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Dynamization of medical drugs – a revolutionary approach in pharmacy

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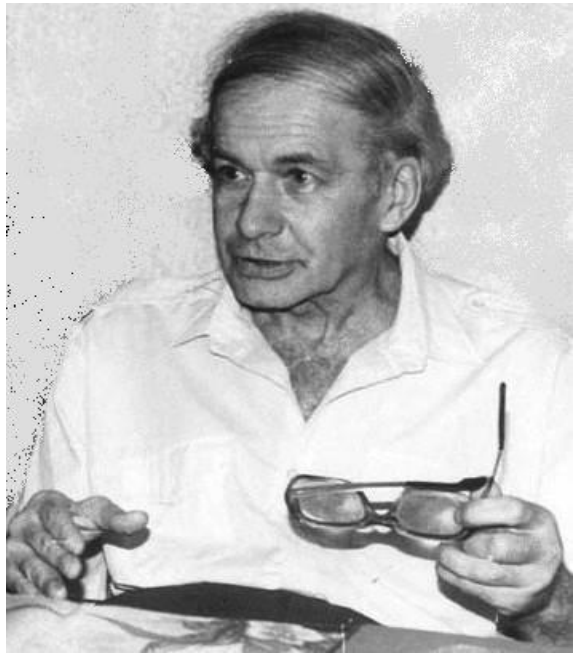
TRIZ is a method of developing New Paradigms



- "Although people who had achieved a great deal in science and technology talked of the inscrutability of creativity, I was not convinced and disbelieved them immediately and without argument. Why should everything but creativity be open to scrutiny? What kind of process can this be which unlike all others is not subject to control?… What can be more alluring than the discovery of the nature of talented thought and converting this thinking from occasional and fleeting flashes into a powerful and controllable fire of knowledge." (From *Creativity as an Exact Science*)

- **In Memory of Genrich Altshuller**

- The authors have introduced a new revolutionary approach Dynamization of medical drugs in pharmacy. Dynamic classes of drugs with variable structures have the ability to adapt to the specific organism of any patient and the target organism such as microorganisms, viruses, or cancer cells. The presentation provides theoretical substantiation, modeling, and practical confirmation for this previously unknown approach based on TRIZ and System evolution.

- Our research in pharma, analysis of the Technical Systems Law trend, and examination of the industry's current state have led us to develop a pioneering approach to drug dynamization. Many companies in the industry are dedicating a larger portion of their net revenues to R&D, surpassing even knowledge-intensive fields like semiconductors and software. Despite an increase in the number of approved new drugs and funding for their development, the effectiveness of some drugs hasn't improved in proportion to the costs. For instance, developing new antibiotics and increasing their dosage doesn't always produce the desired outcome.

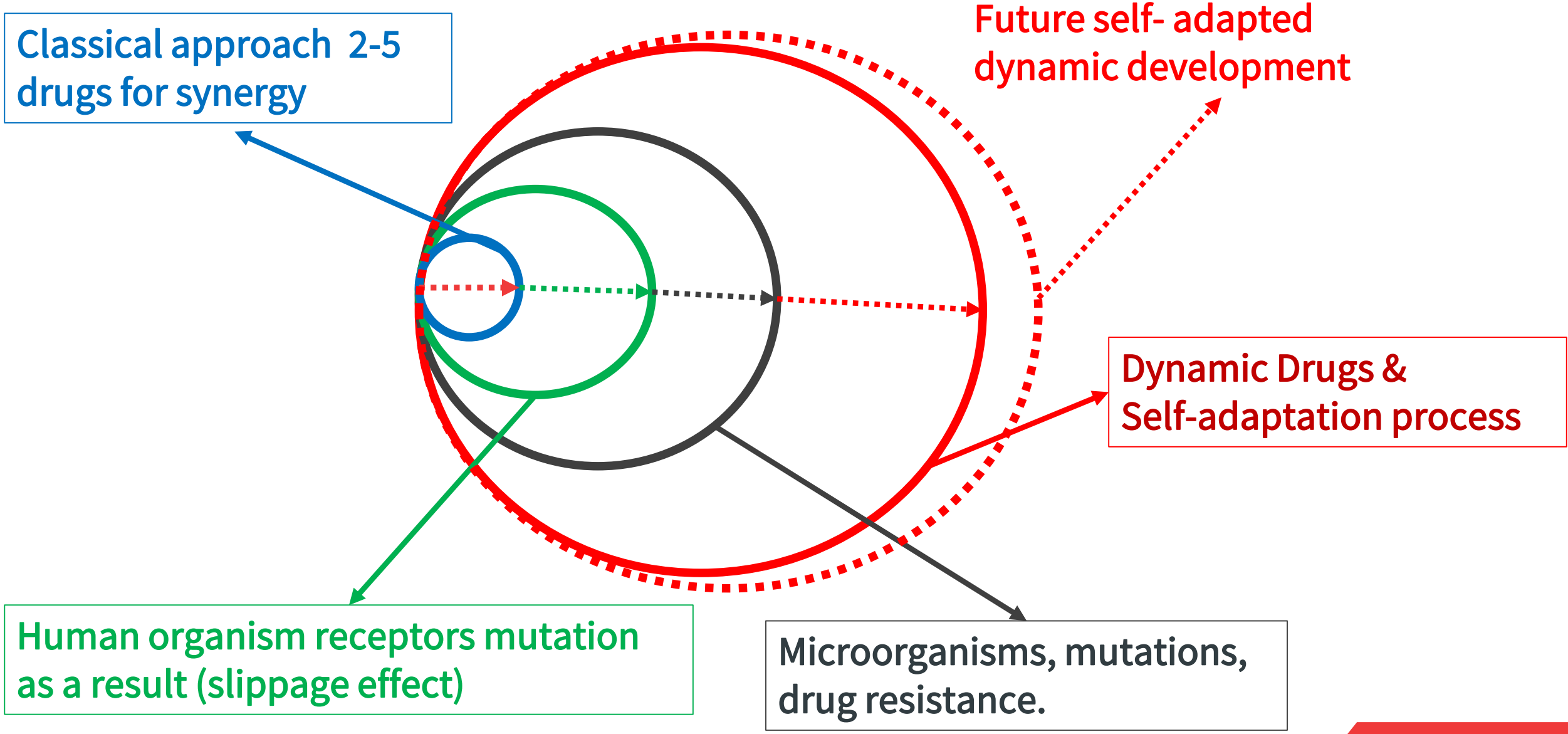
- Improper use of antibiotics can lead to selective selection, which increases the resistance of bacteria to antibiotics. Additionally, antibiotics are ineffective against multidrug-resistant bacteria as they cannot keep up with the bacteria's mutation. After years of research and development, we have created a new class of dynamic drugs that have a variable structure to adapt to the organism they are targeting, whether it is a human body, pathogen, or virus. With these drugs, we no longer need to give large amounts of medication with high dosages or worry about the antibiotic not being effective initially, or the bacteria becoming resistant over time. Dynamic antibiotics prevent bacteria from adapting and becoming resistant.

