ③ **Onpatro (Patisiran):**
 - siRNA therapy using lipid nanoparticles.
 - Treats hereditary transthyretin-mediated amyloidosis.



Abraxis
US FDA approved 2005



Albumin Shell
(Excipient)



• Hydrophobic
• M.W 854 Da
Paclitaxel
(Drug)



• siRNA
• Lipid
• siRNA
• Lipid
• siRNA
• Lipid



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EMERGING APPLICATIONS ...



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- **CRISPR-Cas9 Delivery:** e.g. Nanocarriers for gene editing.
- **mRNA Vaccines:** e.g. Lipid nanoparticles in COVID-19 vaccines.
- **Nanogels:** e.g. Stimuli-Responsive Nanogels that respond to multiple triggers (e.g., pH, redox, or light), typically used for Local Injection or Topical Application.

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Main Purposes Of Nanomedicine:

Transforming Healthcare And Drug Delivery

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Main Purposes Of Nanomedicine:

(مراجعة)



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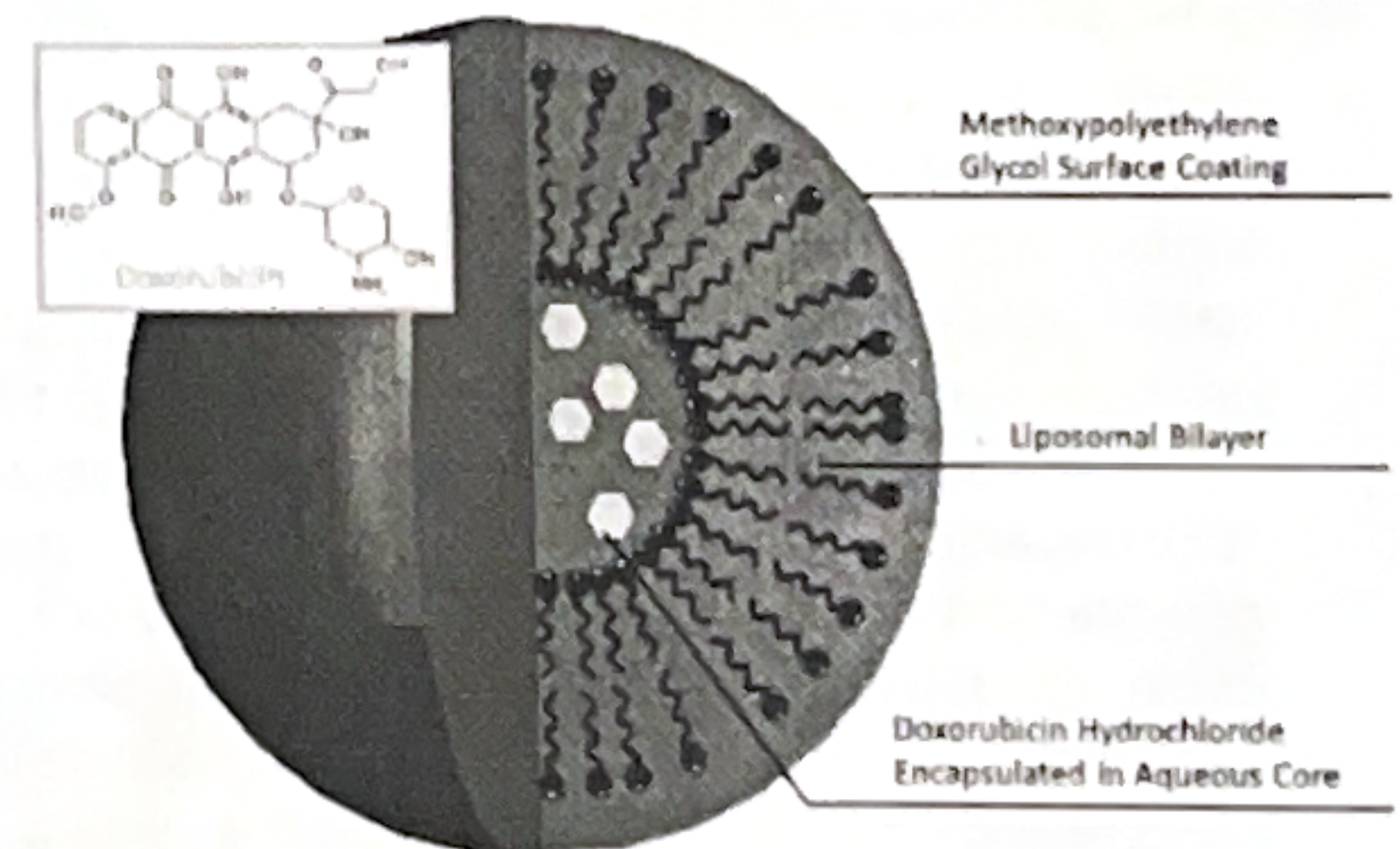


1. Improved Drug Solubility and Bioavailability

- Improve the solubility of poorly water-soluble drugs, ensuring better absorption and bioavailability.

Examples:

- Doxil®**: Liposomal formulations for better bioavailability in cancer therapy,
- Abraxane®**: Nanoparticle albumin-bound paclitaxel enhances solubility and delivery for breast and lung cancer therapy.
- AmBisome®**: Liposomal amphotericin B improves the solubility and bioavailability of the antifungal drug.



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Main Purposes Of Nanomedicine:



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2 Efficient Delivery of Large Biomolecules (Proteins, Nucleic Acids):

- Facilitates the delivery of biologics, such as proteins; monoclonal antibodies, siRNA, and mRNA, DNA which are otherwise challenging due to their size and instability (enzymatic degradation).

Examples:

encapsulation by nano

- Comirnaty® (Pfizer-BioNTech COVID-19 vaccine)** - Utilizes lipid nanoparticles (LNPs) for the efficient delivery of mRNA encoding the SARS-CoV-2 spike protein, a revolutionary application of nanomedicine in vaccines.

- Patisiran (Onpattro®)** - The first siRNA-based therapy approved for the treatment of hereditary transthyretin-mediated amyloidosis, employing lipid nanoparticles for targeted hepatic delivery.



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PFIZER-BIONTECH COVID-19 VACCINE



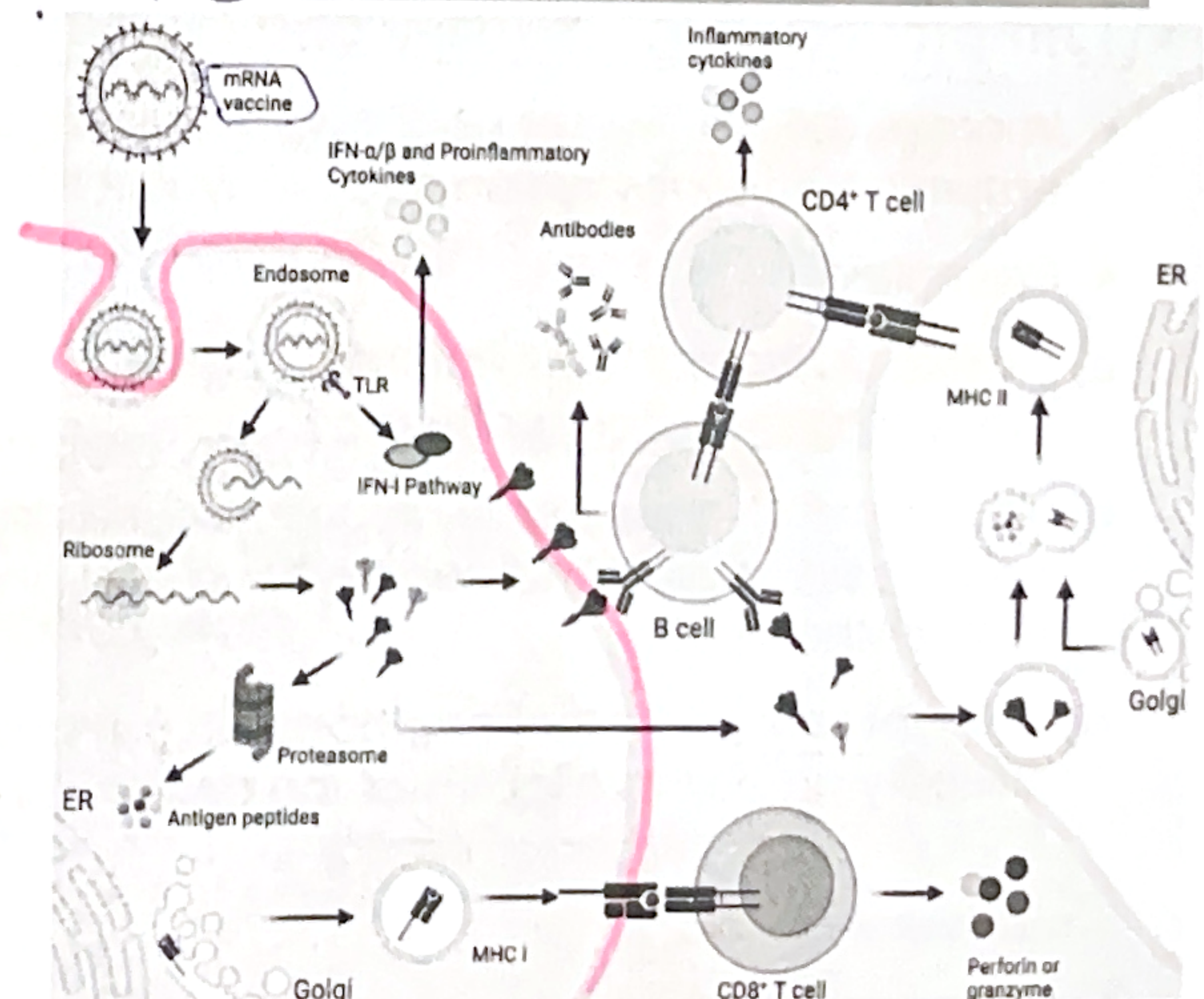
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كيفية وكيفية العمل

- mRNA delivered in an mRNA vaccine enters cells by endocytosis and, after release from the endosome, is translated into protein by ribosomes. Translated proteins can then activate the immune system primarily in two ways: i) proteins are degraded by the proteasome into peptides subsequently presented as antigens on the cell surface by major histocompatibility complex (MHC) class I molecules which bind to the T cell receptor (TCR) to activate CD8⁺ T cells to kill infected cells through the secretion of perforin and granzyme; ii) proteins secreted extracellularly are engulfed by antigen-presenting cells (APCs) and degraded into peptides subsequently presented on the cell surface by MHC class II molecules for recognition by CD4⁺ T cells, which can activate both the cellular immune responses by secreting cytokines and the humoral immune responses by co-activating B cells. In addition, single-stranded RNA and double-stranded RNA delivered in mRNA vaccines bind to Toll-like receptor (TLR) in the endosome to activate the antiviral innate immune responses via the production of type-I interferon (IFN-I) which results in the induction of several IFN-I-stimulated genes involved in antiviral innate immunity, in a mechanism known as the self-adjutant effect of a sequence-engineered mRNA.

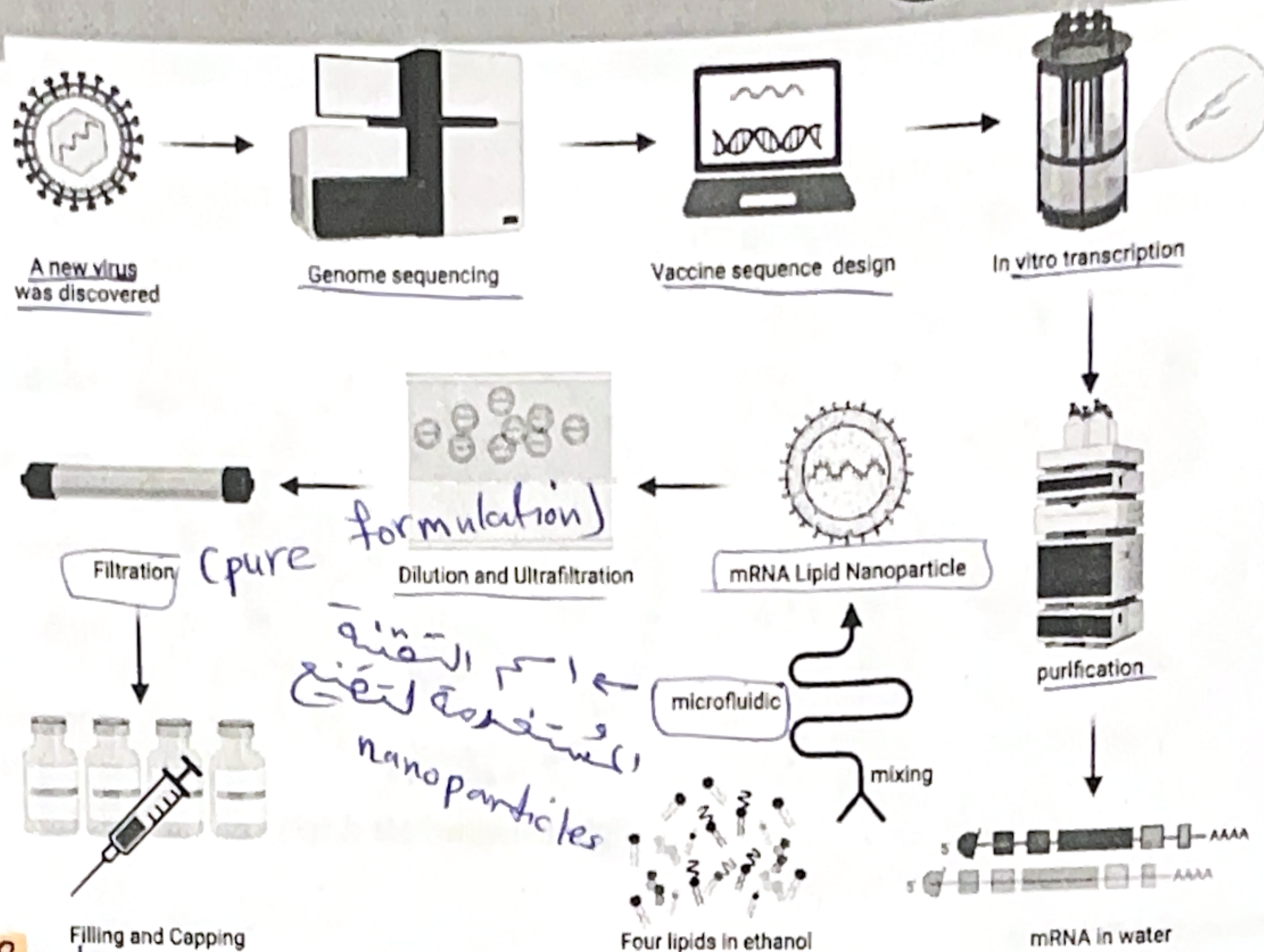
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Production process of mRNA vaccines



