

Improving RNA Stability from Weeks to Years

Kyle Heim, PhD – Owner Alpine Medical Technology, LLC

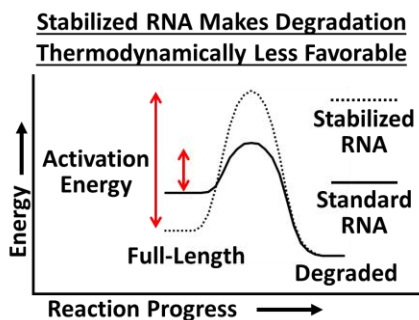
Contact: Kyle@AlpineMed.Tech

RNA Stability Problem: RNA-based products must be stored at freezing or refrigerated temperatures.

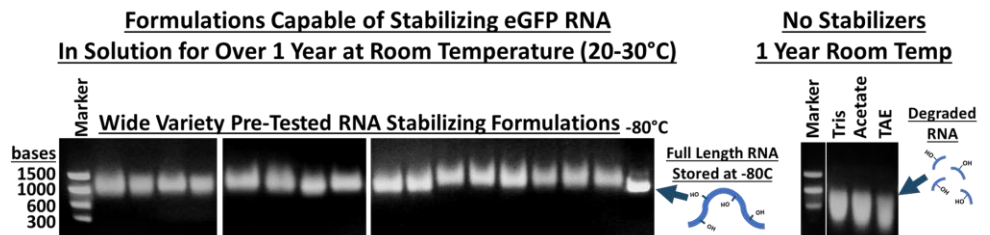
- RNA-based products are often limited by the inherent instability of single stranded RNA.
- mRNA vaccines are limited to storage at room temperature for up to 24hrs or 4°C for up to 90 days.
- Overcoming instability to date has relied on expensive and complex treatments such as lyophilization.

Solution: Alpine Med Tech has Cracked the Code Using Thermodynamics
Developing Dozens of RNA Stabilizing Formulations Stable for Over 1 Year at Room Temperature

Improving RNA Stability by Shifting Activation Energy: Taking advantage of this core thermodynamic principle can dramatically improve RNA stability in solution both with and without lipid-nanoparticles.



Stabilizing Formulations Display Comparable Stability to RNA Stored in Solution at -80°C



Take Advantage of Alpine Med Tech's Highly Stable RNA Formulations!

It's easy to rapidly screen our library of premixed formulations using accelerated stability testing.

Alpine's RNA Stabilizing Technology Can Save You Time and Money

Stability Screening is Simple with Optimized Pre-Mixed Formulations

1. Mix with desired RNA
2. Incubate overnight
3. Analyze next day

Accelerated Stability Screening Saves Time



Quickly Identify the Best Formulations

Easy to Use Just Add & Mix



Works with Free RNA and RNA/LNPs

Not Sequence Dependent

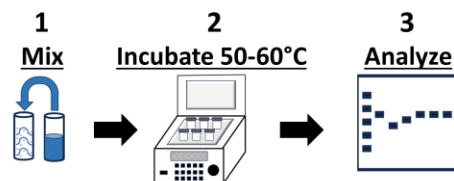


No Modifications or Complex Treatments

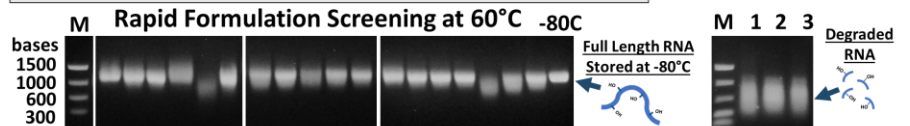
Stable in Solution Without Refrigeration