- We have developed a class of drugs known as "dynamic drugs." One of these drugs is a dynamic anticancer agent that is based on RNA. When tested on animals with inoculated tumors, this drug protected them from death, while the control groups experienced fatalities by the end of the experiment. Another drug, called dynamic insulin, can be taken orally in tablet or solution form. Unlike injectable forms of insulin, dynamic insulin doesn't typically cause hypoglycemia (a drop in blood glucose levels).

NOVEL Drugs Development

NOVEL Drugs with dynamic structures (Dynamic drugs) based on TRIZ expertise

Classic pharmaceutical vs. NOIGEL approach

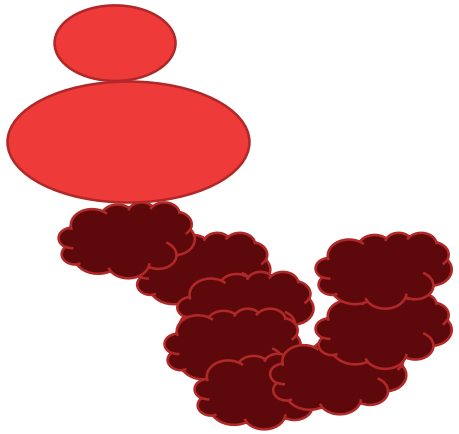


Novel anti-cancer Dynamic Drug Antican

Polyribosome and mRNA mechanism in action

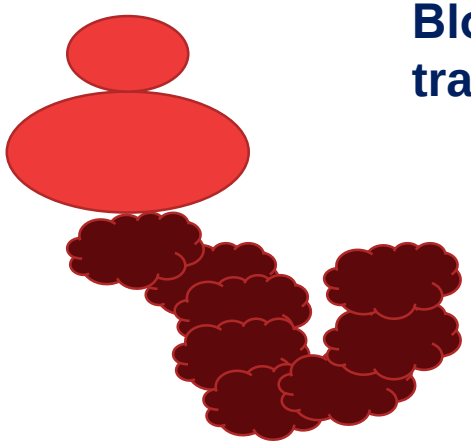
Polyribosome

mRNA



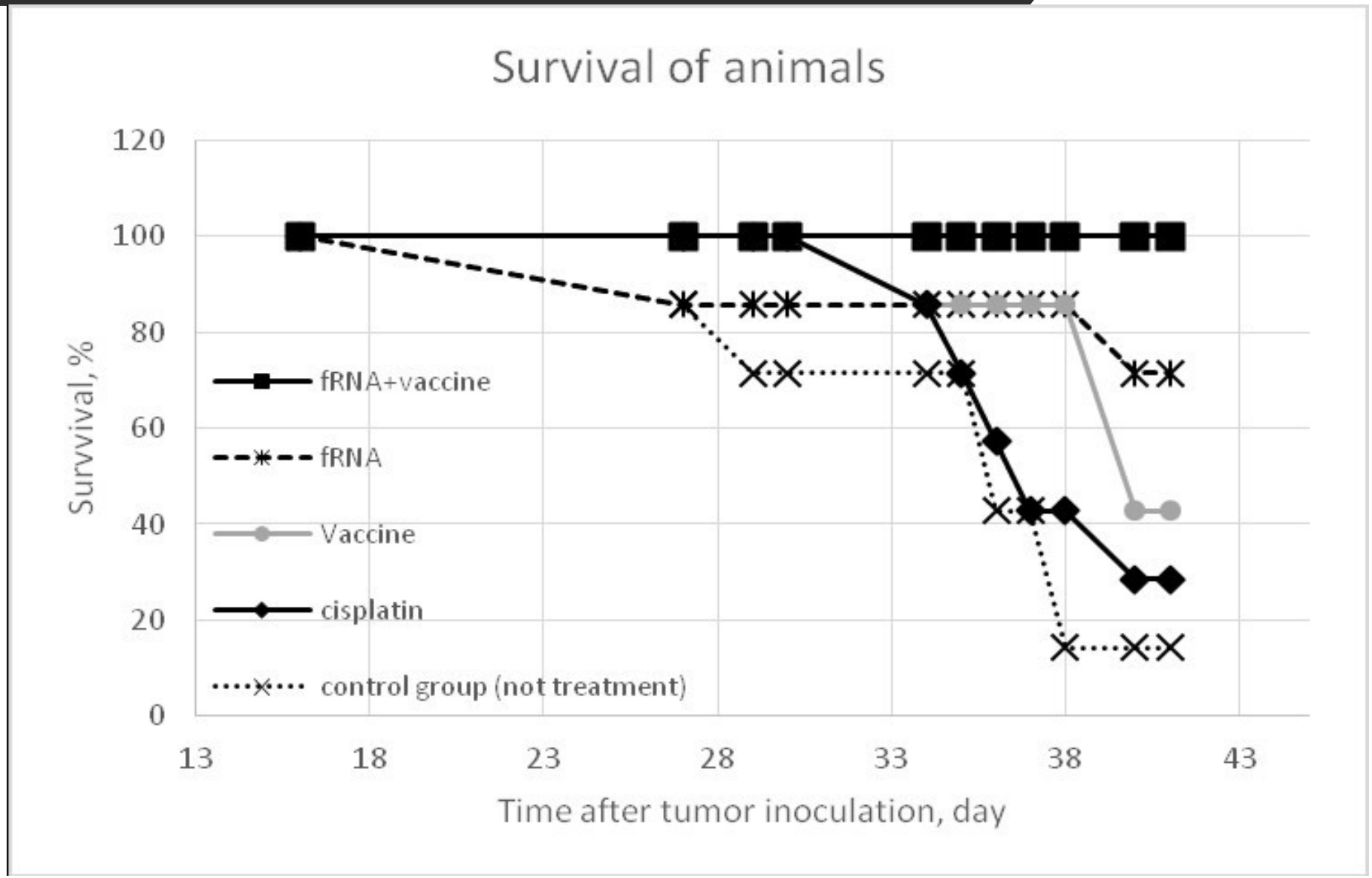
Translated protein

Blockage of protein's translation

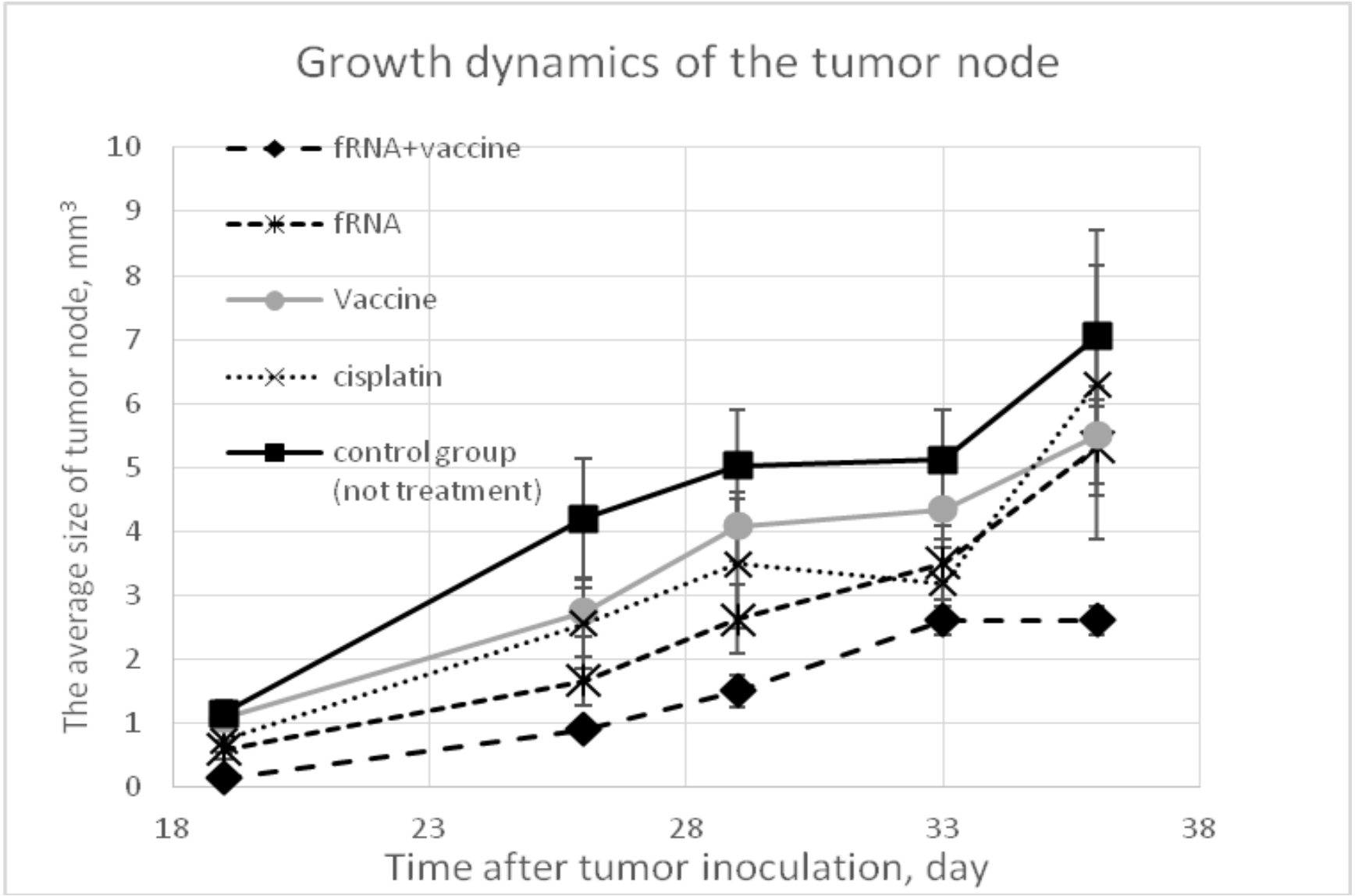


Fragment m-RNA- fRNA

fRNA efficacy in vitro (Lewis lung carcinoma (LLC)

