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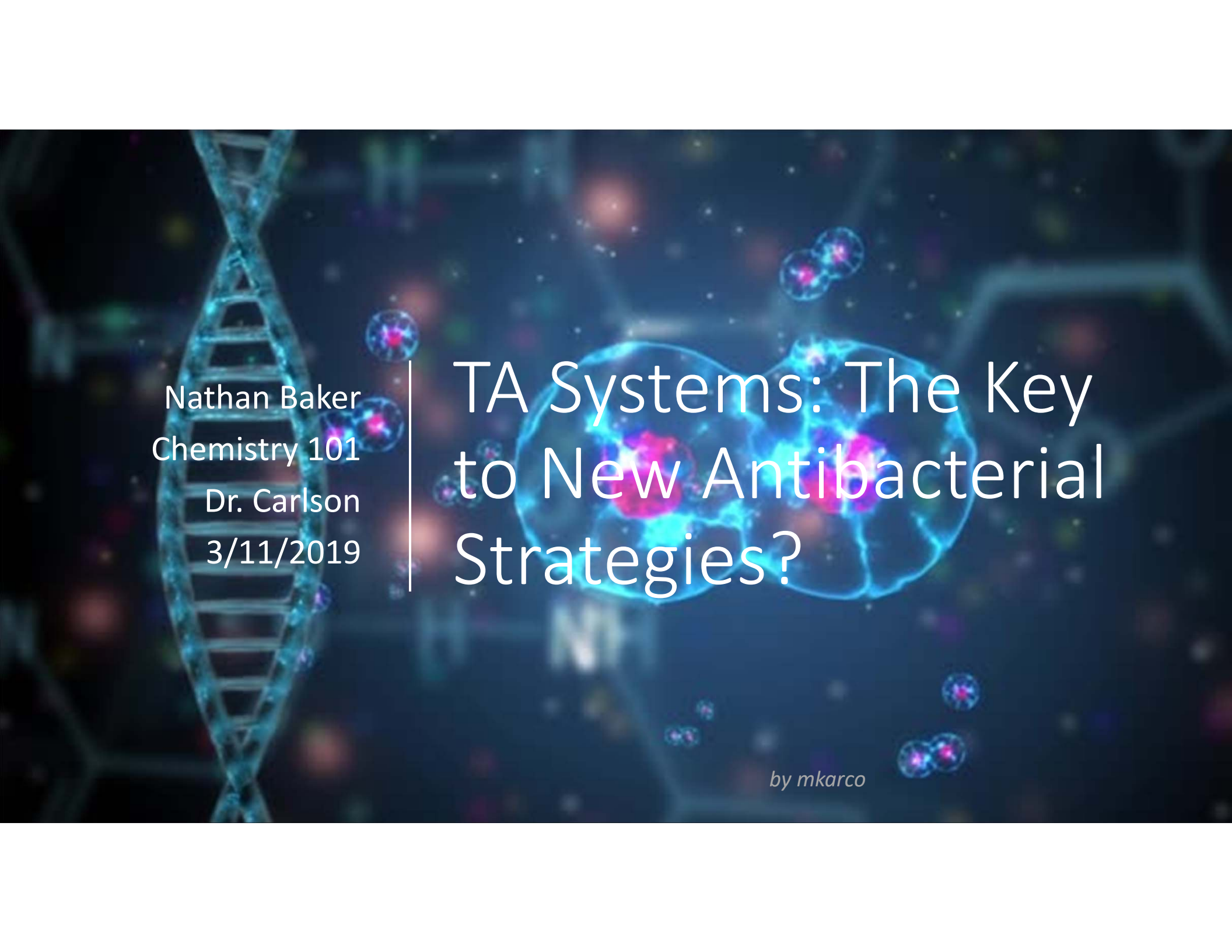
TA Systems: The Key to New Antibacterial Strategies?

