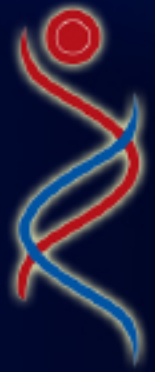

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USA, New York

A New Approach to the Design and Synthesis of Drugs Based on Self-Organizing Quasi-Life Systems

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Drug Discovery & Therapy
Dubai, UAE

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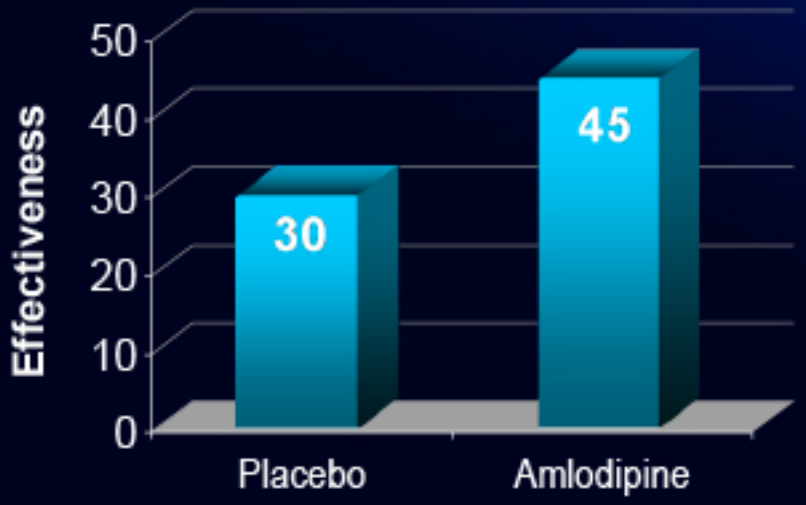
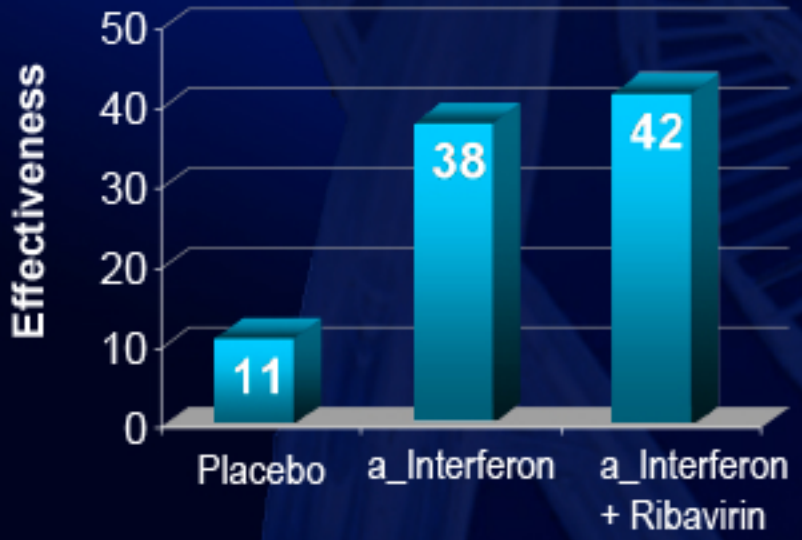
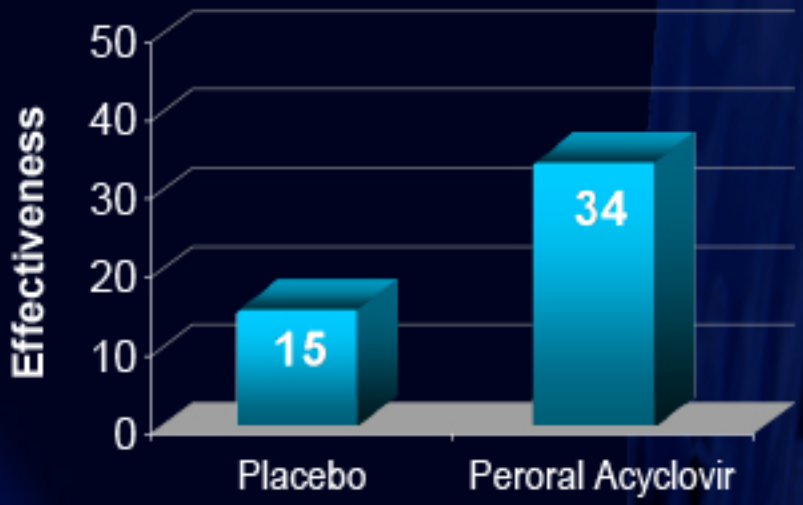
1. The real effectiveness of existing drugs







2. Properties of classical drugs

A) A precisely **conservative** chemical structure

B) The presence of a **"slippage effect"** (A change in the receptor apparatus of a specific person over the course of time. For example, the loss of effectiveness of hypotensive drugs and other substances in the same people over time; ACE inhibitors are the best-studied of these)

C) The drug's **inability** to **adapt** (change) independently to reduce the "slippage effect" or mutations of the causes of infections

D) The average **effectiveness** of these drugs rarely exceeds 50% (not everyone has an identical receptor apparatus)