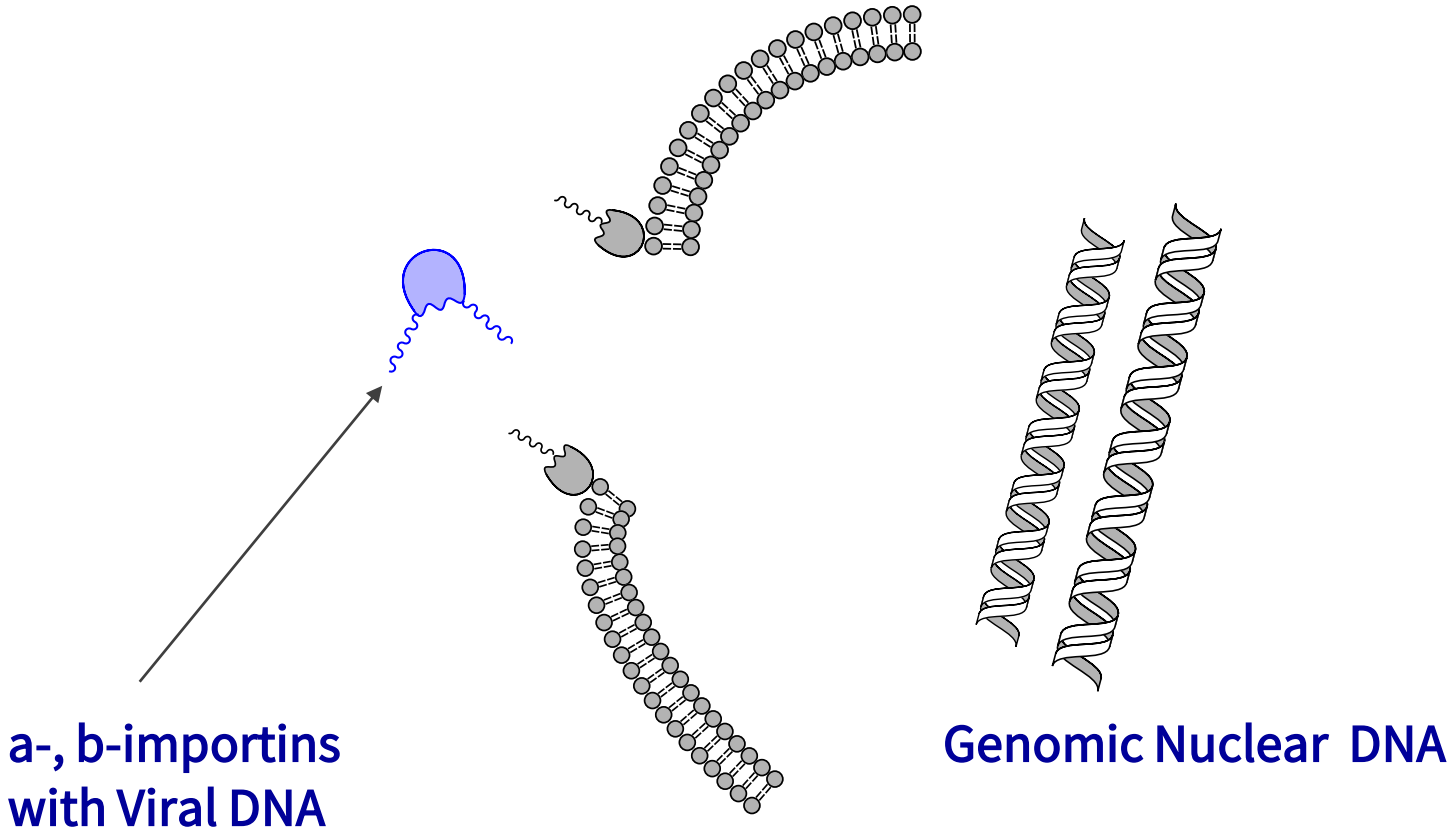


The fRNA influences the dynamics of the tumor node growth

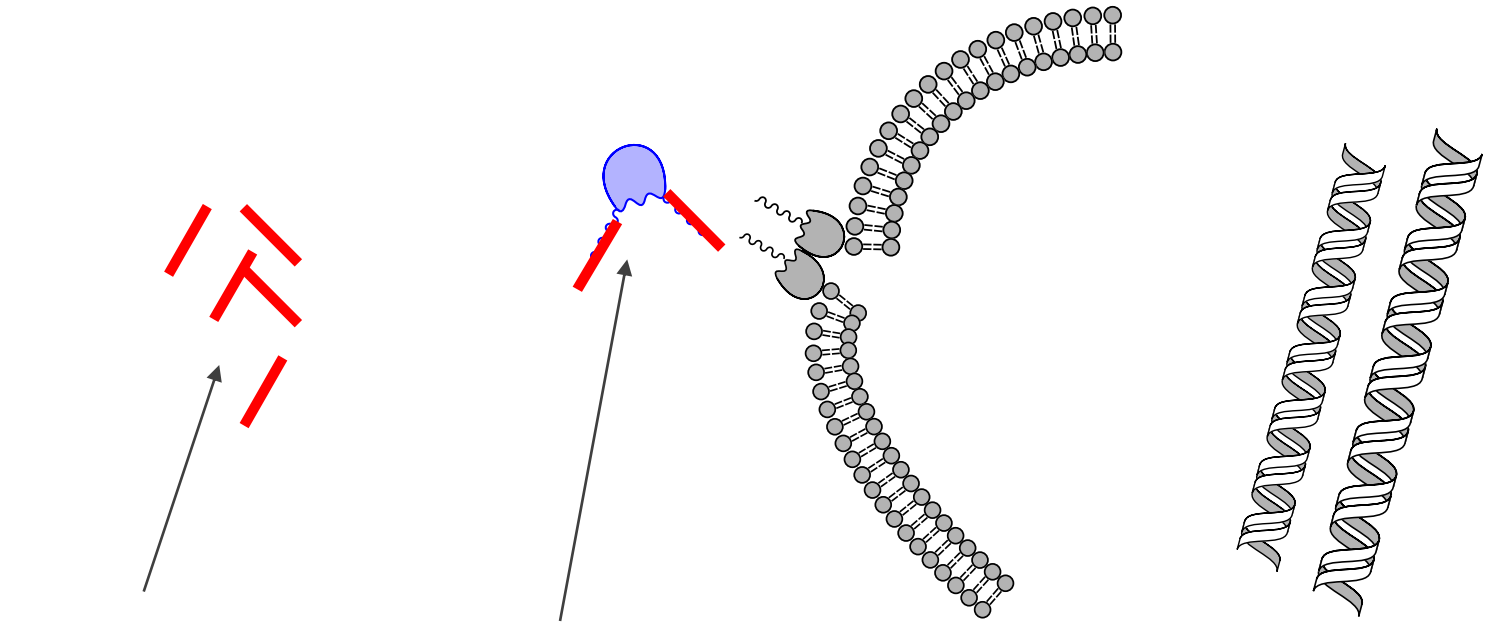


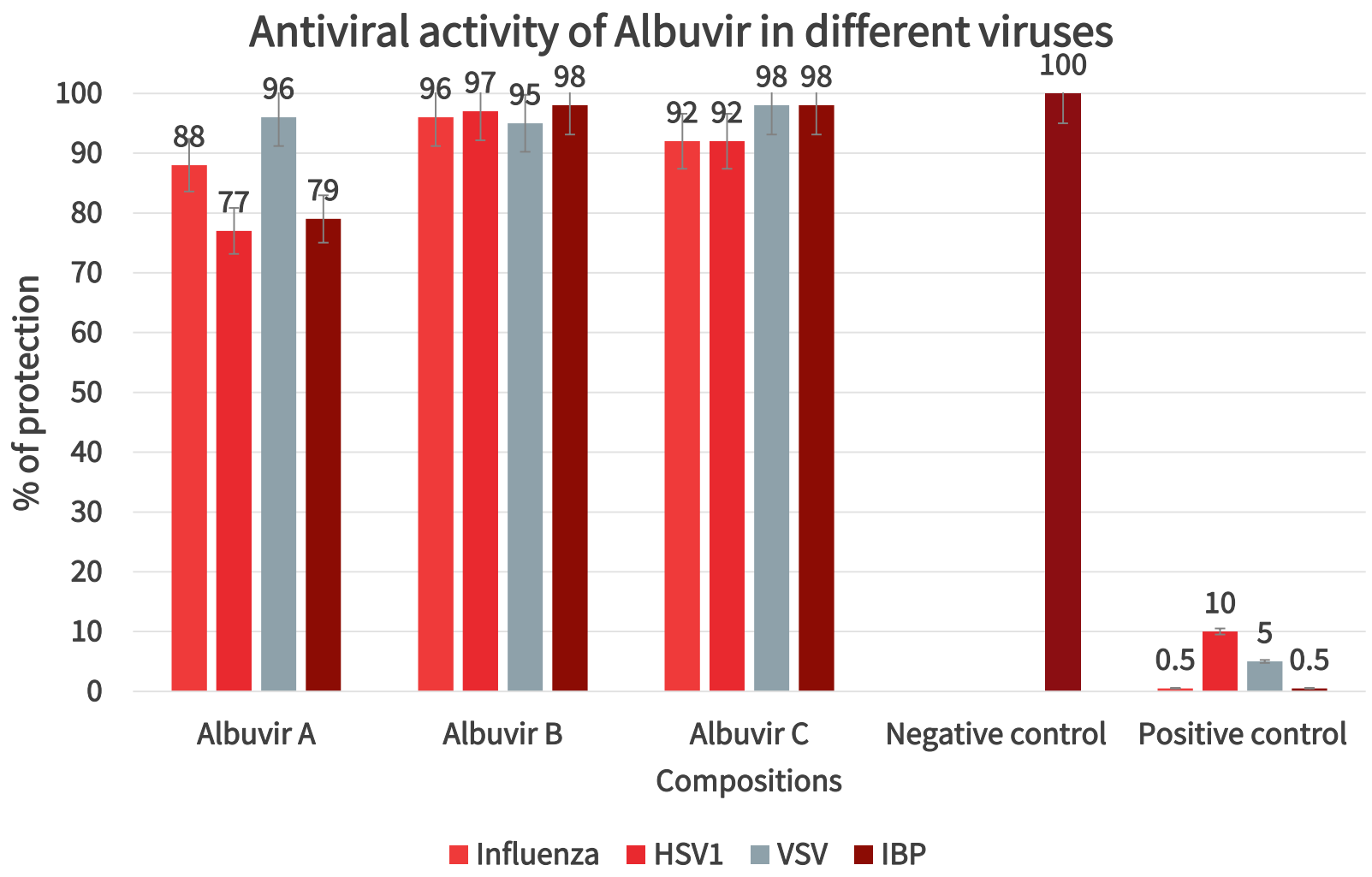
Novel antiviral Dynamic Drug Albuvir

The Mechanism of the Penetration of a Viral Genome through the Nuclear Membrane



Albuvir Mechanism of Action





