Engineering at the interface of RNA-protein complexes for solving difficult problems in biology and medicine

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What does Artic foxes and drug-resistant bacteria have in common?

Summer Environment

Summer Environment

A challenge in fighting pathogenic bacteria

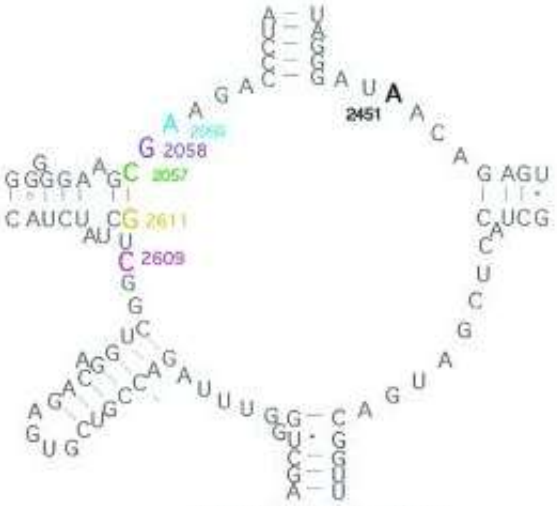
- Disease-causing microbes that have become resistant to antibiotic drug therapy are an increasing public health problem.

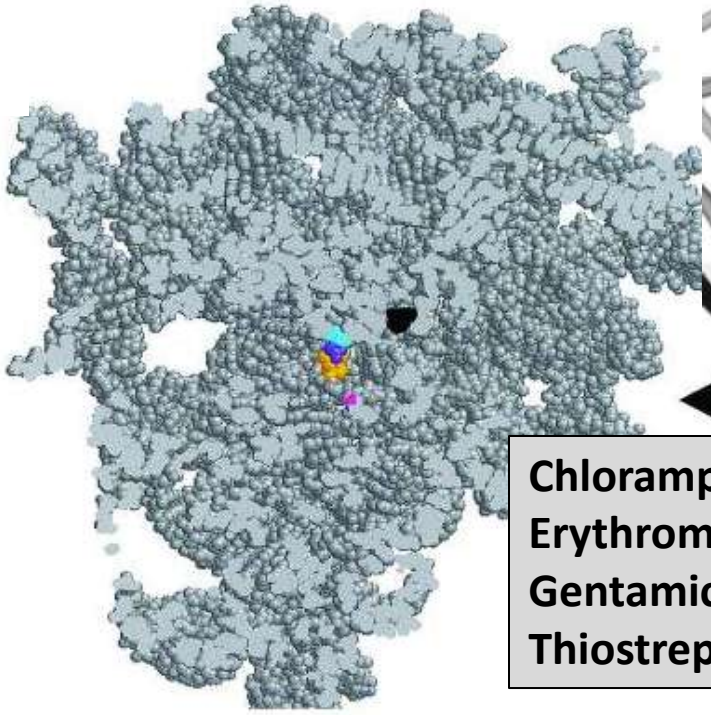
- ~ 70 percent of the bacteria that cause infections in hospitals are resistant to at least one of the drugs most commonly used for treatment.

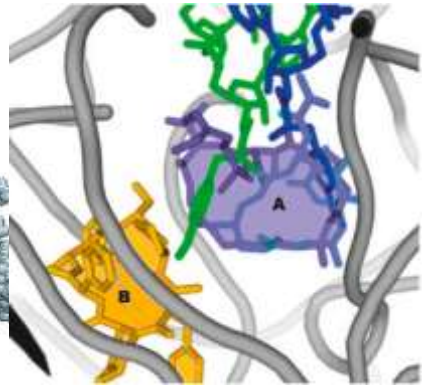
RNA-protein complexes: key anti-bacterial targets

"Possibly the most pregnant recent development in molecular biology is the realization that the beginnings of life are closely associated with the interactions of proteins and nucleic acids" — Florence O. Bell

Example: **Bacterial ribosome critical for survival (Nobel Prize, 2009)**







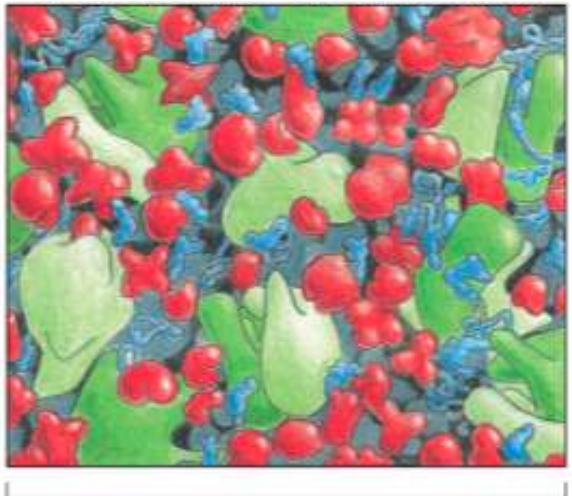
Chloramphenicol, Erythromycin, Neomycin, Gentamicin Tetracycline, Thiostrepton, Spiramycin…

Molecular aspects of RNA-based recognition

***Challenge*: Understanding how to discriminate among all cellular molecules for recognition of a specific target RNA**

- Structural and chemical features of RNAs that allow them to be recognized as drug targets?
- How do these interactions rearrange with environmental changes?
- How do they recognize their natural targets?