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أول ما فلع الفايروس
لازم يعرفو ستوهو
عشان يقدرو يصنحو له
علاج، فلان لازم نعلمه
sequencing

ولانه RNA لازم نحوله
الى DNA اول

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2 كما انكرف sequence الى

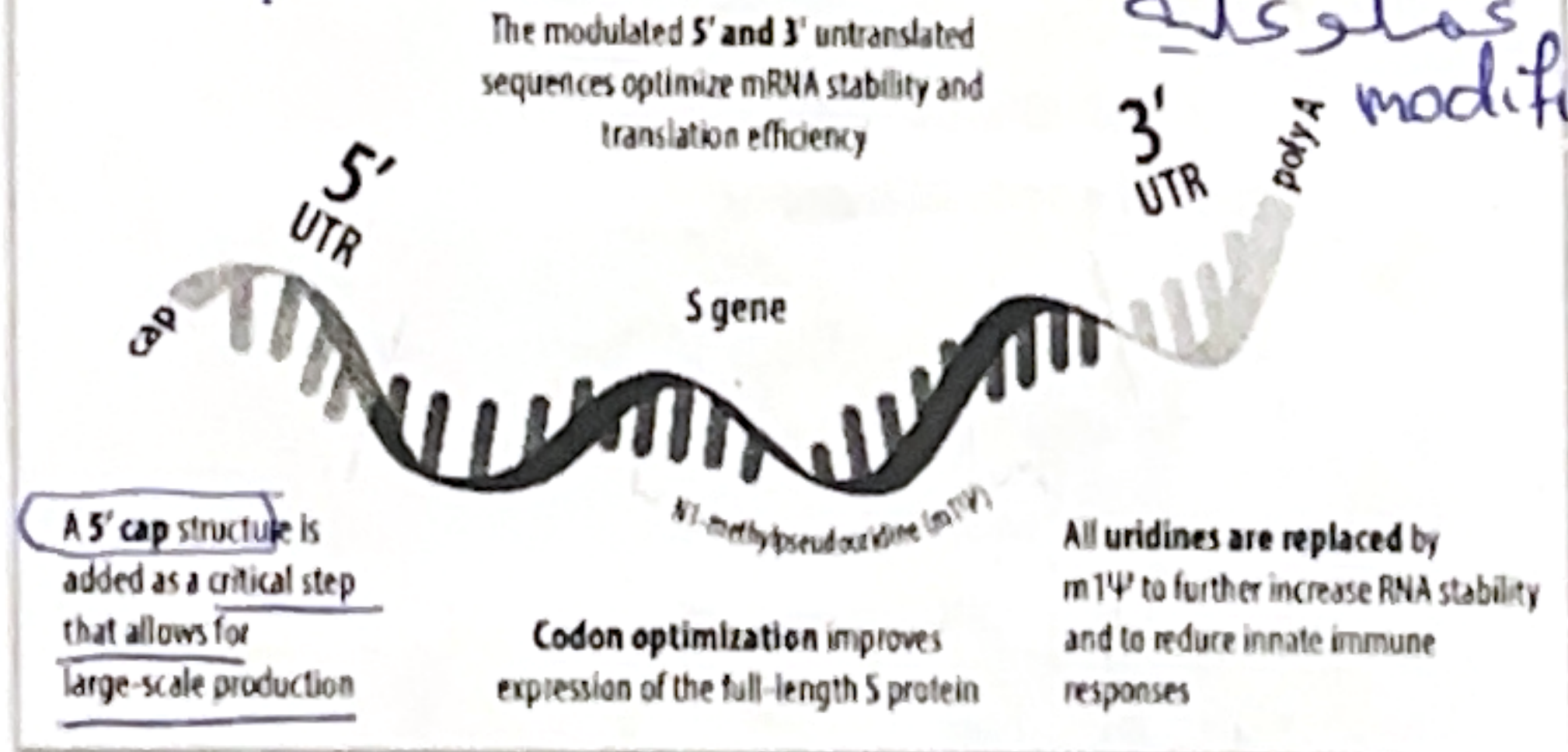
amplification (PCR)

transcription

purification (formulation)

PFIZER-BIONTECH COVID-19 VACCINE

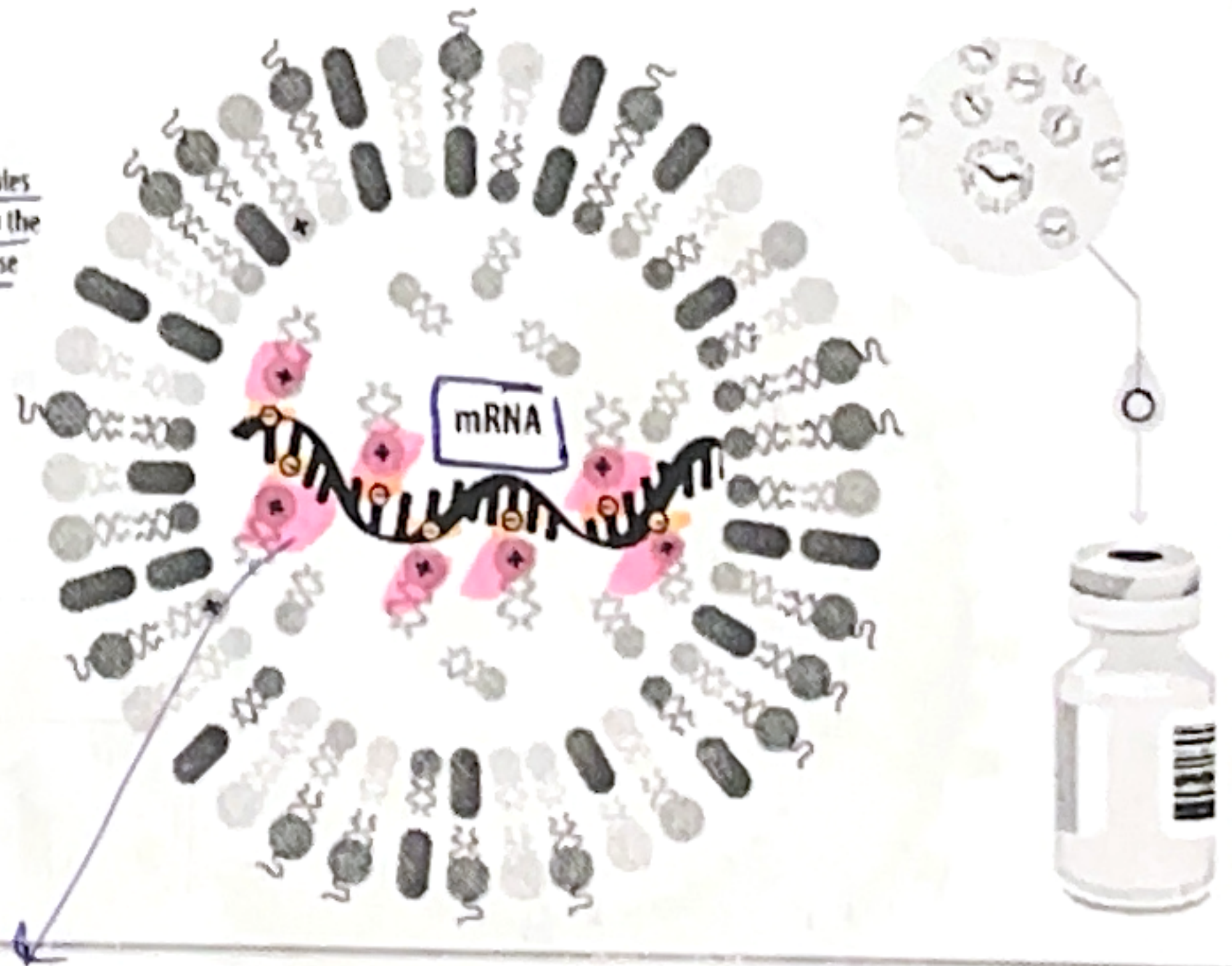
mRNA than encode spike
protein of covid virus



Lipid nanoparticle

Many of the ionizable lipid molecules have a positive charge and cling to the negatively charged mRNA, they lose their charge in the more alkaline conditions of the bloodstream, reducing toxicity in the body