Negative control – cells culture without viruses;
Positive control - cells culture with viruses; %- part of survived cells after infected

Table . Effective Albuvir A concentration in the in ovo influenza infection model

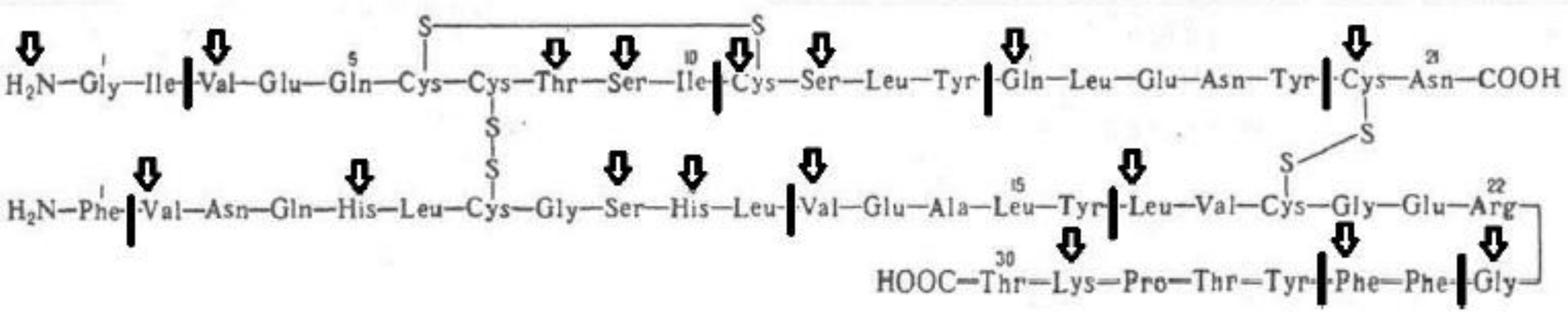
Group	The concentration of the drug (mg / ml)	Virus titer (lg $TCA_{50/мл}$)		Minimal effective concentration (MEC mg / ml)
		Experience (with drugs)	control (without drugs)	
Control (0.9% sodium chloride solution was injected)	-	12	12	-
Experienced Albuvir A	50±5	0	12	0,005
	5±1	0	12	
	0,5± 0,05	1	12	
	0,05± 0,005	2	12	
	0,005± 0,0005	5	12	
	0,0005± 0,00005	10	12	