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3/11/2019

TA Systems: The Key to New Antibacterial Strategies?

by mkarco

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A brief history of antibiotics

- The first major antibiotic, penicillin, was discovered in 1928 by Sir Alexander Fleming (Ventola 1).
- Though the drug was saving lives for a while, resistance to the drug was first observed in the 1950s (Ventola 1).
 - To remedy this, new antibiotics were developed and used (Ventola 1). Unfortunately, the bacteria eventually became resistant to every one of the antibiotics that were created (Ventola 2).
- Antibiotics work by inhibiting the growth of the bacteria's cell wall (Porter, digitalworldbiology.com). Some growth inhibiting antibiotics inhibit the main functions of the bacterium: DNA replication, protein-making, and the making of the cell walls (Porter, 1).



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How do they work?

- Antibiotics work by inhibiting the growth of the bacteria's cell wall (Porter, 8). Some growth inhibiting antibiotics inhibit the main functions of the bacterium: DNA replication, protein-making, and the making of the cell walls (Porter, 8).
- Unfortunately, antibiotic resistance is a serious problem (Ventola 1).

Where are we now?

As of 2015, bacterial infections are still a serious problem (Ventola 2). However, the *artificial activation of TA systems* was shown as a viable method to hinder the growth of *Esherichia coli* (*E. coli*) (Rownicki et al 3). This method has prospects as an alternative strategy to the antibiotic problem (Rownicki et al 3).



By depositphotos

TA Systems

What they are, what they do, and how to use them.

TA systems—what do they do? What are they?

TA systems or "toxin-antitoxin" systems are pieces of genetic "code" in bacteria that contain a toxin and a subsequent, neutralizing antitoxin (Rownicki et al 1). The activation of this system inhibits bacteria growth via *post-segregational killing* (Rownicki et al 1).