ionizable lipid
cholesterol
PEG-lipid*
phospholipid



immune
response

+ stability من

باين من lipid الى استخترتهم من

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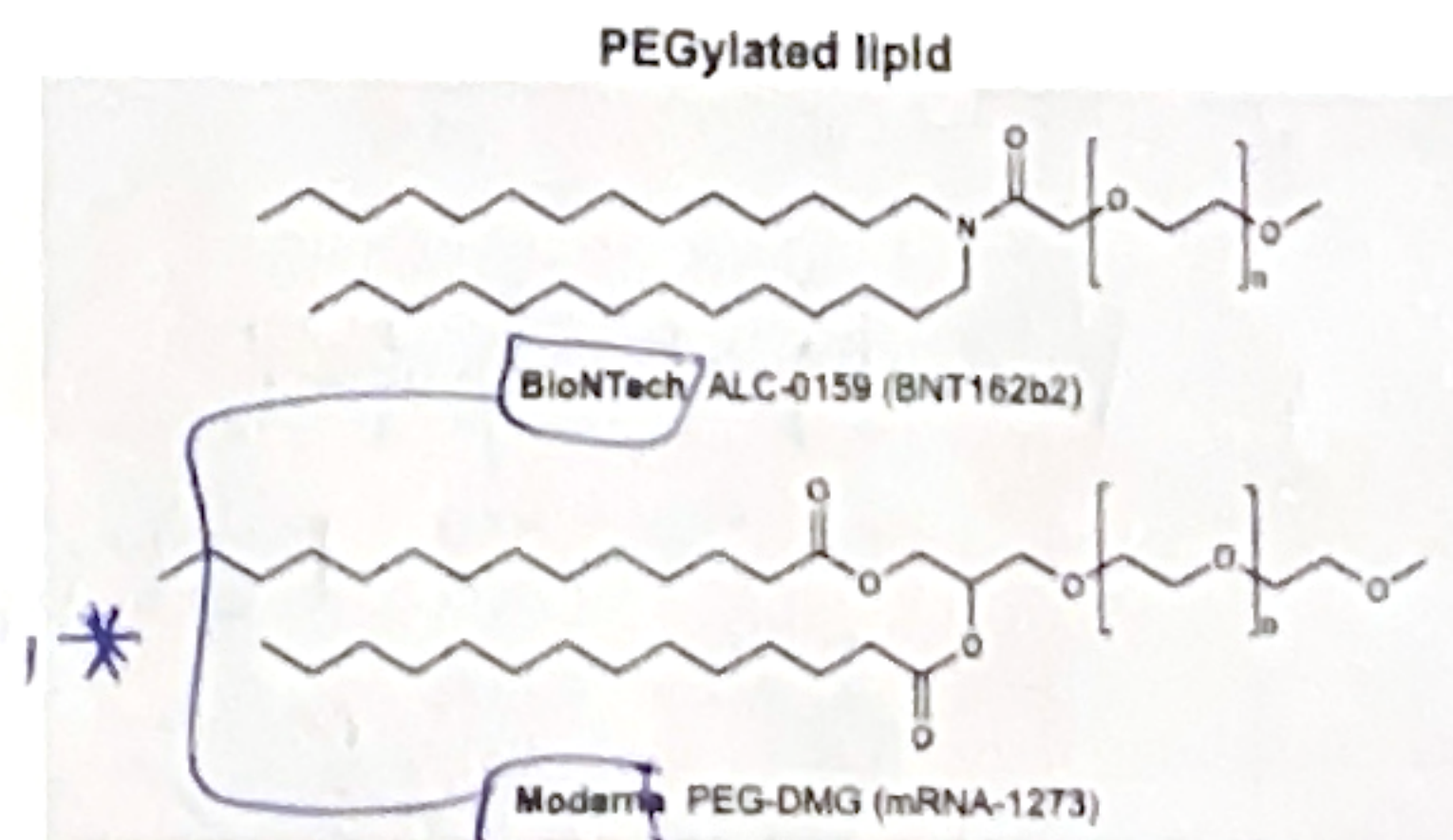
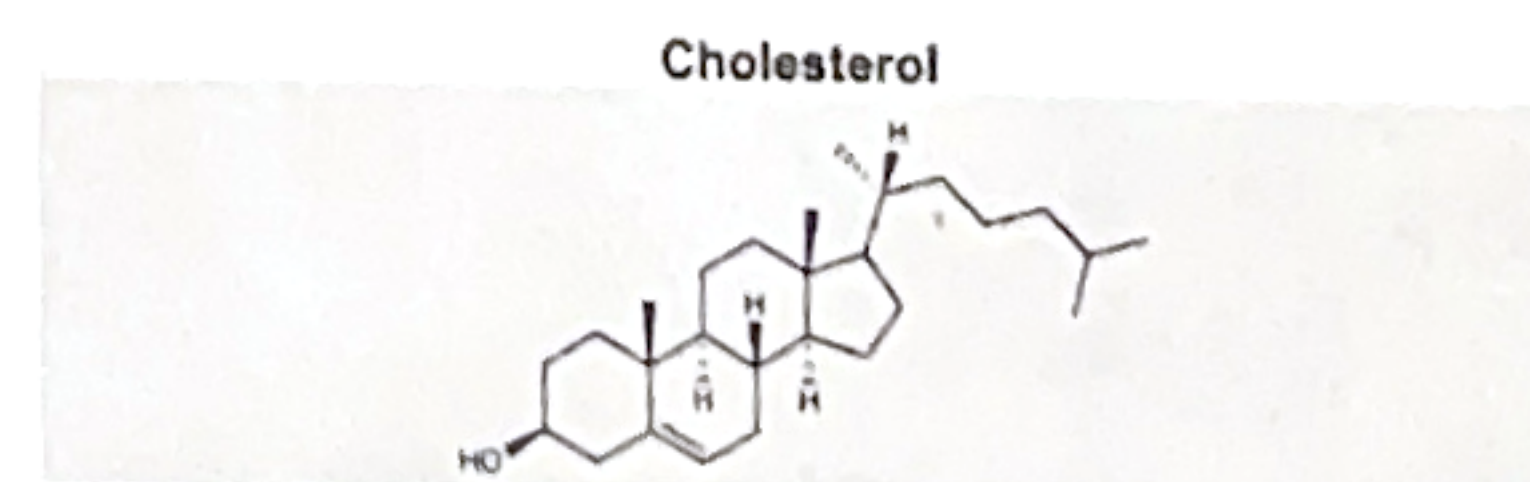
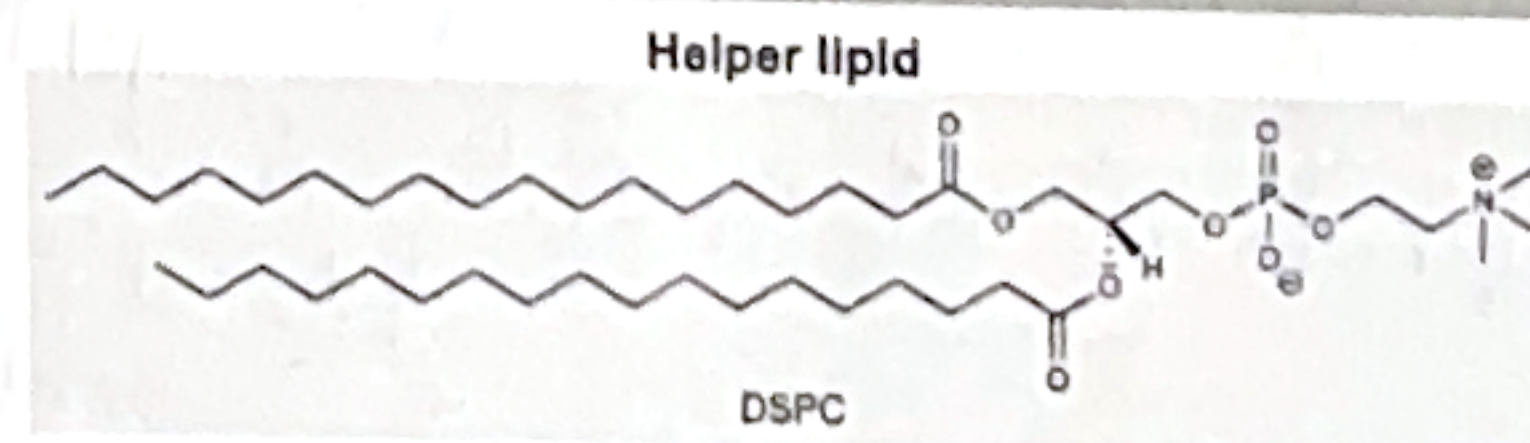
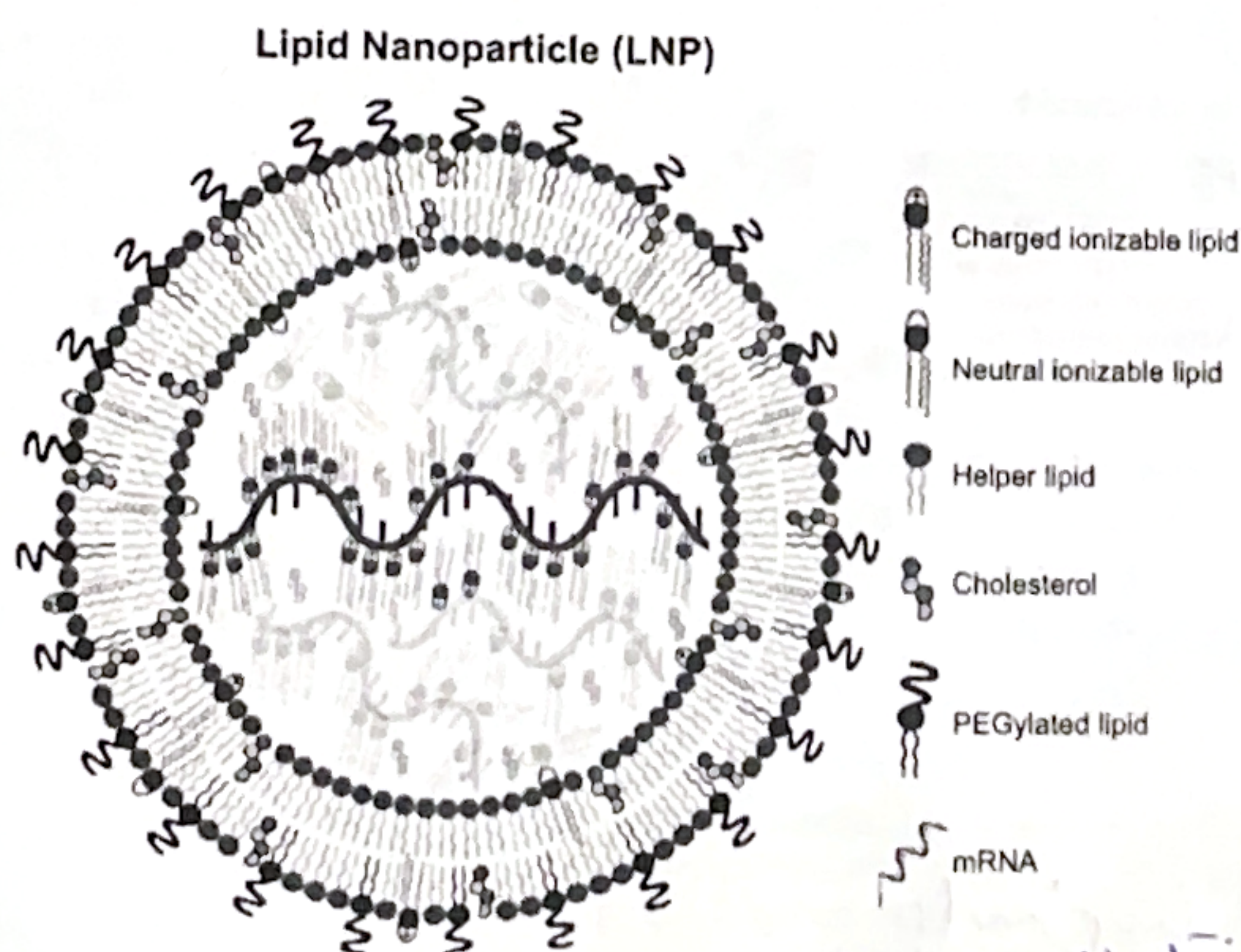
تصنع liposomes، برتبطو electrostatic interaction مع mRNA

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-
- The diagram illustrates the structure of a lipid nanoparticle (LNP). On the left, a syringe is shown drawing a drop of liquid from a vial labeled "COMBINATORY mRNA vaccine formulation". Two lines from the drop point to a large circular cross-section of the LNP. The LNP is a spherical bilayer composed of various lipids. A legend on the right identifies the components: mRNA (represented by a wavy line), ionizable lipid (represented by a grey circle with a wavy tail), helper lipid (represented by a black circle with a wavy tail), PEG (represented by a wavy line), and cholesterol (represented by a steroid ring structure). The mRNA strands are shown encapsulated within the LNP.

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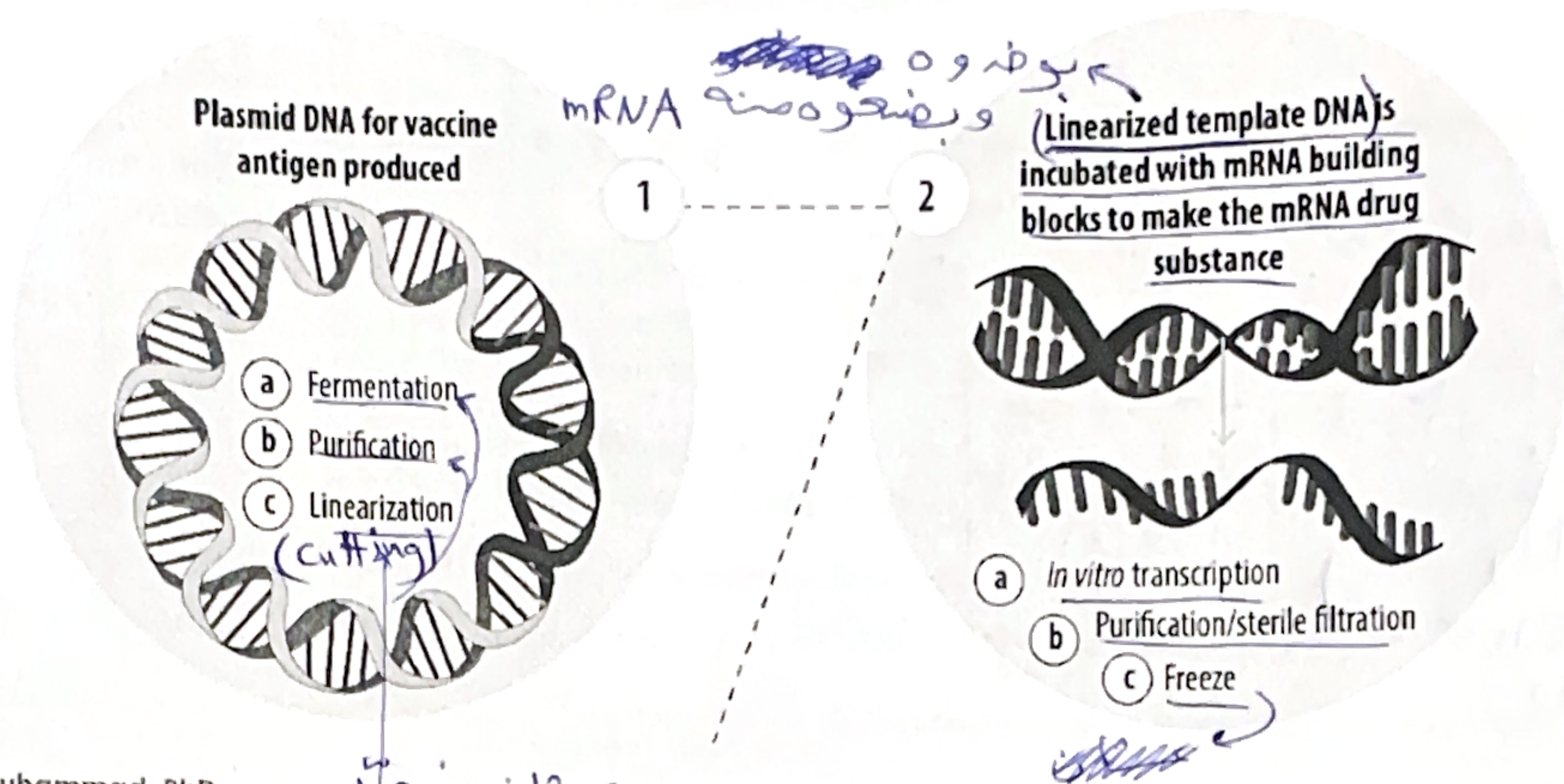


* اختلافات بين اشراك
 المختلفة تكون بسيطة
 (Composition of the lipid)
 efficacy (مورثاتية)
 اعراضه من تجميع
 nano

Steps In The Manufacturing Of: The mRNA Drug Substance & Vaccine Drug Product.