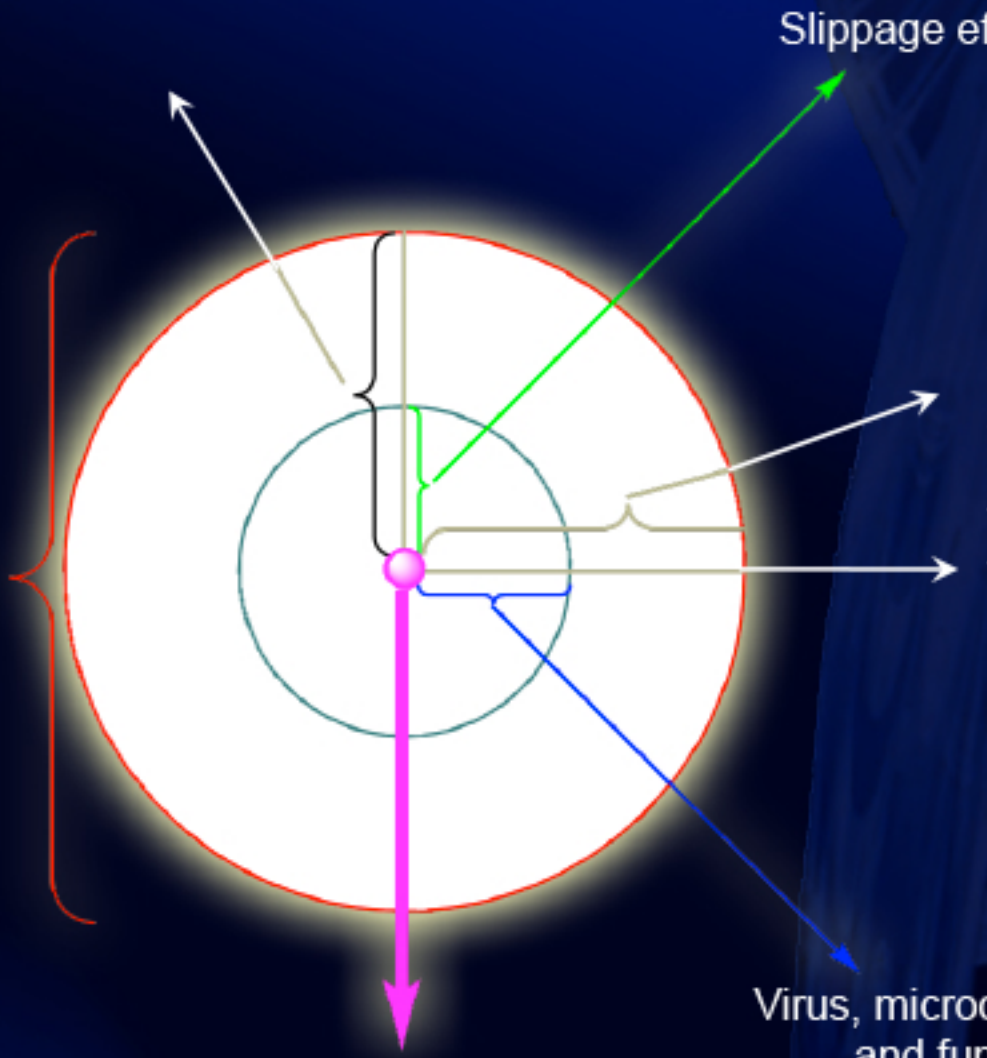
3. Properties of dynamical drugs

A) One **precise polymer** branched irregular structure (protein, DNA, RNA, polysaccharide, tannide) and **millions of derivatives in one mole** of substance are obtained through the **partial modification of the internal groups** of the polymer (acylation of a PART of the lysines in a protein, a PART of the exoclinical amino groups in DNA or RNA). Although it may be one structure out of hundreds of thousands, it conforms to the receptor of a specific patient.

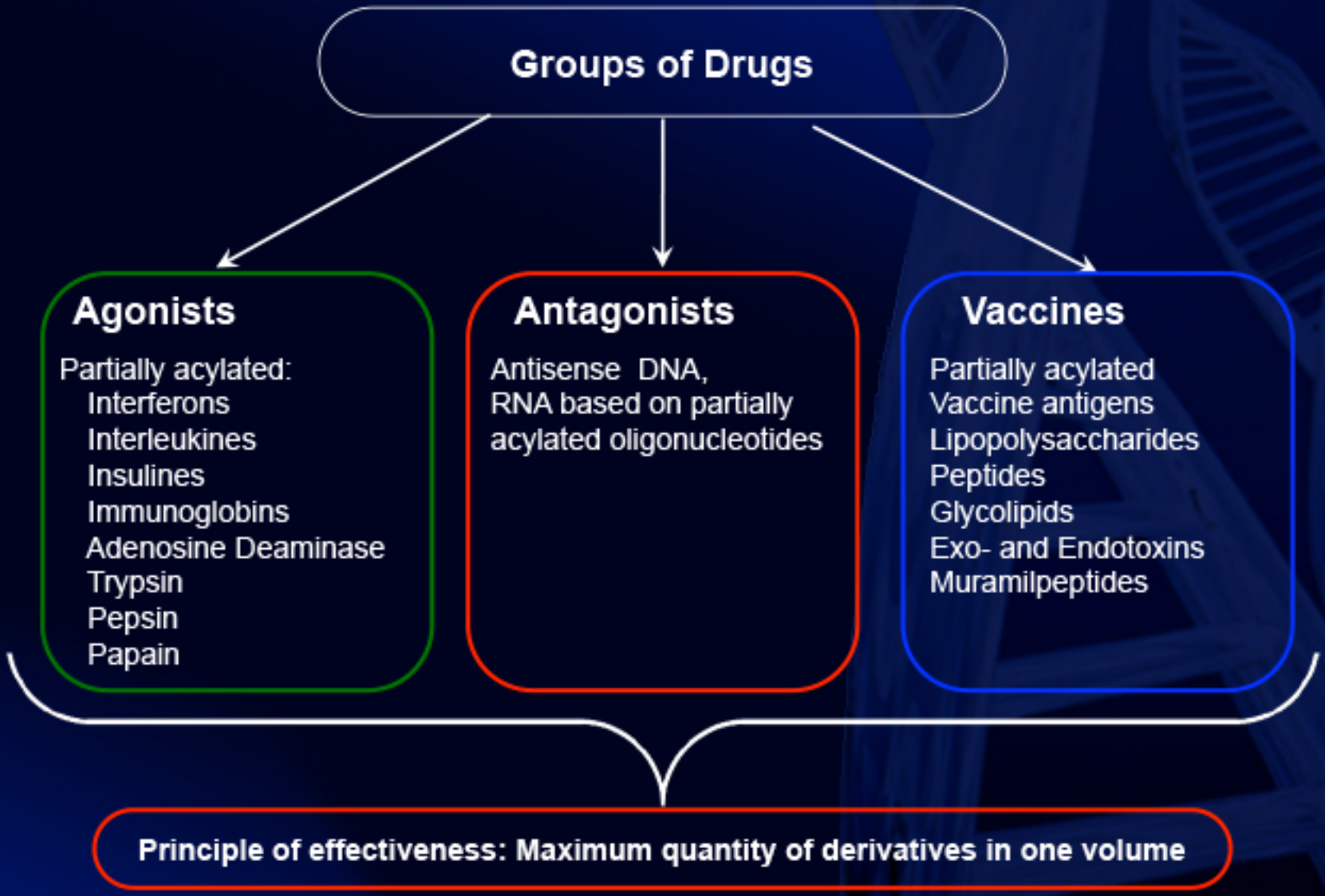
B) **When there is receptor mutation** or delayed receptor polymorphism (**slippage**), the drug will be effective regardless due to the **other derivatives from the content of the same drug**, that did not display effectiveness earlier.