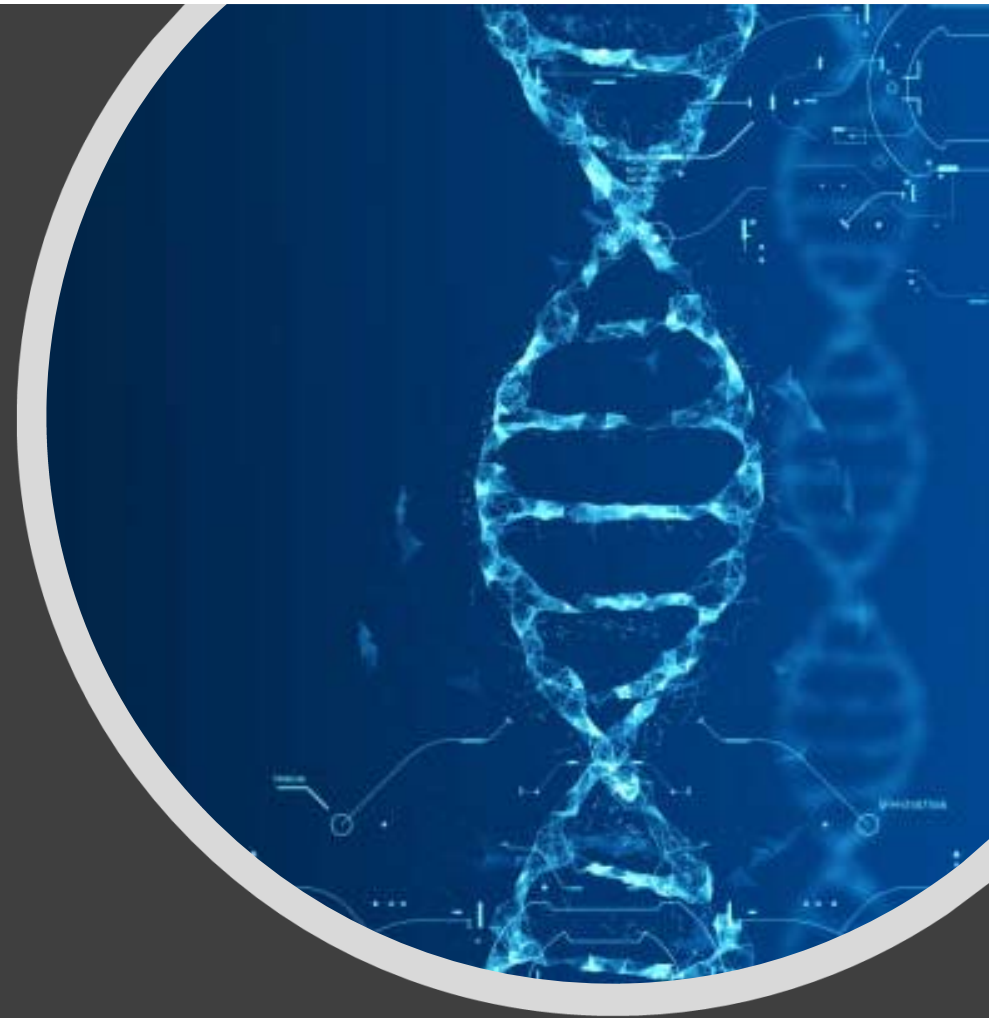
By vchalup

Post-segregational killing

Post-segregational killing is the result of losing the TA gene during the cell division process, which results in the replicated antitoxin to degrade faster than the toxin (Coray et al 1). Once the antitoxin degrades, it can no longer neutralize the toxin, resulting in the cell's death (Coray et al 1).

Utilizing TA systems for antibacterial purposes

The artificial activation of TA systems would result in the inhibition of bacteria growth (Rownicki et al 1). In the study conducted by scientists of the University of Warsaw, the *mazEF* and *hipBA* *E. coli* TA systems were successfully activated (Rownicki et al 3). This resulted in the inhibition of the growth of the *E. coli* (Rownicki et al 3).



By Antiv3D

How to artificially activate a TA system

In the study, PNAs (peptide nucleic acids) were used to target the TA systems in the *mazEF* and *hipBA* *E. coli* (Rownicki et al 2). Peptide nucleic acids are modified antisense oligonucleotides (Rownicki et al 2). Regular antisense oligonucleotides bind to specific sequences of nucleic acids but tend to degrade rapidly when inside a cell (Rownicki et al 2). Instead, PNAs were used because they are more robust when inside a cell (Rownicki et al 2).