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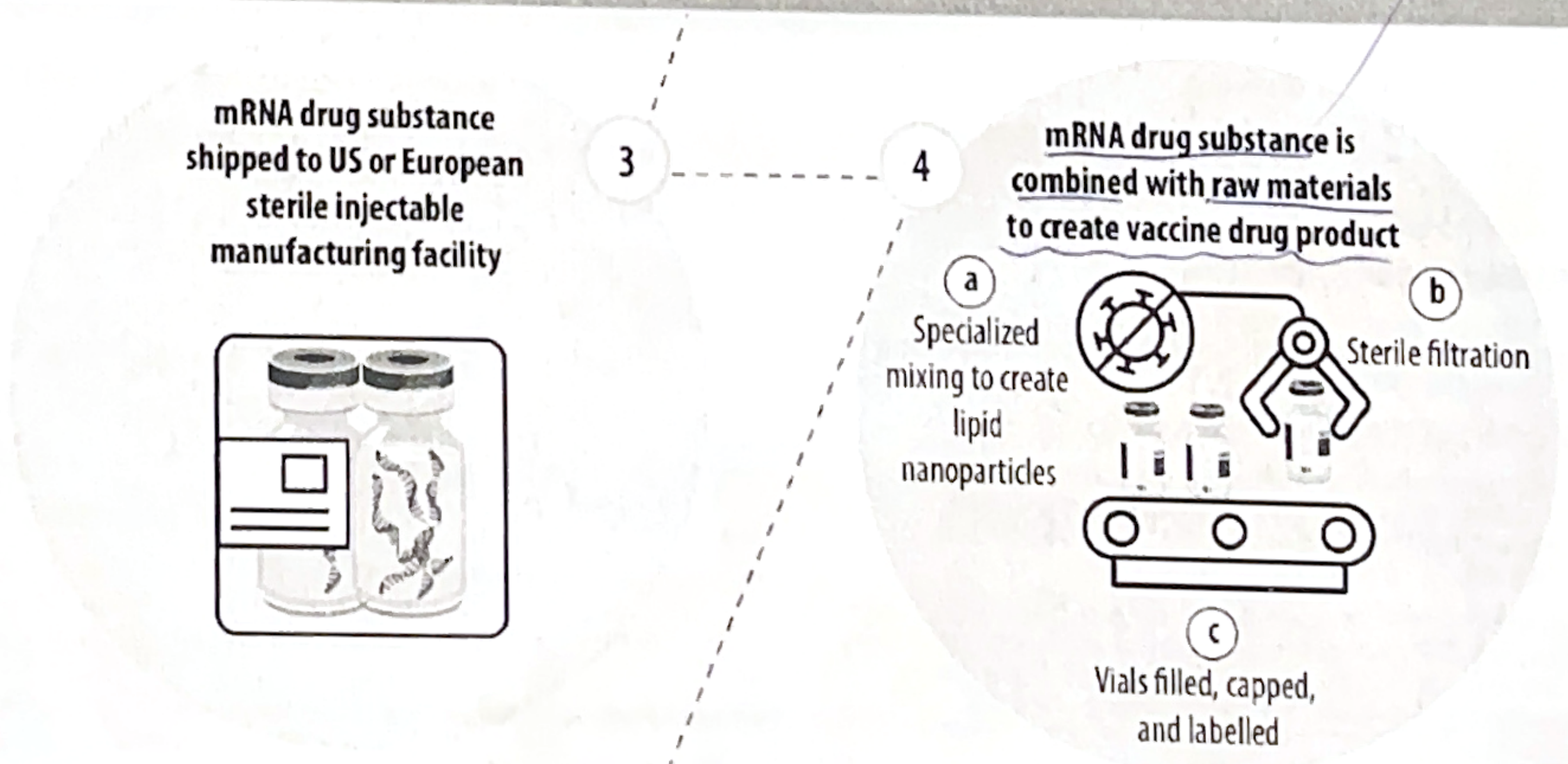
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Steps In The Manufacturing Of: The mRNA Drug Substance & Vaccine Drug Product.



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Steps In The Manufacturing Of: The mRNA Drug Substance & Vaccine Drug Product.



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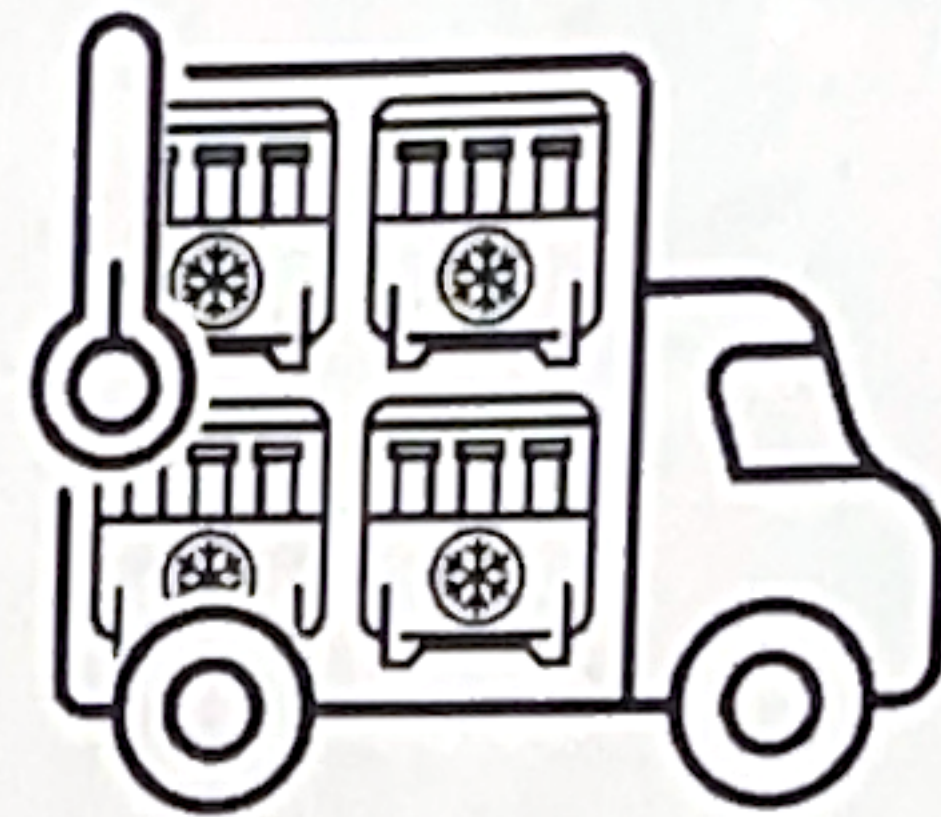
5

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100% of vaccine vials are
inspected and packed into
storage freezers



Vaccine distributed to
vaccination centers



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efficient delivery of large molecules

ONPATTRO® (PATISIRAN):



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Lipid Nanoparticle Delivery:

- The siRNA is encapsulated in lipid nanoparticles to ensure stability and efficient delivery to hepatocytes (liver cells), where TTR is primarily produced.

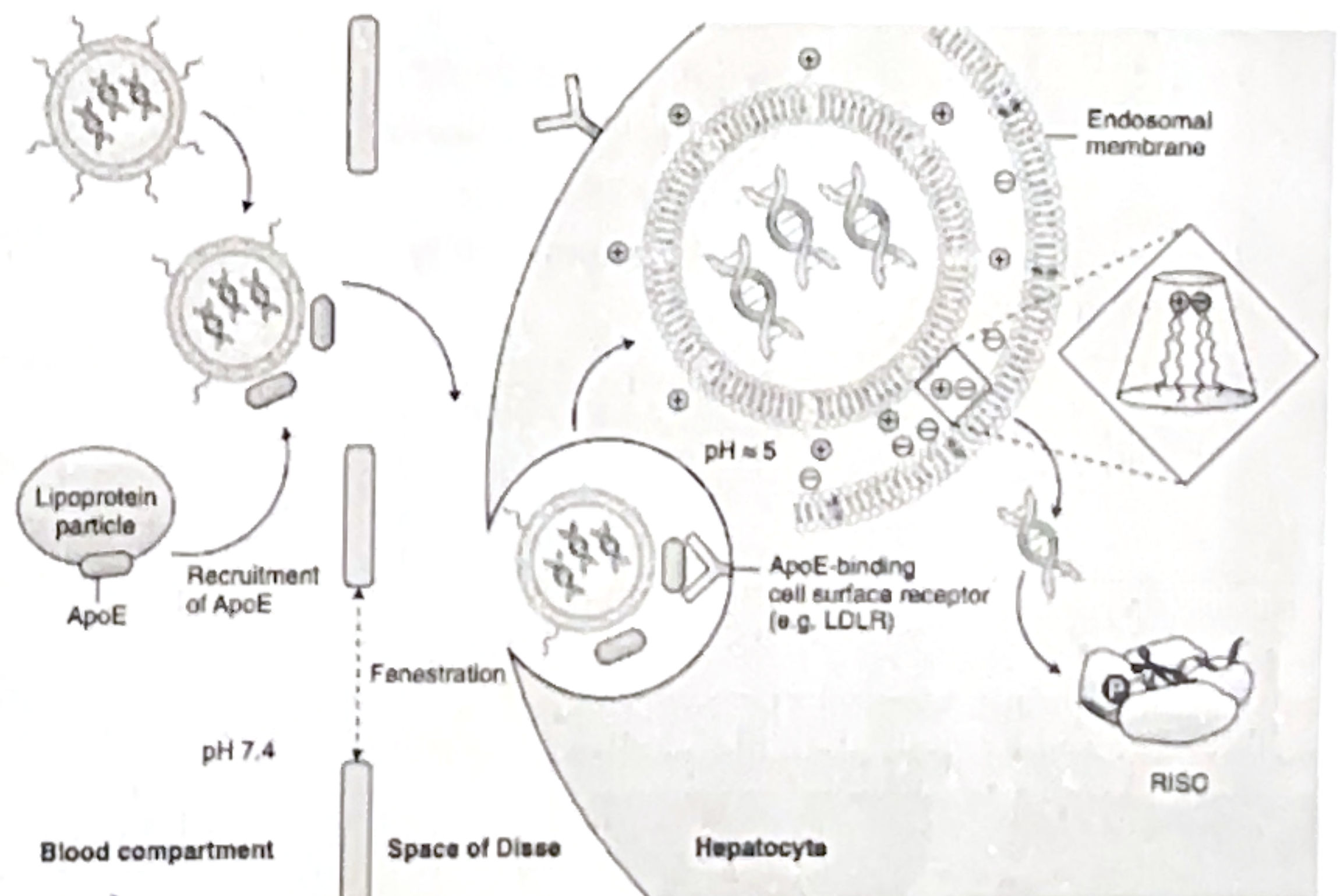
Targeting Transthyretin (TTR) mRNA:

- Patisiran specifically binds to and degrades TTR mRNA in the liver via the RNA-Induced silencing complex (RISC).

Inhibition of TTR Protein Production:

- This prevents the liver from synthesizing both mutant and wild-type transthyretin protein, reducing the accumulation of amyloid fibrils in tissues.

- Onpattro slows or reverses amyloid deposition, by reducing TTR production alleviating symptoms and improving outcomes in patients with hereditary transthyretin-mediated amyloidosis (hATTR amyloidosis).



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← في بروتين مسؤول عن نقل vitA , thyroxin في الجسم
يكون mutated , فببسر له
أعضاء في الجسم مثل heart , kidney , ...
preprecipitation
silencing for the mRNA that encode the mutated gene

that encode the mutated gene

Main Purposes Of Nanomedicine:



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3. Targeted Drug Delivery

- Nanomedicine allows for the precise delivery of therapeutic agents to specific tissues or cells, minimizing systemic toxicity and enhancing therapeutic efficacy.

Examples

Kadcyla®: Antibody-drug conjugate (ADC) targeting HER2-positive breast cancer cells.

- combines trastuzumab (HER2-specific monoclonal antibody) with a cytotoxic agent (DM1).
- How It Targets Cells** - The trastuzumab component binds specifically to **HER2 receptors**, which are overexpressed on HER2-positive breast cancer cells.
- Upon binding, the complex is internalized into the cancer cell.
- Inside the cell, the cytotoxic drug (DM1) is released, disrupting microtubule function and inducing apoptosis selectively in HER2-positive cells.
- Advantage:** Provides targeted therapy with reduced systemic toxicity compared to conventional chemotherapy.

① **Nanotherm:** Magnetic nano particles functionalized with antibodies targeting glioblastoma cells

② **Myocet®:** Liposomal doxorubicin targeted for breast cancer, sparing healthy tissues. (® utilizes passive targeting through the Enhanced Permeability and Retention (EPR) effect.)