E. coli cytoplasm ~6mg/ml RNA



Engineering RNAs and RNA-targeting molecules with novel functionality

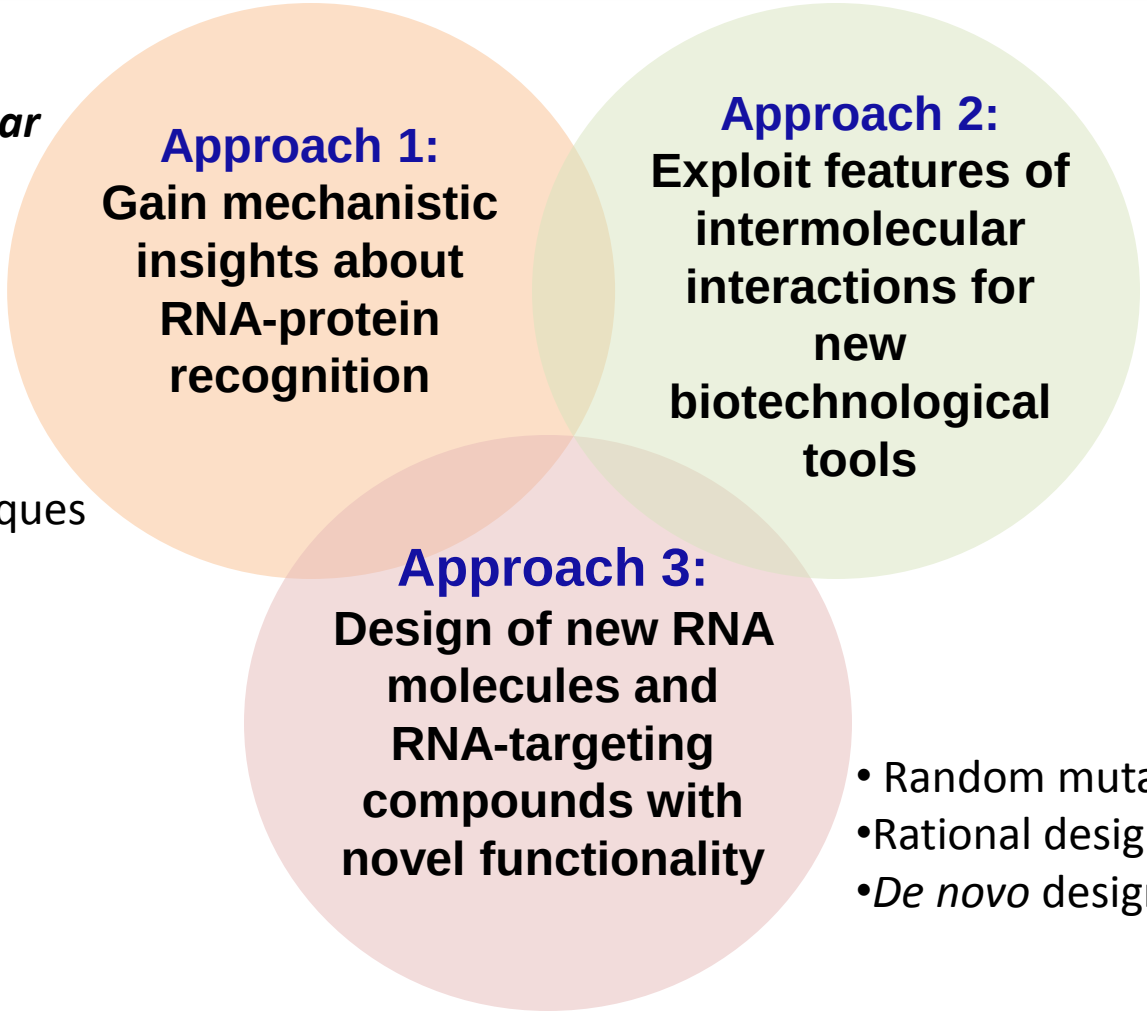
Can we exploit these sophisticated recognition methods for the design and development of new biotechnologically and therapeutically relevant RNAs?

Understanding and Engineering RNAs

Engineer molecular tools to study:

- Structure
- Particle physics
- Chemical composition

•Modeling Techniques



- reconfigure cellular behavior
- Controllable RNA elements
- RNA-based sensors
- Predict resistance

- Random mutagenesis
- Rational design
- *De novo* design

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