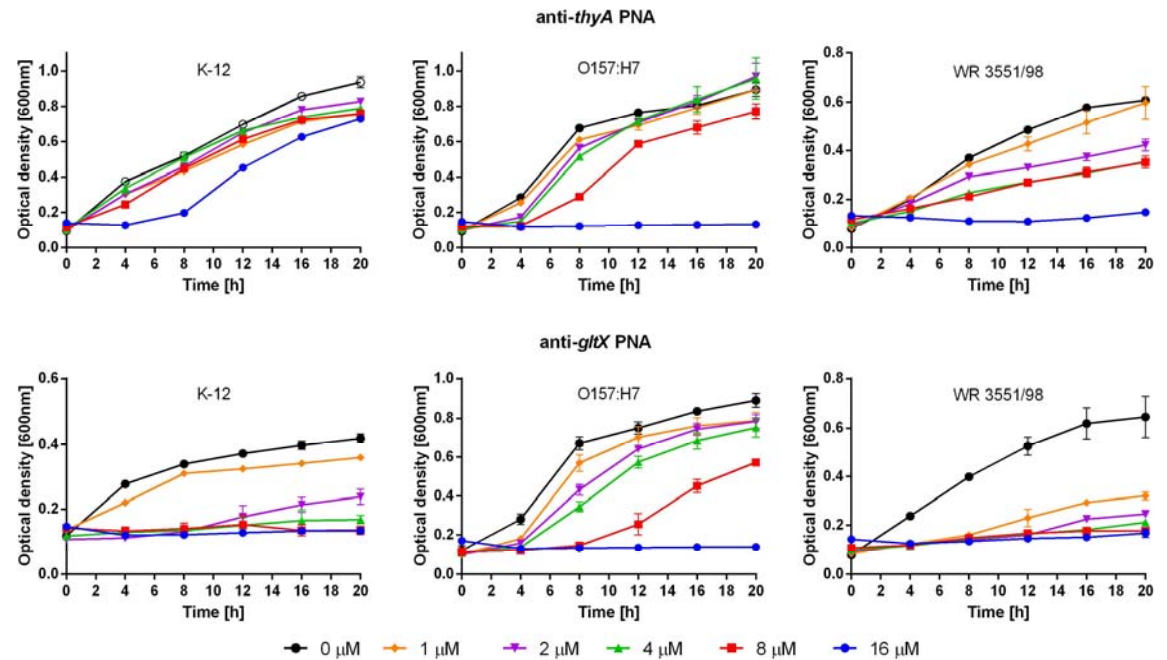


By Cinemarama

The Results

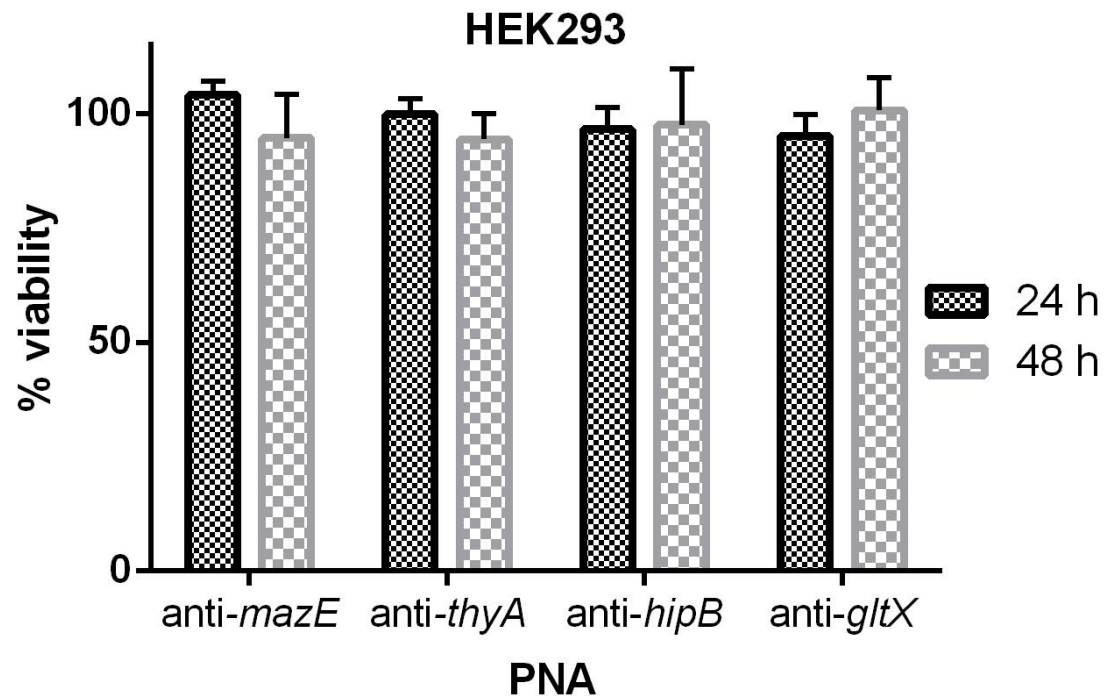
It was found that the PNAs caused the growth of the *E. coli* to be hindered (Rownicki et al 4).

The colored bars on the graph represent the different concentrations of PNAs applied (Rownicki et al 4).