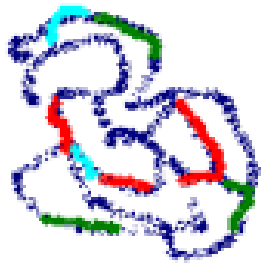
The level of inhibition of the Epstein-Barr virus reproduction under the influence of various concentrations of the studied drugs. PCR method

Concentration µg / ml	Epstein-Barr virus reproduction inhibition rate (%)		
	N 1	N 2	Acyclovir
0,1	20	0	0
0,5	50	10	0
1	56	50	0
5	67	62	0
10	80	70	10

Novel Dynamic Derivative of an Insulin

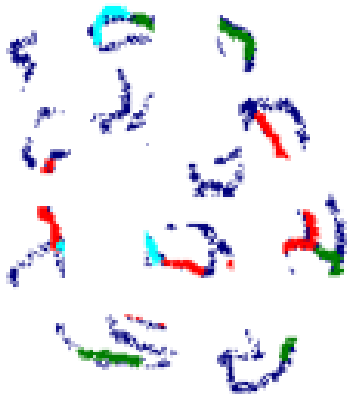
Black bars show places of insulin hydrolysis, when it is treated with pepsin: only seven peptides are produced, the amino group that should be attacked by anhydride are shown by black arrows (the number of groups available for acylation-n = 17).