C) **When microorganisms and viruses mutate,** the drug will **be effective regardless**, as among the millions of similar structures, at least one will be effective. The effect is the presence **of predictive structures for targets that do not yet exist.**

4. Predictive structures cover the slippage spectrum



5. Groups of Quasi-life Self-assembled Drugs



6. Molecular modeling as part of the new proposed concept

Classic methods

1. Creation of a 3D model
   - Optimization of the structure based on methods of **molecular mechanics**
   - Refinement and optimization of the inhibitor structure with the use of **semiempirical methods**
2. **Docking** between the model of the inhibitor and the receptor
3. Selection of the models with the maximum **affinity**

Actual effectiveness: 10-15%, which is 100 times higher than that of the screening method

Methods for systems with imprecise structures

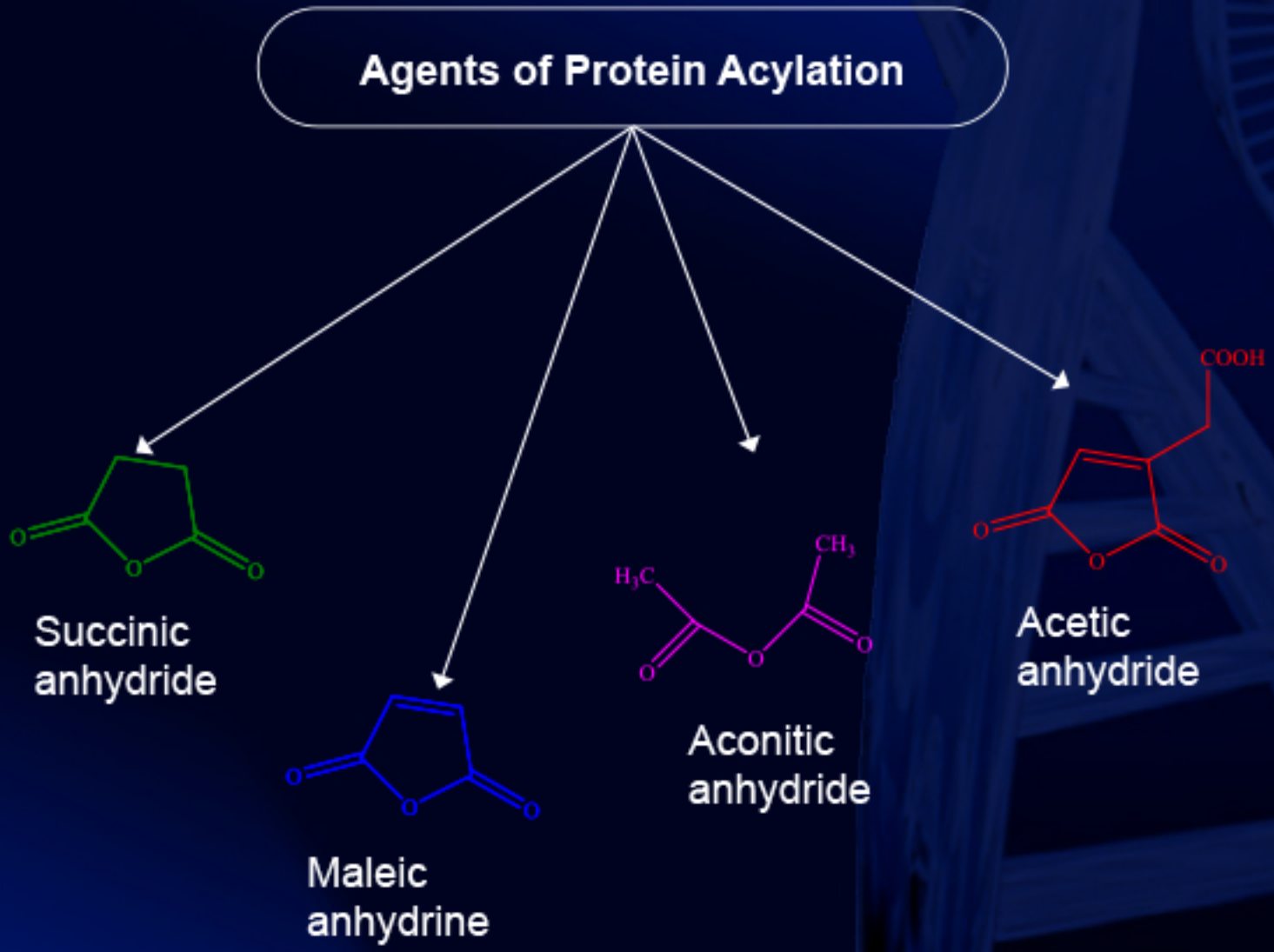
1. Creation of a 3D model
   - Use of long-known structures (amino acids in protein and mononucleotides in DNA and RNA as inhibitor components) to create an inhibitor through the **BIO+** method.
   - Selection of an inhibitor as an ANTIPODE by charge and architechtonic inhibitor surface due to the partial modification of structures **docking with Fourier transformation based on neural networks)**