Safety concerns

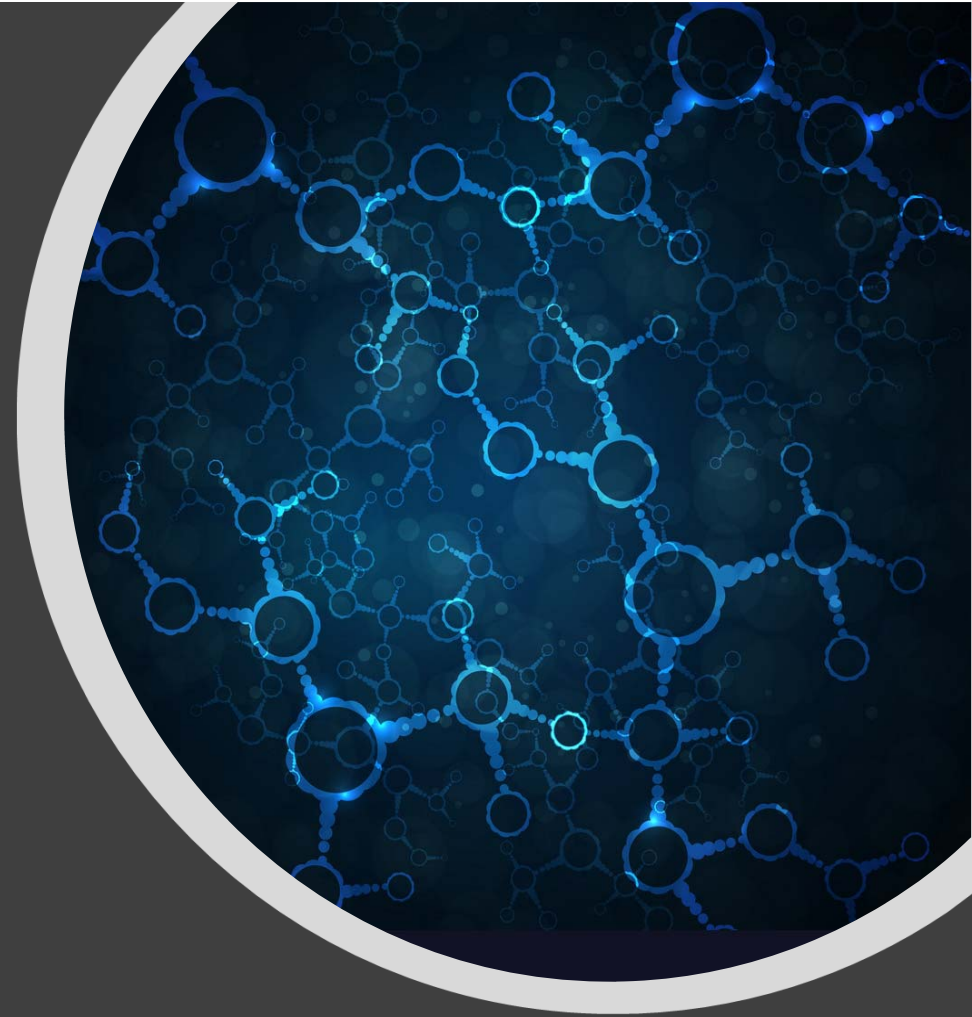
The sequence-specific PNAs actually have a negligible effect on human cells. According to the study, no toxicity was observed in the human test cells after 24 and 48 hr treatments with PNAs. (Rownicki et al 5).



This illustrates the cytotoxic effect of the PNAs at a concentration of 32 μ M. This was tested on HEK-293 cells. The bars are illustrated as the relative viability (%) compared to natural, unmodified control cells (Rownicki et al 6). (Image taken from study: Rownicki et al 6)

Conclusion

Using the PNAs as a method to activate the TA systems is a viable option (Rownicki et al 4). PNAs do not harm the human cells either (Rownicki et al 5).



By majcot

Works cited

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