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application : hyper-thermia therapy for glioblastoma multi-forme (brain cancer cells)

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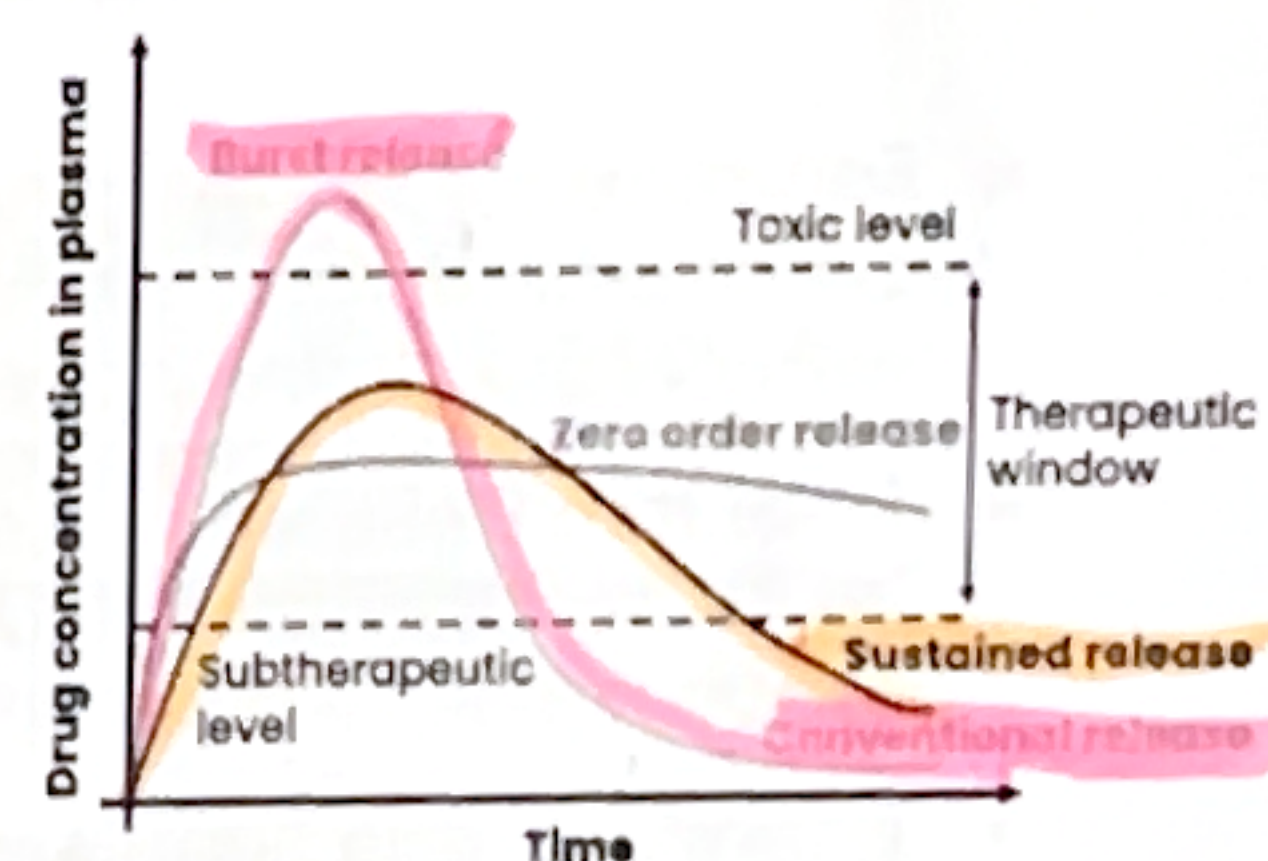


4. Controlled and Sustained Release

- Offers controlled release of drugs over time, reducing the frequency of dosing.
- Example: PLGA nanoparticles for sustained delivery of anti-inflammatory drugs.

What Are the Four Drug Delivery Methods?

- Immediate Release**
 - The dosage form that is designed to give a rapid and complete release of the drug.
- Non-Immediate Release**
 - The dosage form encompassing drugs that do not fully release upon administration
- Site-Specific Release**
 - The dosage form that offers targeted delivery of a drug directly to the location where it is administered.
- Sustained Release**
 - The dosage form that releases a drug continuously at a slow or controlled rate over a prolonged period of time.



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Main Purposes Of Nanomedicine:



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(أقراة)

5. Enhanced Imaging and Diagnostics

Enhanced Diagnostic Imaging

- Nanoparticles improve the sensitivity and specificity of imaging modalities such as MRI, PET, and CT, aiding in the early detection and monitoring of diseases.
- Ferumoxytol®** - Iron oxide nanoparticles used as a contrast agent in MRI for vascular imaging and detecting inflammation.
- Nanoparticle-based PET tracers** - Gold nanoparticles functionalized with radiolabels for enhanced tumor imaging with improved resolution and accuracy.
 - Improves contrast and specificity in imaging technologies like MRI, CT, and PET.
 - Example: Iron oxide nanoparticles for magnetic resonance imaging.

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FERUMOXYTOL®

diagnostic
therapeutic

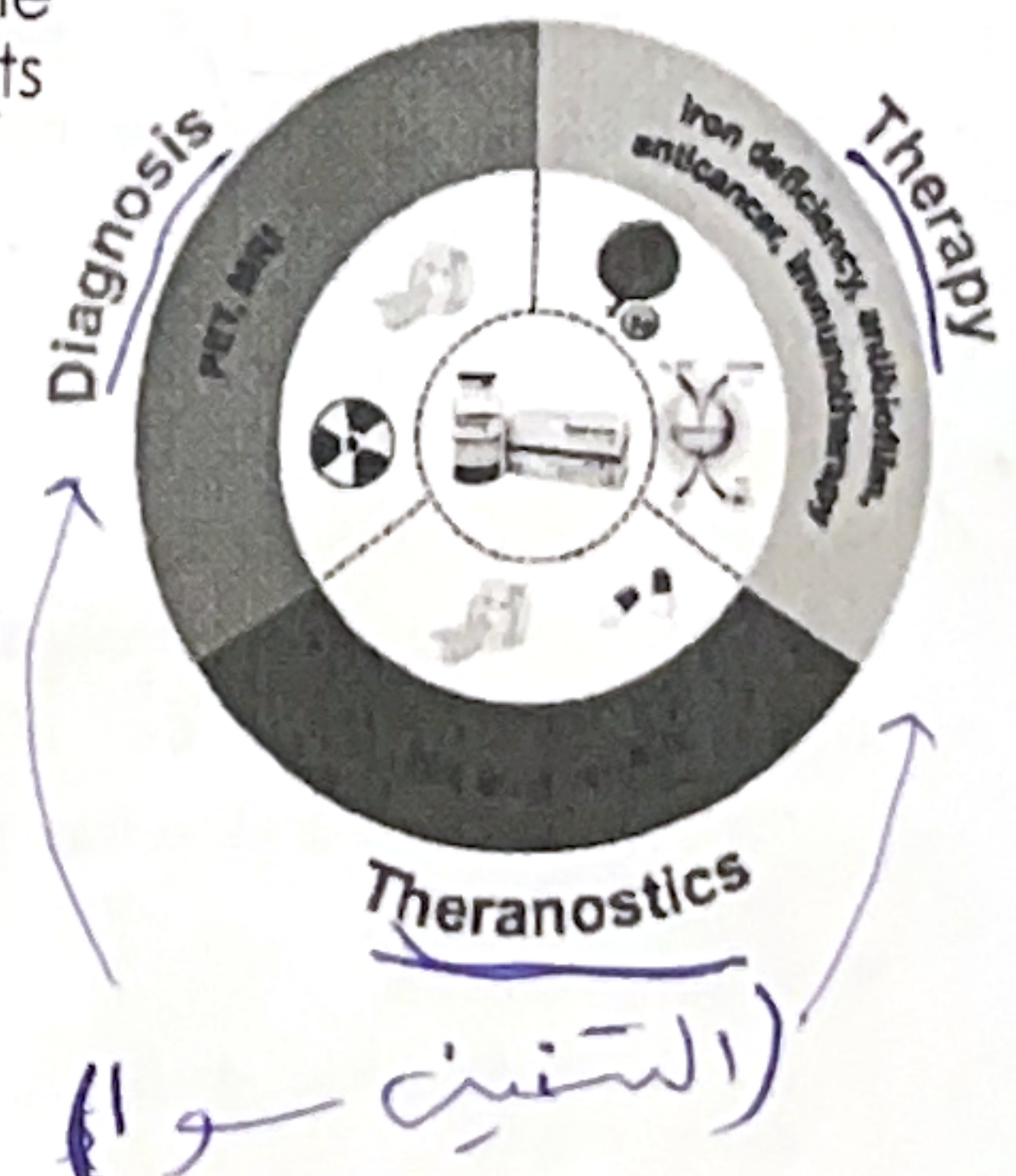


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- Ferumoxytol®** is an iron-based nanoparticle used primarily for the treatment of iron deficiency anemia (IDA), particularly in patients with chronic kidney disease (CKD). It is used to:

- Treat Iron Deficiency Anemia:** Ferumoxytol is used to restore iron levels in patients with IDA who cannot tolerate oral iron supplements or when oral iron is ineffective.
- Parenteral Iron Supplementation:** It is administered intravenously to rapidly replenish iron stores, especially in patients with chronic diseases like CKD, inflammatory bowel disease, and cancer-related anemia.
- MRI Imaging:** Due to its magnetic properties, ferumoxytol is sometimes used as a contrast agent in magnetic resonance imaging (MRI) for enhanced imaging of tissues and vessels.



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TFR1 (transferrin receptor 1) and FPN (ferroportin) are two key proteins involved in iron homeostasis in the body

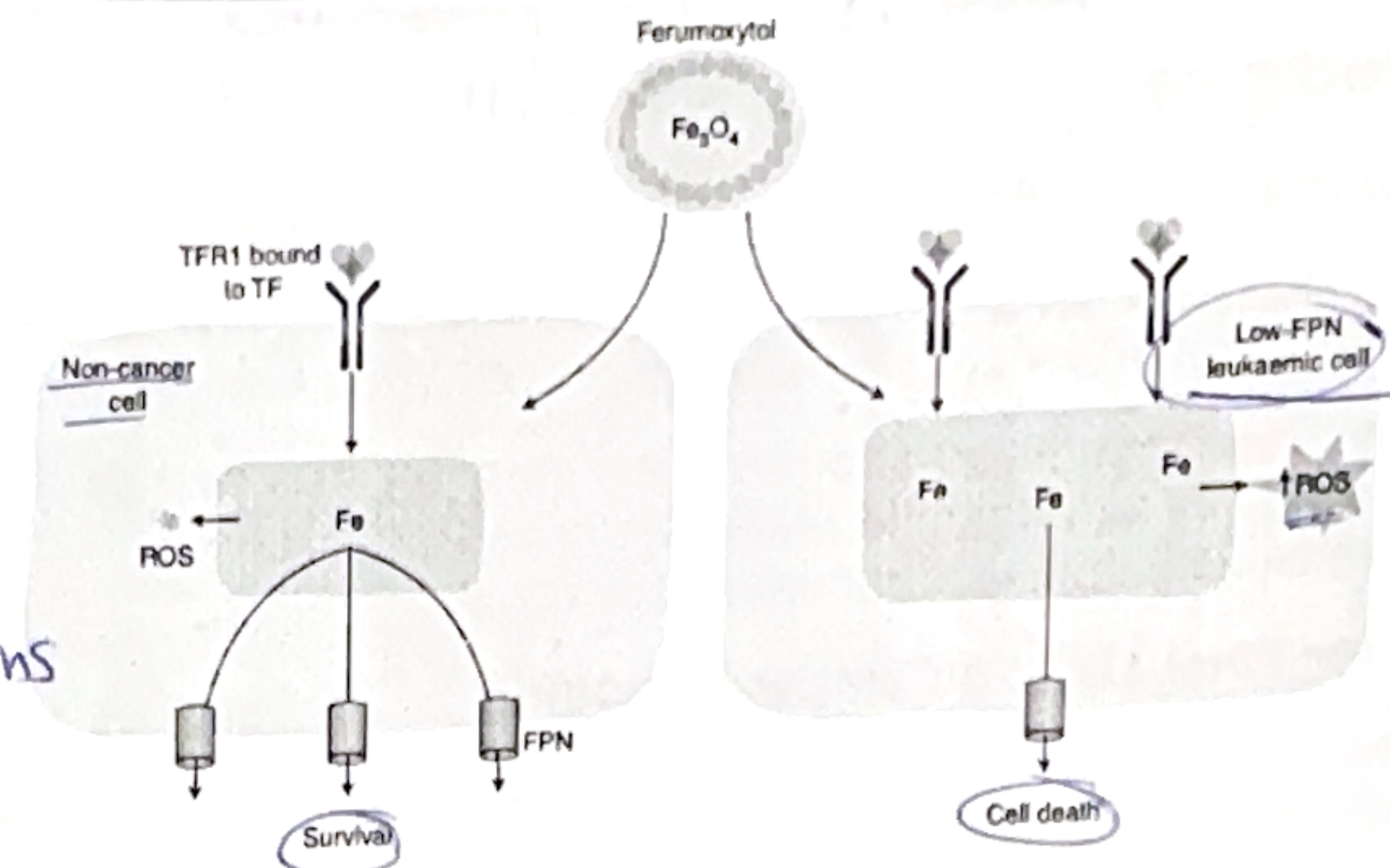


Fig. 1 | Proposed mechanism by which ferumoxytol induces selective cell death in leukaemic cells that express low levels of FPN. Left image depicts a non-cancer cell with moderate levels of TFR1 and high levels of ferroportin; right image depicts a leukaemic cell with high levels of TFR1 and low levels of FPN. When both cell types are exposed to the iron oxide nanoparticle ferumoxytol, non-cancer cells survive, presumably by exporting the excess iron through FPN. In contrast, owing to their low levels of FPN, leukaemic cells are unable to export excess iron, which remains in the cell, catalyses the production of excess reactive oxygen species and leads to cell death. ROS, reactive oxygen species; TF, transferrin.

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← Ferumoxytol يعبره تراكم في
هذه الخلايا عن الخلايا الطبيعية من ناحية
عشان يحافظ على homeostasis للحديد في الجسم بس مع
(normal cells) اما في cancer cell فPN (يعني موجود أو قليل)
بالتالي يعبره تراكم للحديد ← ROS (تكون موجود أو قليل)
leukaemia cell بسبب اختلاف FPN expression (تجمع accumulation for ferrous)

Main Purposes Of Nanomedicine:



6. Personalized Medicine

- Supports the development of therapies tailored to individual genetic and molecular profiles.
- Nanoparticles for precise cancer therapy based on tumor biomarkers.