Actual effectiveness: 45-60%

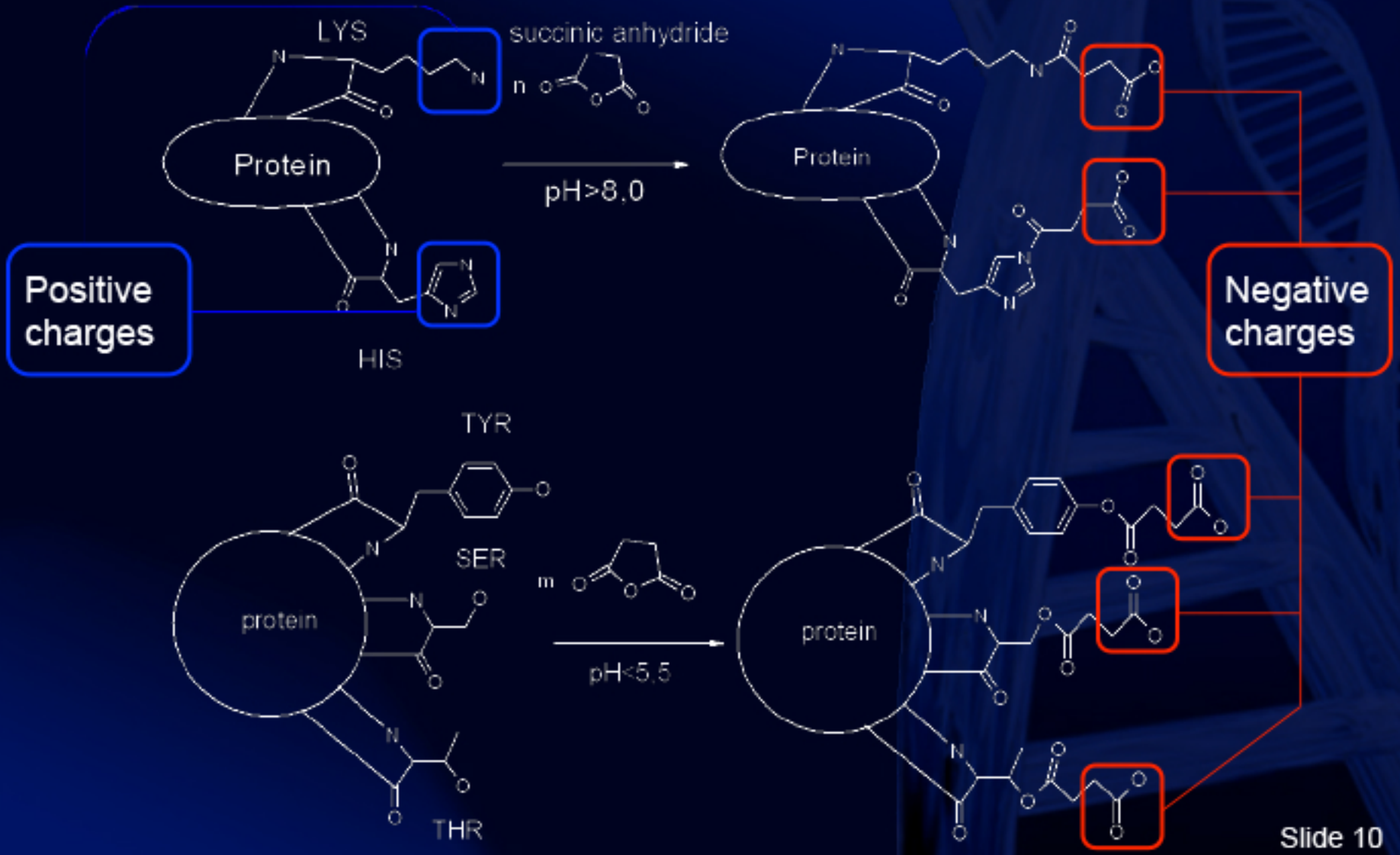
7. Agonist modeling (non-fermented whole molecules)

1. From the x-ray bank, a known structure is taken (**interferon, interleukine**, etc.)
2. A structure is built by a program according to empirical data
3. The quantity of **lysine amino groups, histidines, serines, and threonines** accessible for modification is calculated
4. The necessary **level of modification is calculated** that will provide for the *maximum quantity of various derivatives from one volume of solution*
5. As a result, there is an increase in the activity of these modified proteins by a factor of 10-1000, an increase in the spectra and breadth of activity, and effectiveness in the population is up to 100%.
6. The increase in activity is also facilitated by the change to the molecular charge of the proteins to negative, Through which its affinity to its own receptors are increased *(proven in the example of the increase in virulence of succinylated anti-Legionelle's phages, activity and spectrum of immunoglobulins and interferon)* ***(the drugs Albuvir and Anticanum)***

8. Acylation agents that change a protein's molecular charge



9. Change of molecular charge to negative after acylation (succinylation, maleylation, aconitylation)

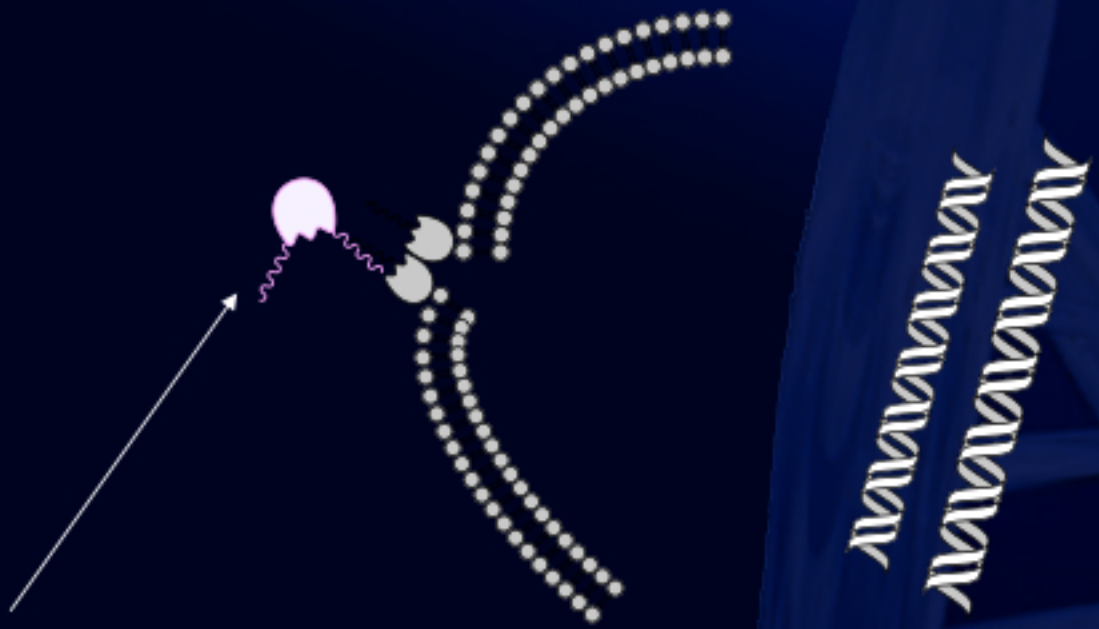


10. Examples of dynamical drugs

Albuvir Contains more than 1 million acylated peptides. It effectively inhibits the process of nuclear importation of viral polynucleotides from those viruses that depend on the cell nucleus (FLU, HERPES VIRUSES, HIV/AIDS)