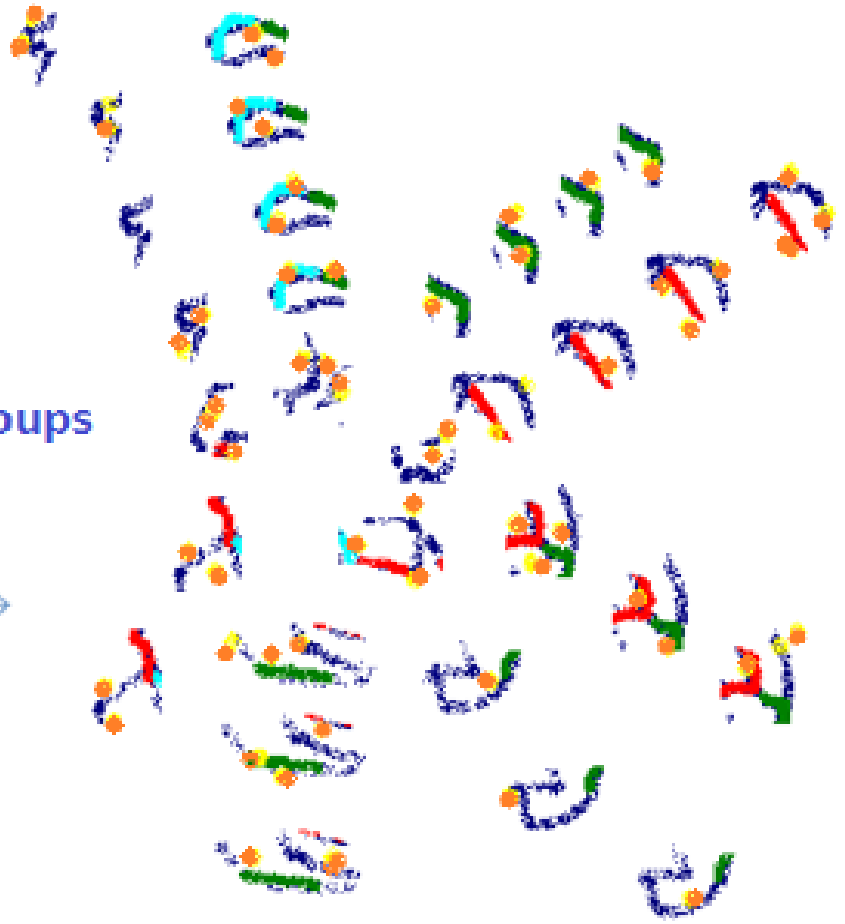
Insulin

Partial hydrolysis



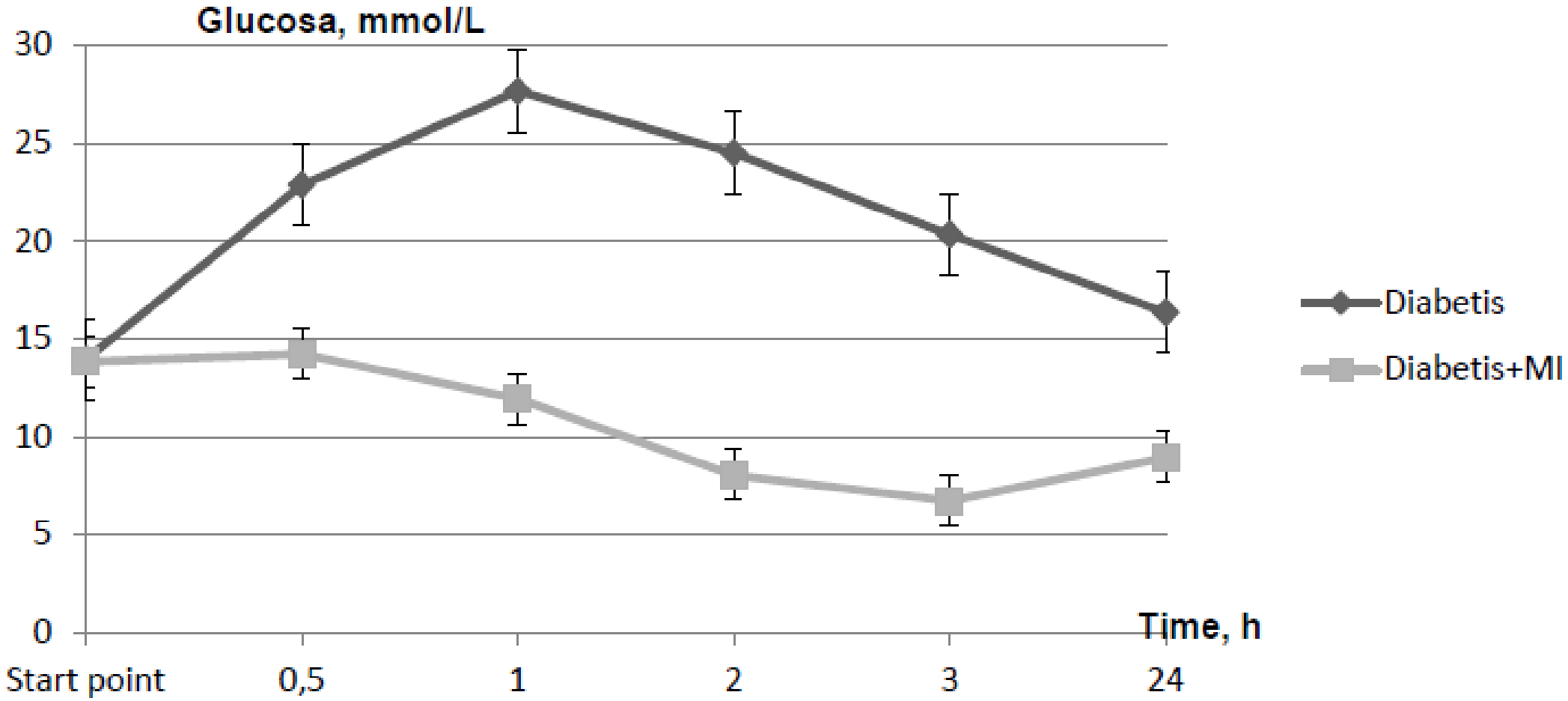
Partial Chemical
Change of -NH2 - groups
in -COOH groups

generates huge quantities of fragments with the same basic structure but different charges and placement of substituted groups (shown in orange)



self-organization is ensured by the fact that all the fragments were previously part of the whole and fit together like hand in glove to

The effect of MI on after-load glucose level in blood of rats with alloxan diabetes



- The quasi-living system based on **dynamic derivatives of insulin** has shown high biological activity when administered **orally** in rats with alloxan diabetes. The system promoted a reduction in glucose level to 10 mmol/L on average and maintained this level within 24 hours after a single application. It can be considered a candidate for development and implementation in the capacity of oral insulin. The efficiency of the preparation was confirmed in animals by using both fasting and glucose load.

- New dynamic peptide drugs such as alpha-interferon, gamma-interferon, and interleukin-2 have a wider range of effects on tumors compared to traditional drugs. Other dynamic drugs are also being developed using low molecular weight compounds. This approach involves creating a new class of dynamic drugs with a variable structure that can adapt to the patient's needs. The authors have obtained patents for these dynamic drugs in various countries worldwide to protect their development.

The optimistic vision of a new approach for the design and synthesis of Dynamic & Synergistic drugs.

2023

Q&A

SESSION

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THANK YOU!

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