1) Gene Delivery Systems for Genetic Disorders (e.g., CRISPR-Cas9 Nanoparticles):

- Nanoparticles, such as lipid nanoparticles (LNPs), are being explored for delivering gene-editing tools like CRISPR-Cas9 to target mutations in diseases such as cystic fibrosis, Duchenne muscular dystrophy, and certain types of cancer.
- Personalization:** These nanoparticles can be engineered to deliver the CRISPR components specifically to the target tissue based on an individual's genetic profile, ensuring precision in gene editing to correct disease-causing mutations.

2) Targeted Drug Delivery with Antibody-Conjugated Nanoparticles (e.g., Kadcyra®):

- Kadcyra® (ado-trastuzumab emtansine) is a HER2-targeted antibody-drug conjugate (ADC) that delivers a cytotoxic agent directly to HER2-positive breast cancer cells.
- Personalization:** This therapy is tailored to patients with HER2-positive breast cancer, where the HER2 receptor is overexpressed. The nanoparticle-conjugated drug selectively binds to HER2-expressing cells, ensuring that the chemotherapy is delivered directly to the cancer cells while minimizing off-target effects.

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Main Purposes Of Nanomedicine:



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6. Personalized Medicine

نانو تصنيع على شكل
S.E من قبل

3) Nanoparticles for Immune Modulation in Cancer Immunotherapy:

- Nanoparticles can be used to deliver immune checkpoint inhibitors, like PD-1/PD-L1 blockers, directly to the tumor microenvironment, enhancing immune responses against the tumor.
- Personalization:** These nanoparticles can be designed to target specific tumor-associated antigens (TAAs) based on the patient's tumor profile, which increases the efficiency and reduces side effects compared to systemic administration of immune checkpoint inhibitors.

4) RNA Nanomedicines for Personalized Cancer Vaccines:

- Nanoparticles can encapsulate mRNA or other nucleic acids encoding tumor antigens to stimulate the patient's immune system against specific tumor markers.
- Personalization:** mRNA vaccines can be tailored to express antigens derived from the patient's own tumor, enabling a more personalized immune response. This has been explored in personalized cancer vaccines, particularly for melanoma and other cancers.

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Main Purposes Of Nanomedicine:



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7. Minimizing Systemic Toxicity

- Reduces systemic drug exposure, decreasing adverse effects.
- Nanocarriers enable controlled drug release, reducing off-target (side) effects and improving patient compliance.
- BIND-014** - A polymeric nanoparticle delivering docetaxel with high precision, reducing systemic toxicity in cancer therapy.
- Liposome-encapsulated **(amphotericin B)** (Ambisome®) - Reduces nephrotoxicity associated with conventional amphotericin B formulations.

antifungal → اول دواء قف

الكافق على

لصالح antifungal (liposome encap - amphotericin B)

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AMPHOTERICIN B (AMBISOME®)

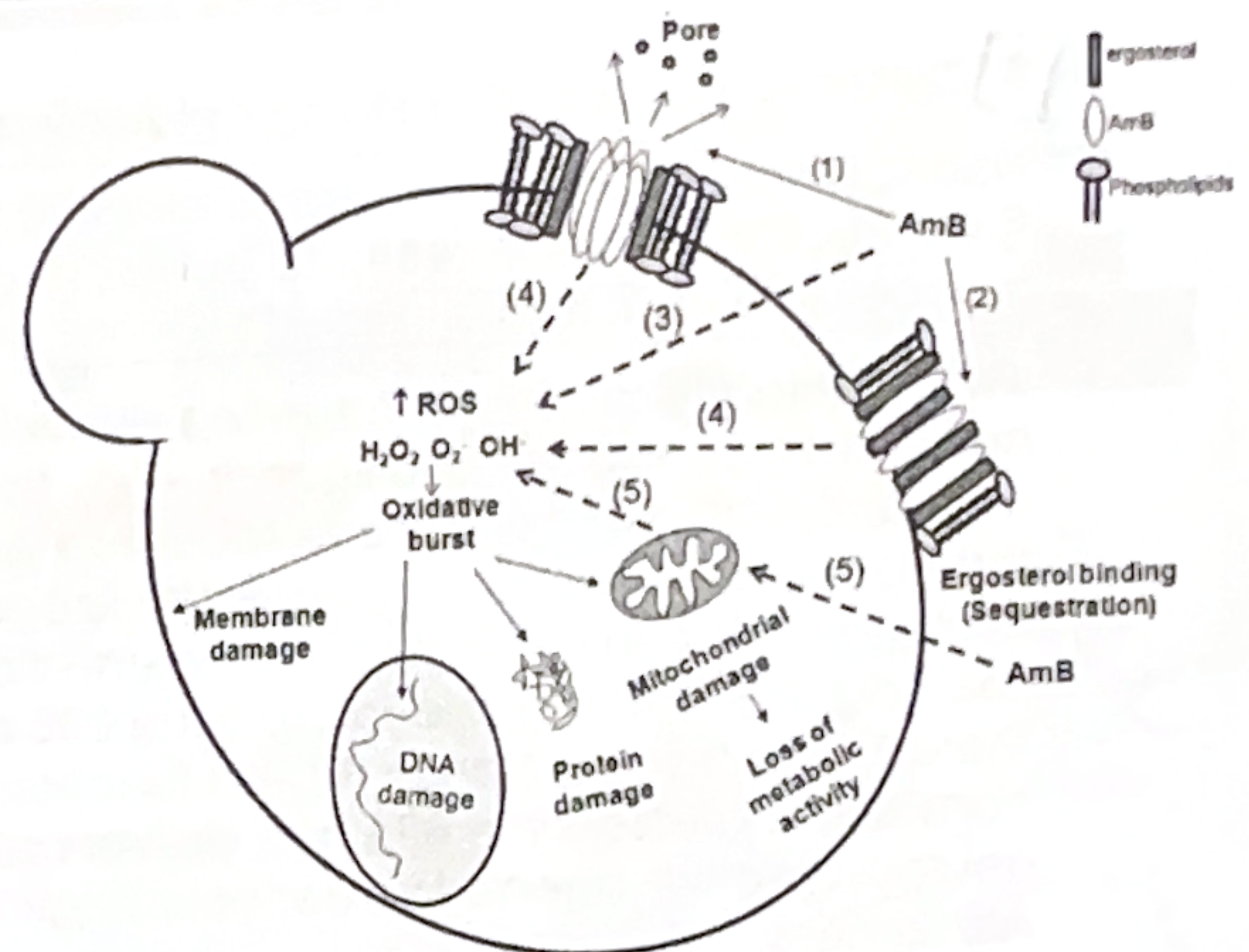


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- It only takes one to do many jobs: Amphotericin B as antifungal and immunomodulatory drug!
- The mechanism of action of AmB still is not completely elucidated. AmB has effects on the fungal cell at two different levels: Binding to the ergosterol at the membrane, inducing pore formation and ergosterol sequestration, and induction of oxidative damage.

(موت الخلايا)



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DID YOU KNOW?



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- amphotericin B** can be produced through biotechnological processes, particularly using microbial fermentation. The process typically involves the use of **Streptomyces nodosus**, a bacterium that naturally produces amphotericin B.
- Fermentation Process:**
 - Amphotericin B is produced by **Streptomyces nodosus** during fermentation in a controlled bioreactor environment. The microorganism is cultured in a nutrient-rich medium under specific conditions that promote the production of amphotericin B.
- Genetic Engineering:**
 - Advances in genetic engineering have been employed to optimize the production of amphotericin B. By modifying the genes of **Streptomyces species**, researchers can enhance yield, improve production efficiency, and even alter the chemical structure of the compound to produce analogs with potentially better efficacy or reduced toxicity.
- Purification:**
 - After fermentation, amphotericin B is extracted and purified through processes like filtration, solvent extraction, and chromatography to obtain the final product suitable for clinical use.

amphotericin B

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nanoparticle

Main Purposes Of Nanomedicine:

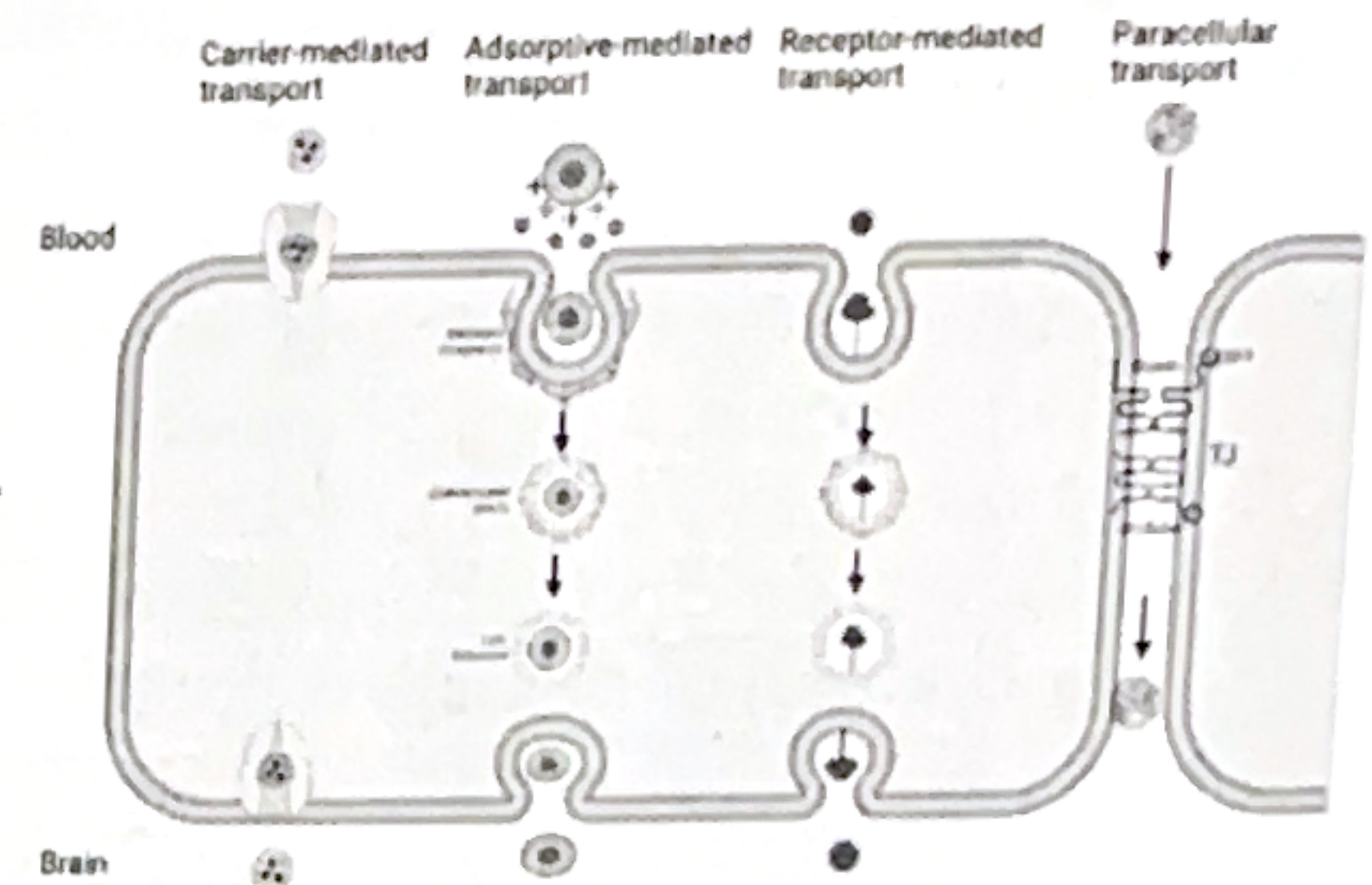


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8. Crossing/ Overcoming Biological Barriers

- Nanoparticles can cross complex biological barriers, such as the blood-brain barrier (BBB), to deliver drugs to otherwise inaccessible sites, for neurological treatments.
- Surface Modification with Targeting Ligands: Functionalizing nanoparticles with specific ligands (e.g., transferrin, peptides, or antibodies) that can bind to receptors on the BBB, such as the transferrin receptor or low-density lipoprotein (LDL) receptor. This can facilitate receptor-mediated endocytosis, allowing the nanoparticle to cross the BBB and deliver therapeutic agents. Nanoparticles functionalized with transferrin can cross the BBB and deliver anticancer drugs or neuroprotective agents to treat neurological disorders like Alzheimer's.



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RYBELSUS® (ORAL SEMAGLUTIDE)



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- the 'Trojan Horse' Approach: Encapsulating the therapeutic drug within nanoparticles that mimic biological substances capable of crossing the BBB. This can be done by coating nanoparticles with natural or synthetic carriers that the BBB recognizes, like liposomes or exosomes. Liposomal formulations or exosome-based nanoparticles have been explored for delivering gene therapies or chemotherapeutic drugs across the BBB to treat conditions like glioblastoma.