Anticanum Contains more than 100,000 acylated oligo-RNAs. Only adenocarcinomas and macrophages have the ability to pick up oligonucleotides. The acylated oligonucleotides that have been picked up selectively bond with their predecessors, inactivating them. These predecessors are cancer RNA: transport, matrix, and ribosomal. Basically, there is a full cessation of protein synthesis only in the adenocarcinoma cells (healthy cells do not pick up negatively charged oligonucleotides)

11. The mechanism of the penetration of a viral genome through the nuclear membrane

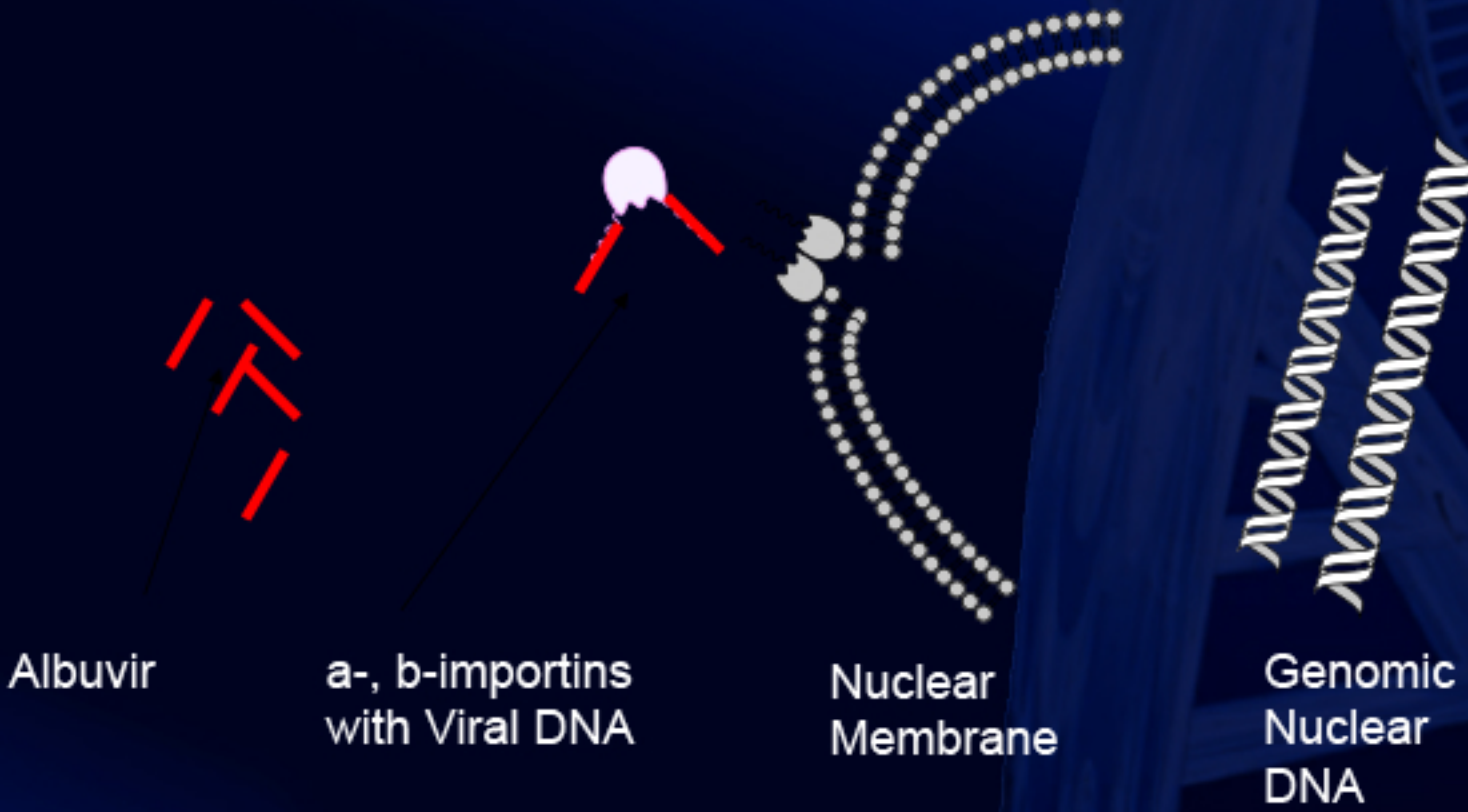


a-, b-importins
with Viral genome

Nuclear
Membrane

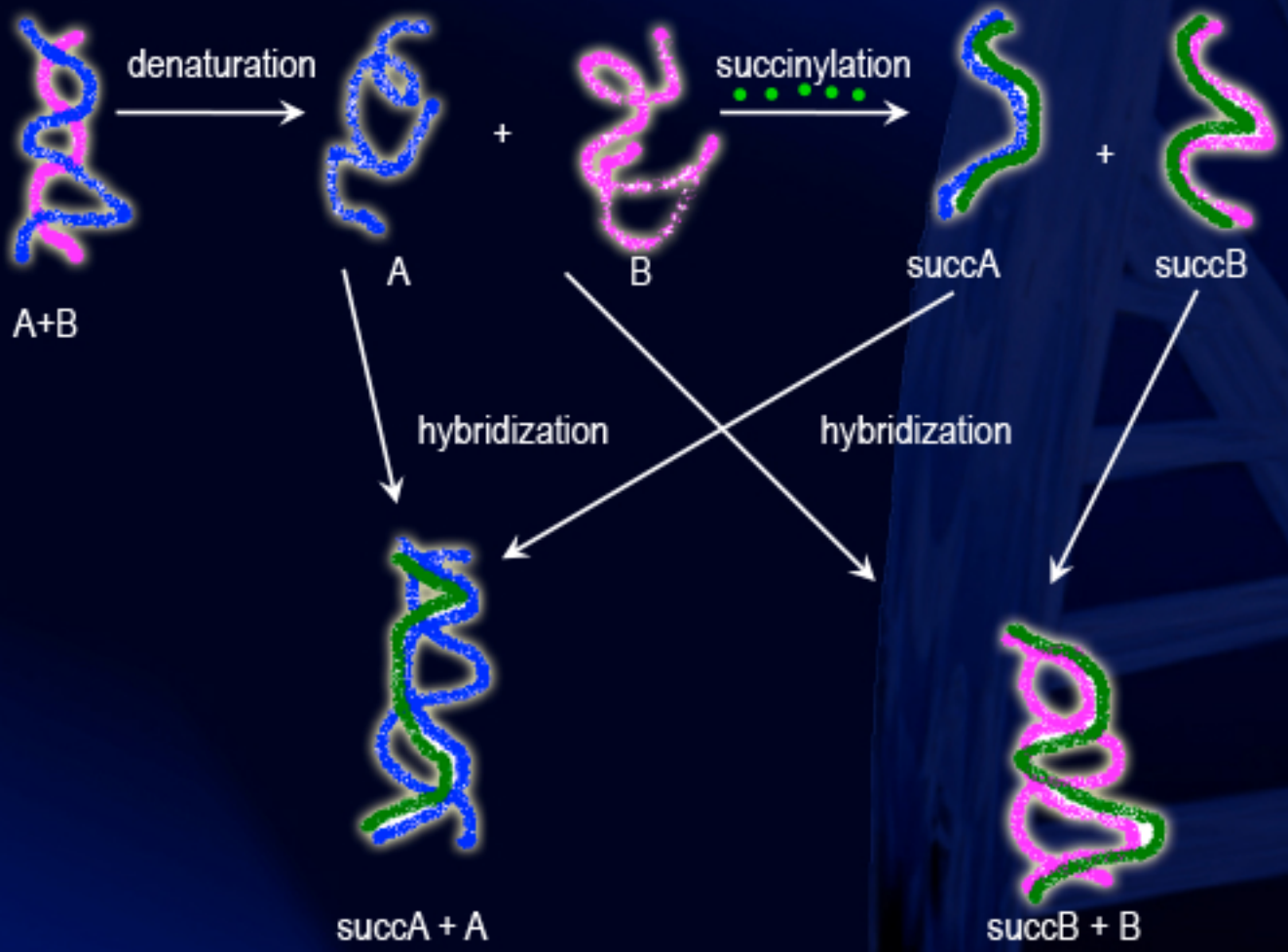
Genomic
Nuclear
DNA

12. Albuvir's mechanism of action

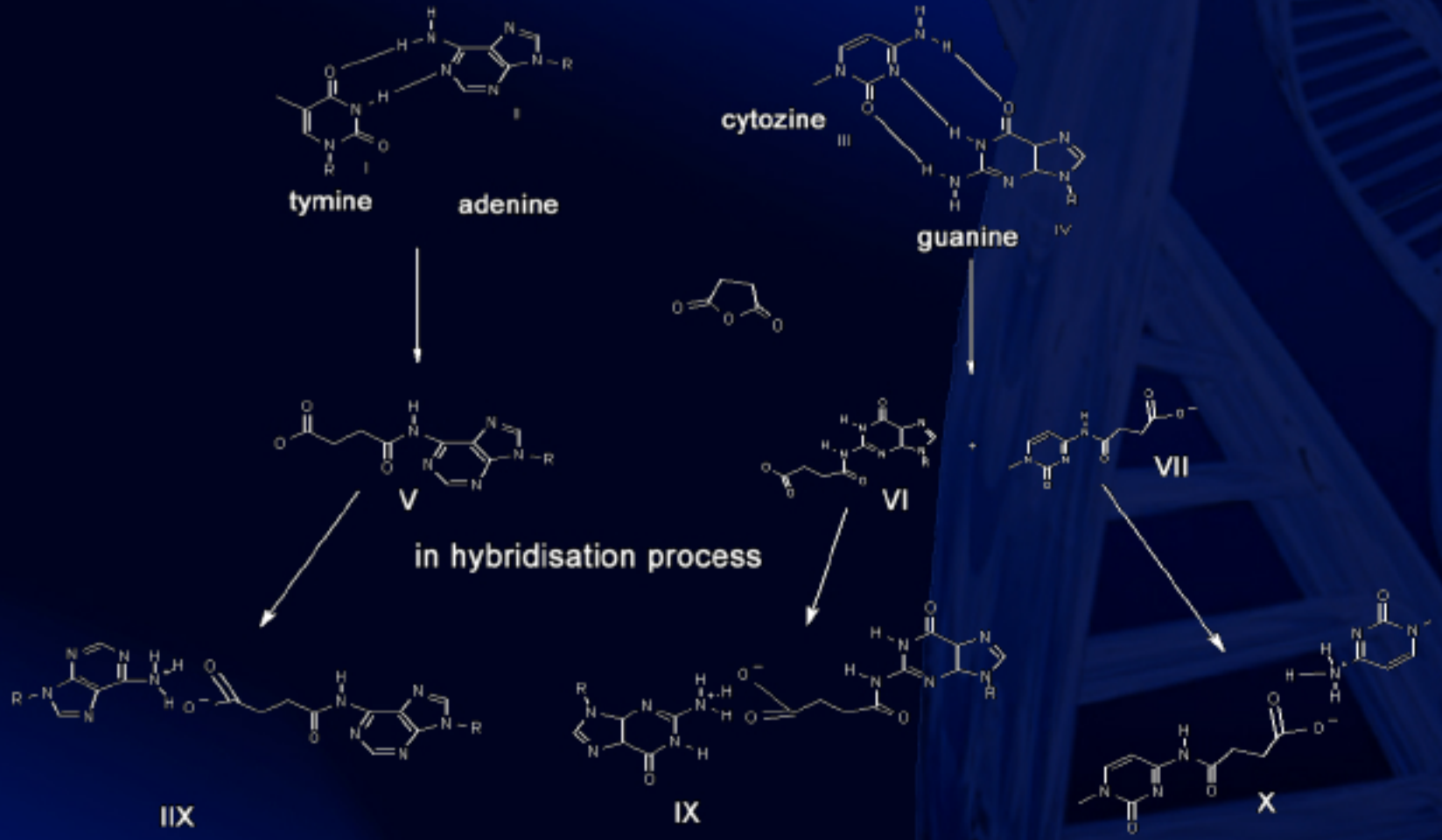


13. Action mechanism of antisense polymorphic RNA

1. The Principle of Selective Specific Hybridization of Acylated RNA with its Predecessors

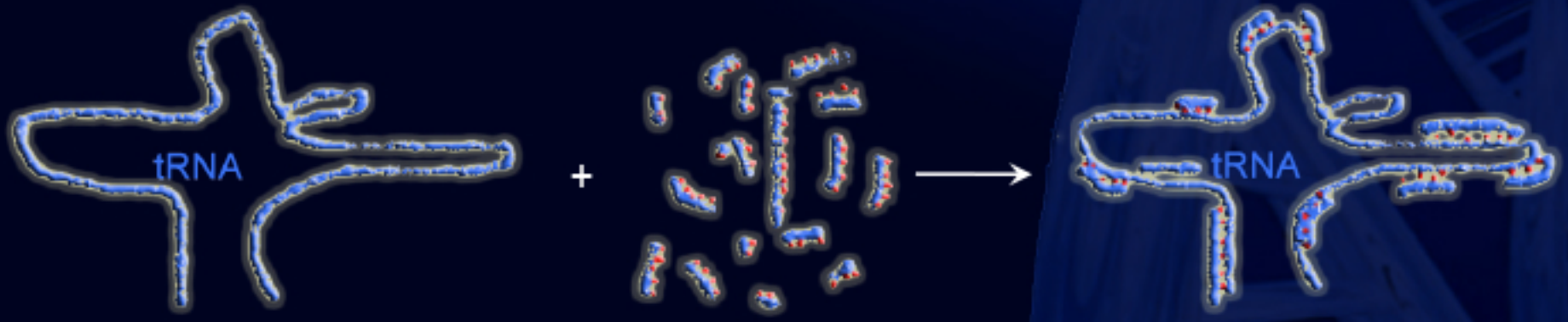


14. The principle of substituting hydrogen bonds in RNA in hybridization with ionic bonds, which are inaccessible to helicase and nuclease