عملوهان كبير وتخبو الكبود داخله
فكر الفكرة بال nano
تقدر تفرقة من BBB
بخصي الدواء جوعان

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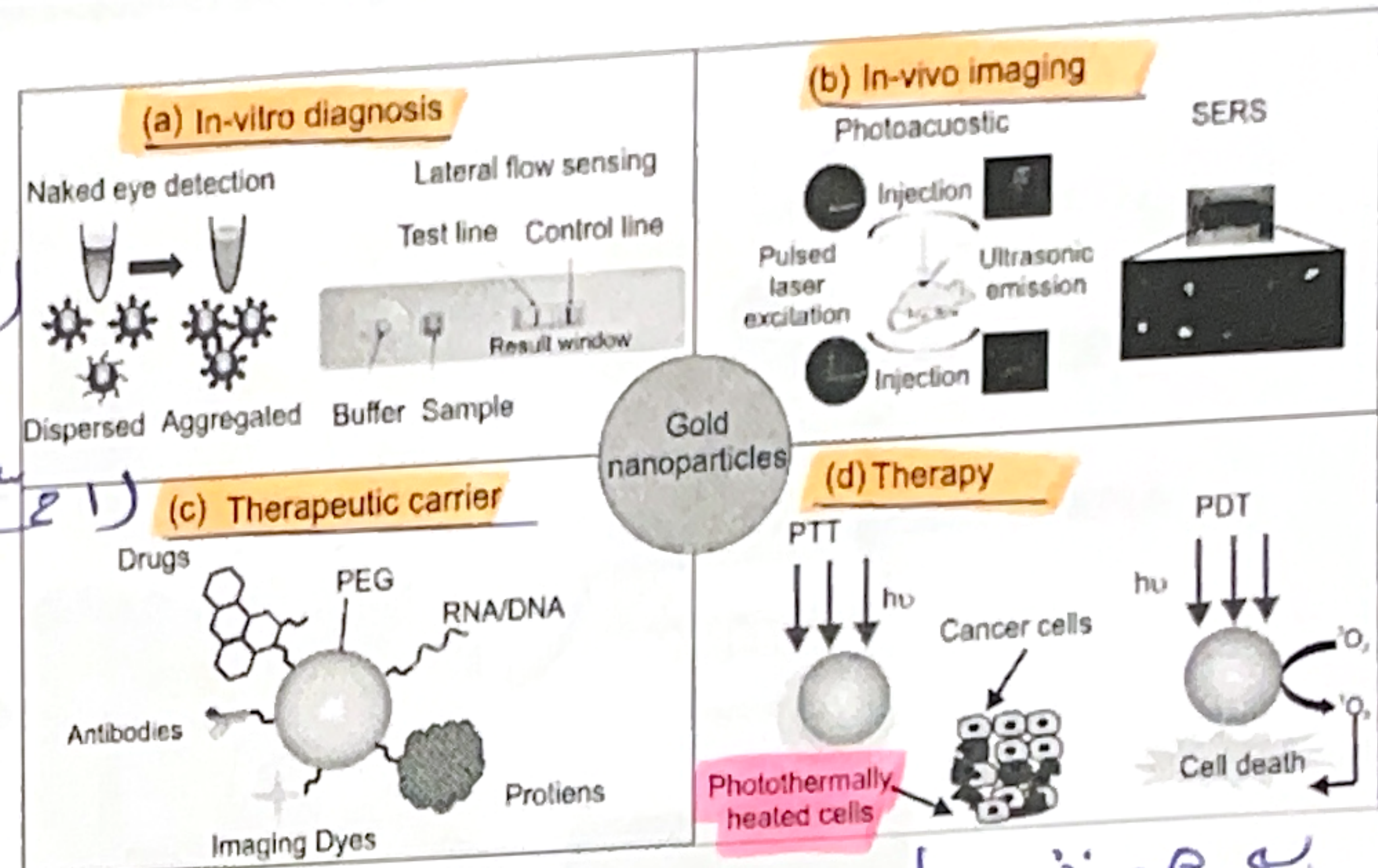
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Main Purposes Of Nanomedicine:



9 Theranostics (Combination of Therapy + Diagnostics)

- Combines therapeutic and diagnostic capabilities in a single nanoplatform.
- Example: Gold nanoparticles for both cancer imaging and hyperthermia treatment.
- Nanomedicine integrates diagnostic and therapeutic functionalities into a single platform, enabling personalized medicine approaches.
- Nanotheranostics using gold nanoshells - Used for photothermal therapy while simultaneously enabling imaging of tumors via near-infrared absorption.



therapeutic effect يكون nano
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Main Purposes Of Nanomedicine:



10 Regenerative Medicine and Tissue Engineering

- Aids in tissue engineering and repair using nanomaterials.
- Example: Nanofiber scaffolds for bone or cartilage regeneration.
- Nanomedicine aids in tissue repair and regeneration by delivering growth factors, stem cells, or scaffolds at the site of injury.
- Nanostructured hydrogels - Used for localized delivery of stem cells and growth factors to promote wound healing and cartilage repair.
- Nanofibrous scaffolds - Electrospun nanofibers functionalized with bioactive molecules for improved osteogenesis and bone tissue engineering.

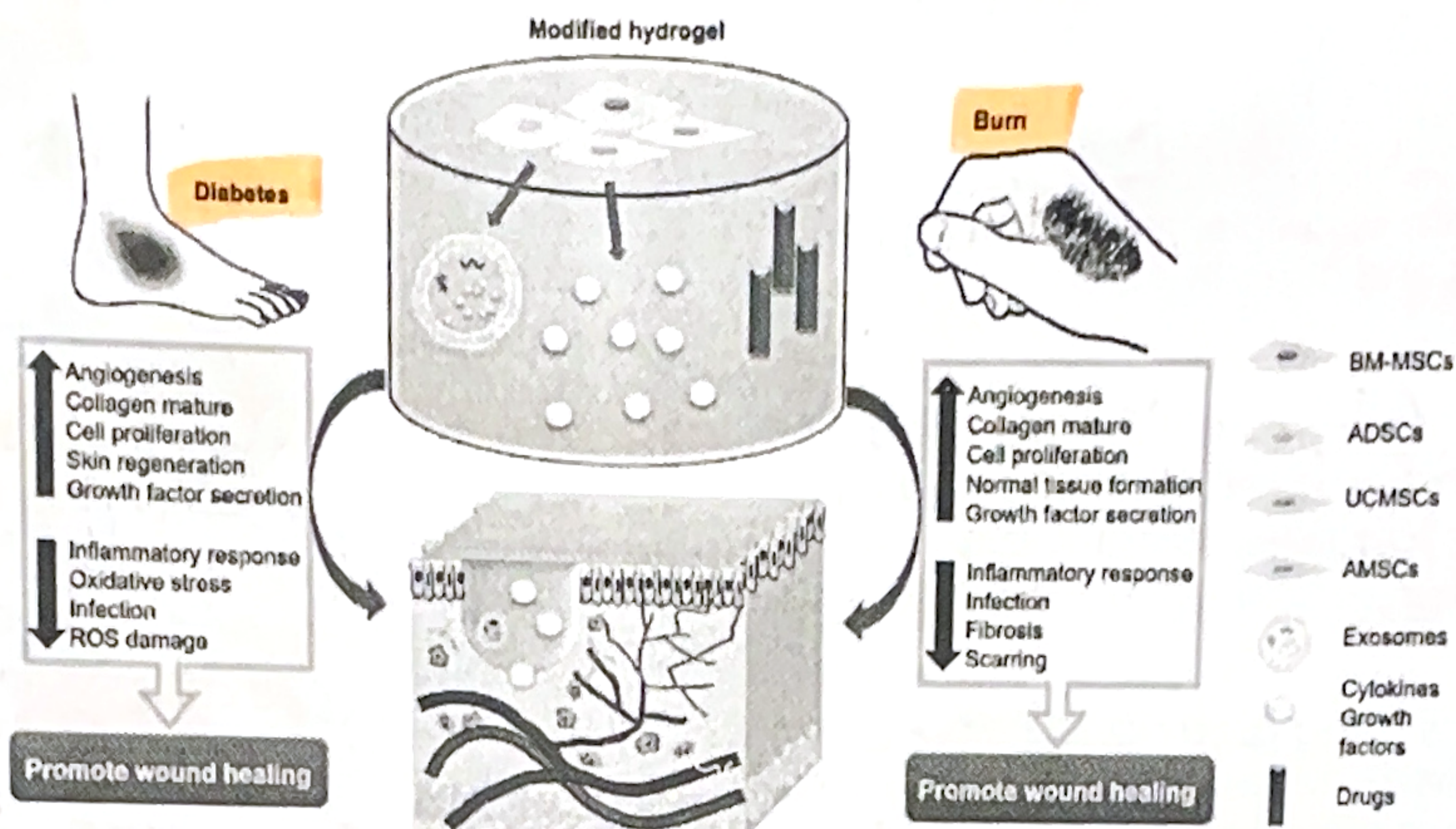
wound healing and repairing

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Main Purposes Of Nanomedicine:



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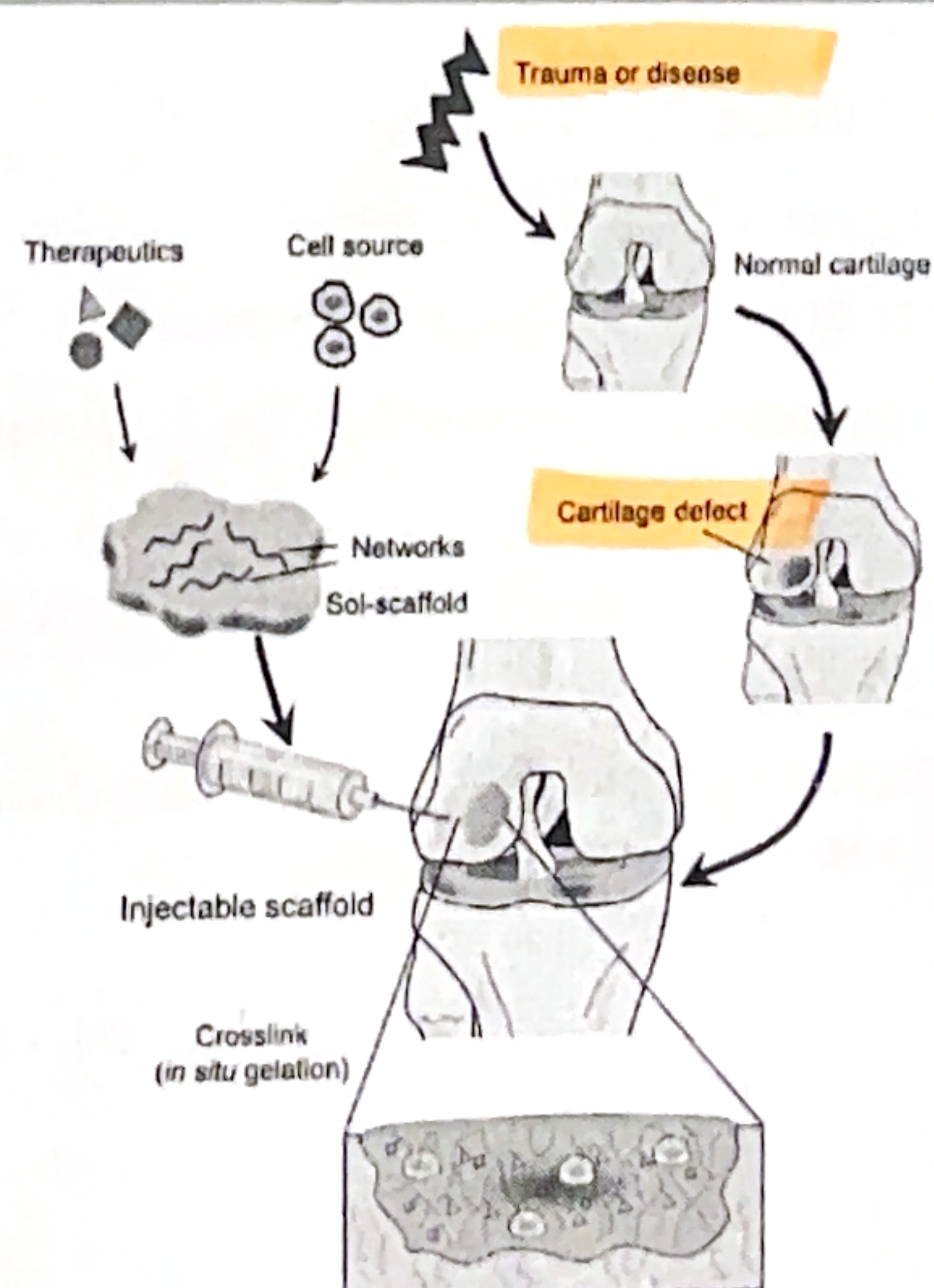
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Main Purposes Of Nanomedicine:



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Main Purposes Of Nanomedicine:



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11. Immune Modulation and Vaccines

- Nanoparticles can act as adjuvants or carriers to enhance immune responses for infectious diseases, cancer, and autoimmune disorders.
- CureVac's lipid nanoparticle vaccine candidates - Designed for infectious diseases, utilizing nanoparticles for optimal antigen delivery and immune stimulation.
- Checkpoint inhibitor delivery using nanoparticles - Nanocarriers delivering antibodies or RNA molecules to modulate immune checkpoints in cancer immunotherapy.

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Nano-Biopharmaceutical Formulations: Key Components



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1. **Nanocarriers:** Liposomes, lipid nanoparticles (LNPs), polymeric nanoparticles, dendrimers.

2. Therapeutic Payloads:

- Small molecules (e.g., paclitaxel in liposomes).
- Biologics (e.g., mRNA in lipid nanoparticles).
- Combination therapies (e.g., docetaxel and siRNA co-delivery).

3. **Surface Modifications:** PEGylation, targeting ligands, stealth coatings.

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NANOBIOINTERACTION



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لا بد من أن نذكر كيف يتفاعل مع الجسم ومن safety

Key Considerations

Particle Characteristics:

- Size, shape, and surface charge influence biodistribution and cellular uptake.
- For instance: Smaller particles (~50-100 nm) exploit the enhanced permeability and retention (EPR) effect for tumor targeting.