15. The principle of obtaining the anti-cancer drug anticanum based on antisense RNA

16. The principle of the activity of the anti-cancer drug anticanum based on antisense RNA

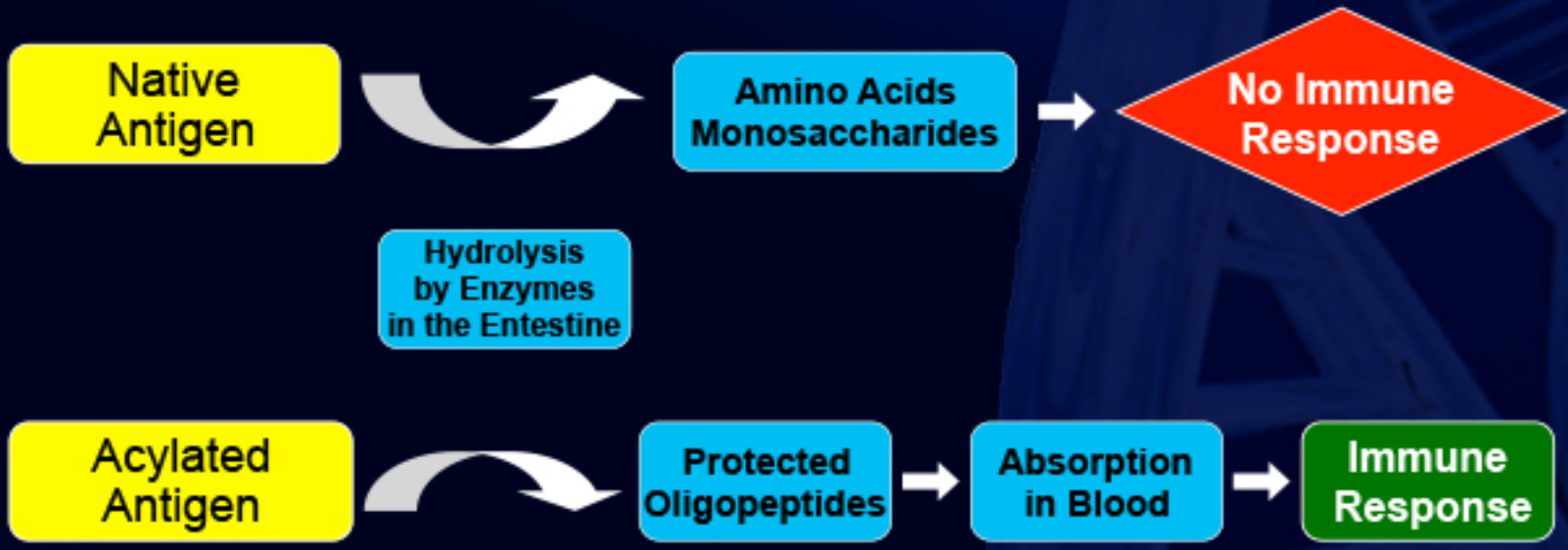


Cancer tRNA

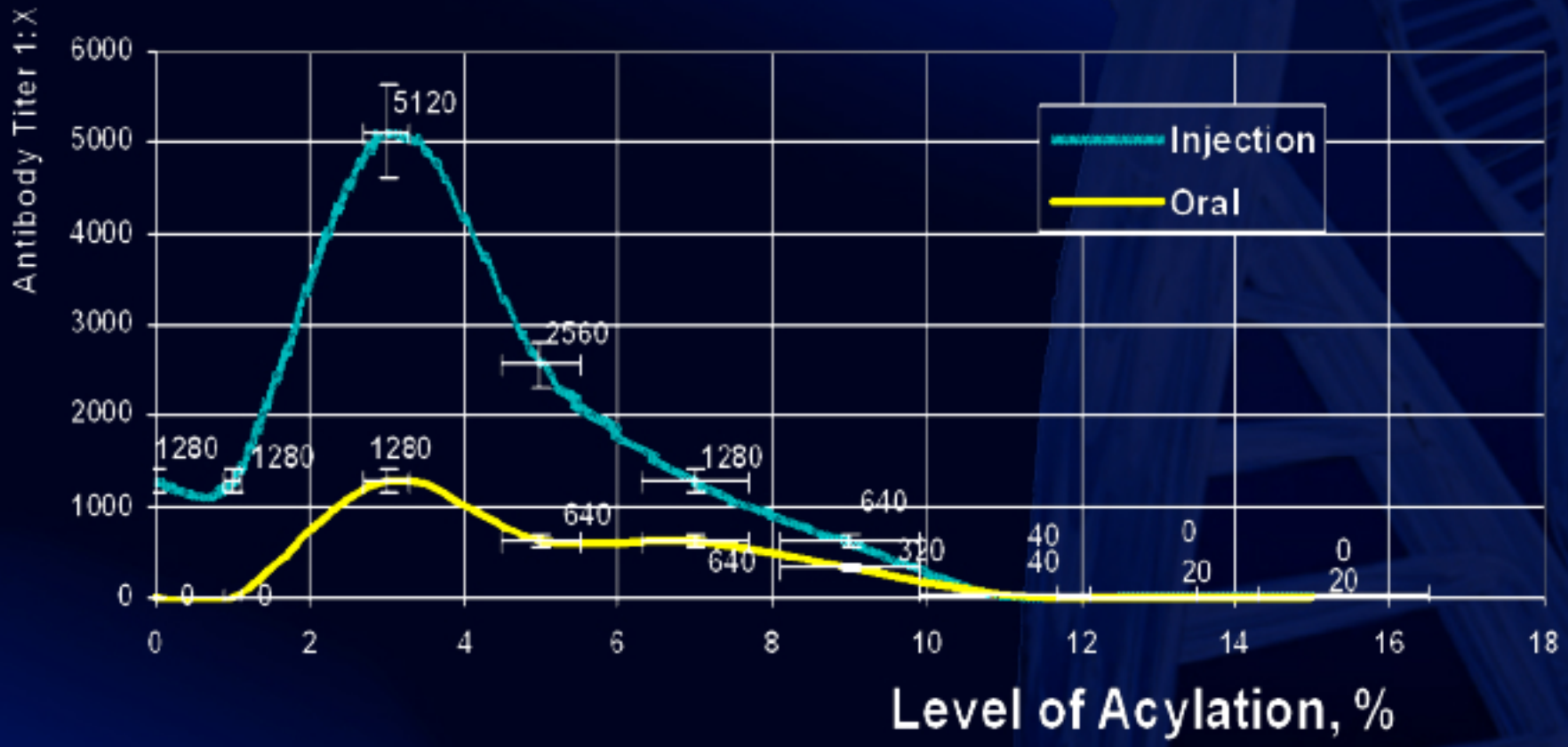
Anticanum

tRNA inactivation through its hybridization with Antacanum fragments

17. The mechanism of action of oral vaccines with partially acylated antigens



18. Dependence between the titer of induced specific antibodies and the level of acylation of a solution of high-molecular acylated pseudomonas antigen



19. Pharmacological properties of the proposed drugs

Albuvir → **Effective in the treatment of:**

LD50=**2880** mg/kg
ED50=25 mg/kg
Ti=115.2
T1/2=29 min
Application method
peroral

1. Influenza
2. Herpes Types 1 and 2
3. Cytomegalovirus Infection
4. Herpes Zoster Virus
5. Epstein-Barr Virus
6. Coronavirus

Anticanum → **Effective in the treatment of (adenocarcinomas only):**

LD50=**340** mg/kg
ED50=5 mg/kg
Ti=68
T1/2=350 min
Application method
Only **intravenous**
slow drip

1. Mammary Gland Cancer
2. Lung Cancer
3. Prostate Cancer
4. Stomach Cancer
5. Carcinoma Metastasis
6. Leukoses, Lympholeukoses, Leukemias

20. Clinical data on volunteers' use of Albuvir

Number of Patients	Name of Disease	Diagnosis Method	Laboratory Diagnostics (name of method and results)		Time of Initiation of Clinical Improvement	Treatment Course
			Before Treatment	After Treatment		
38 (12 women & 26 men)	Influenza (ARD)	Clinical Symptoms	- -		3-6 hours	2 days
2 (1 man and 1 woman)	Hepatitis C	Laboratory diagnostic polymerase chain reaction (PCR) quantitative test	PCR 20-40 thousand genomes in 1 ml	PCR 0-3 thousand genomes in 1 ml	20 (only one subtype "b", resistant to interferon)	40 days until disappearance or decrease of number of genomes in the blood
6 (4 women and 2 men)	Combined infection CMV + HSV-1, -2 Encephalitis	Laboratory diagnostics immunofluorescence method (IFM) quantitative test	IFM from 40 to 60% antigen in lymphocytes	IFM from 0 to 20% antigen in lymphocytes	4-16 hours	20- 30 days until disappearance of antigen from blood
8 (6 women and 2 men)	Combined infection CMV + HSV-1, -2 Dermatitis, etc.	Laboratory diagnostics immunofluorescence method (IFM) quantitative test	IFM from 30 to 50% antigen in lymphocytes	IFM from 0 to 10% antigen in lymphocytes	2-6 hours	2- 3 days to disappearance of dermatitis symptoms
8 (7 women and 1 man)	Epstein-Barr Chronic Fatigue Syndrome	Laboratory diagnostics immuno-fluorescence method (IFM) quantitative test	IFM from 90* to 50% antigen in lymphocytes	IFM from 0 to 10% antigen in lymphocytes	8-12 hours 20	30 days until disappearance of antigen from blood

21. Clinical data on volunteers' use of anticanum

Number of Patients	Name of Disease	Diagnosis Method	Effects of Use	Treatment Course
3	Cervical Cancer (terminal stage, class IV group)	Cytoscopy Histology	Regression of metastasis, halving of tumor size (on the third course)	10 IV drips every other day once a day for 20 days
2	Prostate cancer (terminal stage, class IV group)	Cytoscopy Histology	Regression of metastasis, halving of tumor size (on the third course)	10 IV drips every other day once a day for 20 days
2	Mammary Gland Cancer (terminal stage, class IV group)	Cytoscopy Histology Mammogram Ultrasound	Regression of underarm lymph nodes, decrease in size of tumor (on the third course) to group II	10 IV drips every other day once a day for 20 days
2	Lympholeukosis (terminal stage, class IV group)	Cytoscopy	Five-month remission after 20 days	10 IV drips every other day once a day for 20 days
2 men	Lung cancer (large cell terminal stage, class IV group)	Cytoscopy Histology	Regression of metastasis, full tumor regression (on the third course)	10 IV drips every other day once a day for 20 days

Optimistic vision of a new approach to the design and synthesis of drugs

A new approach to the design and synthesis of drugs will help millions people to survive