Protein Corona Formation:

- Interaction with serum proteins affects targeting and clearance.
- Strategies: PEGylation to reduce protein adsorption.

Cellular Uptake Pathways:

- Endocytosis, transcytosis, or receptor-mediated pathways.
- Example: Trastuzumab-coated nanoparticles target HER2-positive cells.

Diagram showing nanoparticle interactions with cells and the formation of a protein corona.

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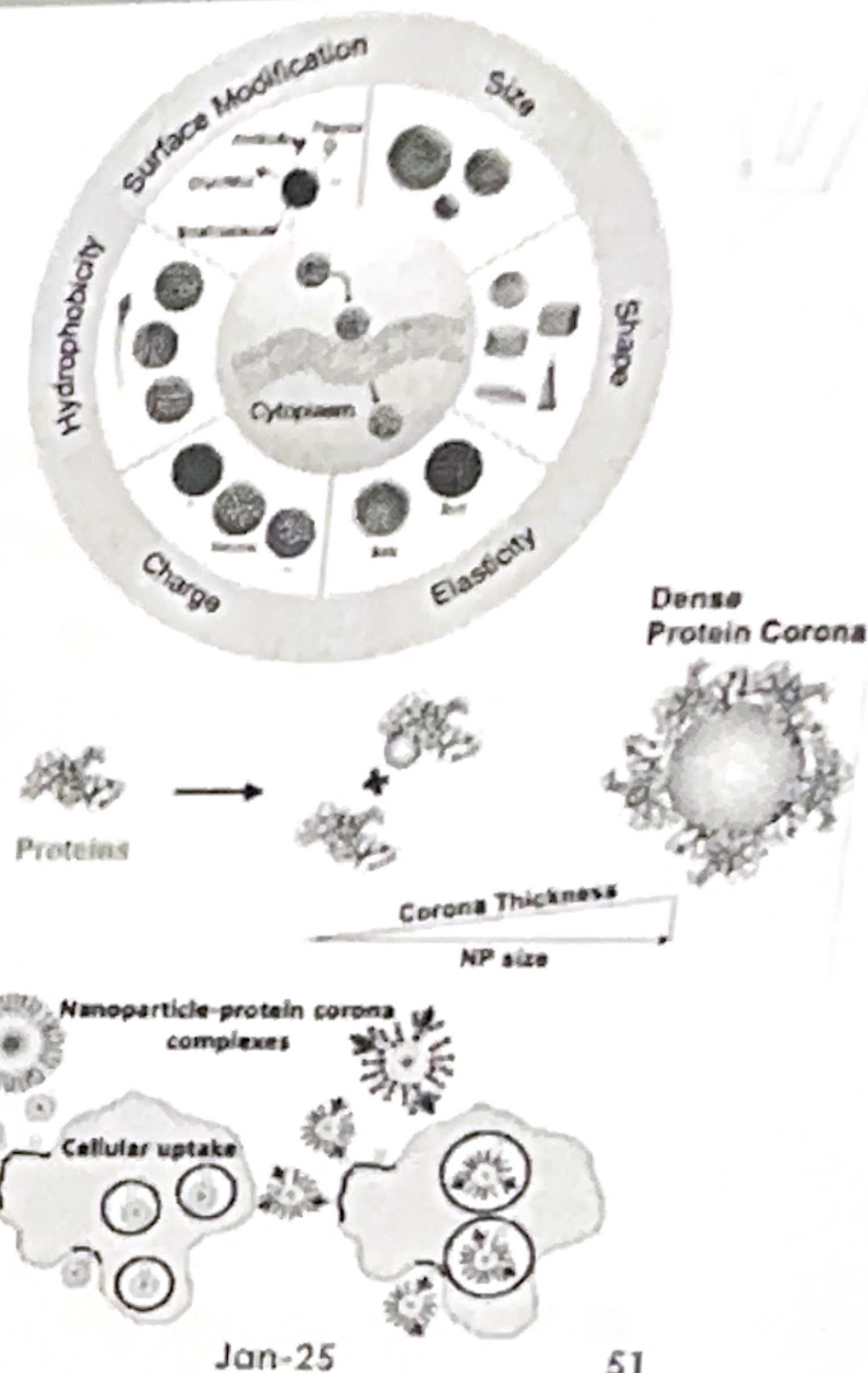
② nano particle بين تدخل الجسم، البروتينات (بشحنة سالبة)

بعضهم adsorption على سطح nano particle

immune cells يتغير تنوع ما ي nano Coated with protein

Coat بـ (protein corona)، كل مراد ما دال

protein corona thickness راجع لـ size والـ surface charge targeting clearance



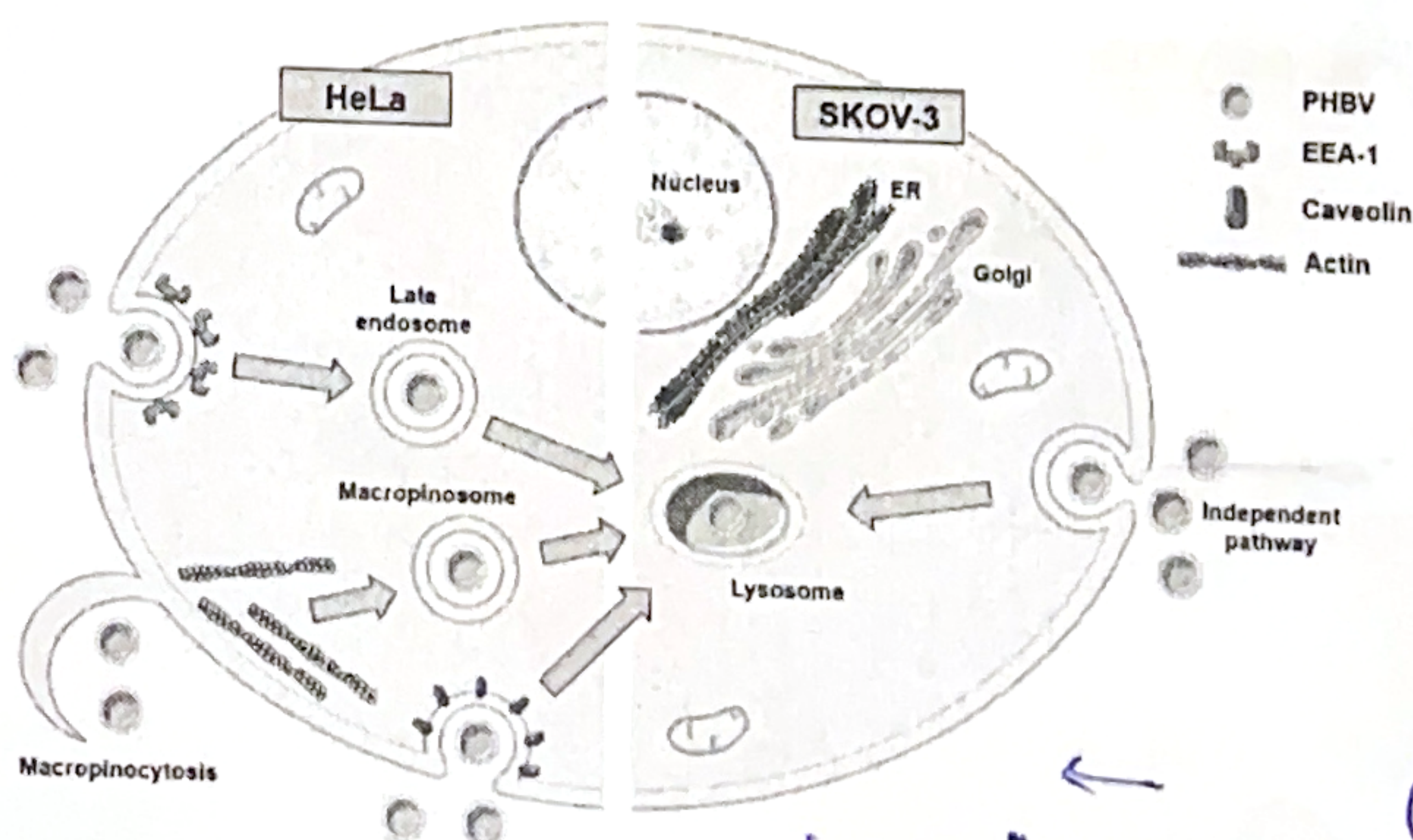
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NANOBIOINTERACTION



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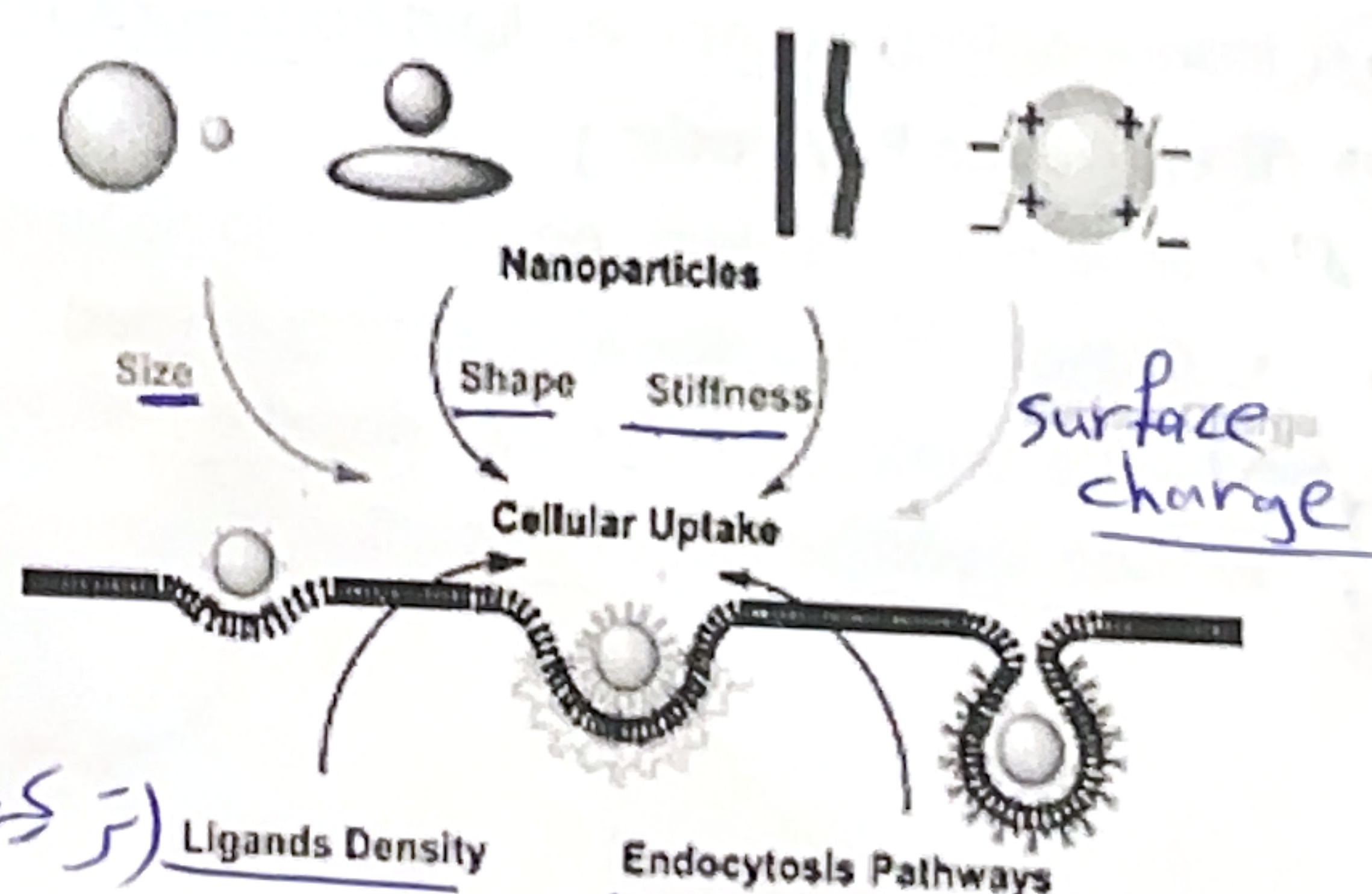


هون بفرجنا انه نفس (nanoparticle) two type of cells

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different pathways

لكنهم استعملو



(تركيز) Ligands Density

Endocytosis Pathways

← العوامل التي تؤثر على uptake

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Practical Aspects In Biopharmaceutical Formulations



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Manufacturing Techniques:

- ← Solvent evaporation, and Microfluidics (e.g., NanoAssemblr), high-pressure homogenization, and solvent evaporation.
- Example: Microfluidic systems for LNP production in mRNA vaccines.

Stability and Storage:

- Addressing aggregation, precipitation, and degradation.
- Example: Lyophilization for long-term storage of mRNA-based nanoparticles.

Quality Control:

- Particle size, zeta potential, encapsulation efficiency, drug release profiles.

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CHALLENGES IN NANOTECHNOLOGICAL FORMULATIONS



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- ① Bid compatibility and immunogenicity issues.
- ② Scale-up and reproducibility in manufacturing.
- ③ High production costs and economic feasibility.
- ④ Cost: High initial development and production costs.
- ⑤ Toxicity Concerns: Long-term effects of nanoparticles on health and the environment.

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FUTURE DIRECTIONS IN NANOBIO TECHNOLOGY



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- Development of multifunctional nanocarriers for combination therapies.
- Sustainable manufacturing practices in nanobiotechnology.
- Precision medicine and personalized nanomedicine.