No Lyophilization No Special Equipment

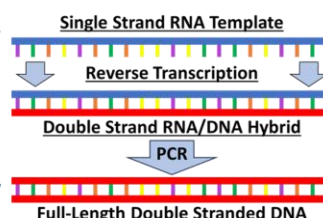
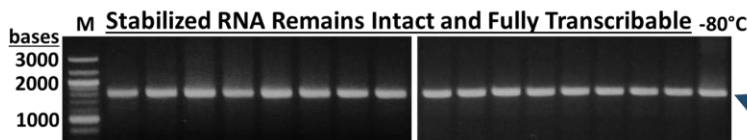


Quickly Screen RNA Stability in Formulations at 60°C



Accelerated Testing Shows Excellent Correlation to Long-Term Stability: RNA formulations screened by accelerated stability testing remain intact and fully readable by RT-PCR after over 1 year at room temperature.

1+ Year at Room Temp Stabilized eGFP RNA Displays Comparable Readability to RNA Stored at -80°C as Measured by RT-PCR

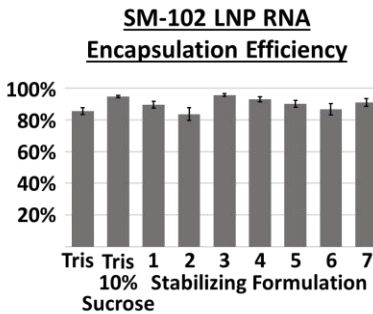


Many Applications

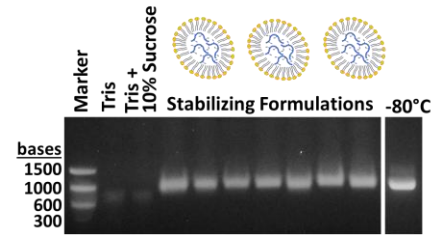
- Diagnostics & Sequencing
- mRNA Therapeutics & Vaccine Preparedness
- Compatible with LNPs, Polymers & Alternative Delivery Agents

Thermodynamically Stabilizing Formulations are Compatible with Lipid Nanoparticles

eGFP RNA encapsulated in SM-102 LNPs stored in stabilizing formulations displays comparable encapsulation efficiency to LNPs stored in Tris-HCl or sucrose while maintaining RNA integrity for over 100 days at room temperature.

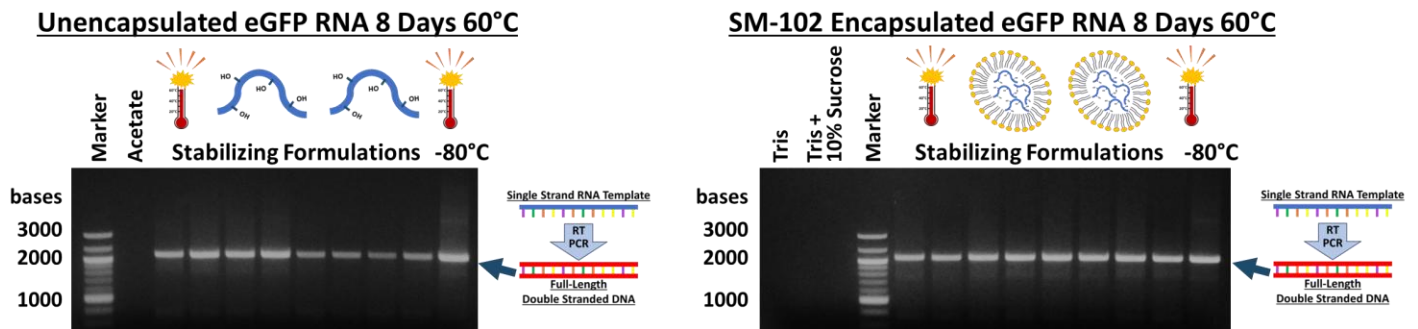


SM-102 Encapsulated eGFP RNA Stability Following 100+ Days at Room Temp (20-30°C)



Stabilizing Formulations Push the Limits of RNA Stability When Stored Under Extreme Conditions

Stabilized eGFP RNA Remains Transcribable by RT-PCR Under Extreme Storage Conditions of 60°C for Over 1 Week

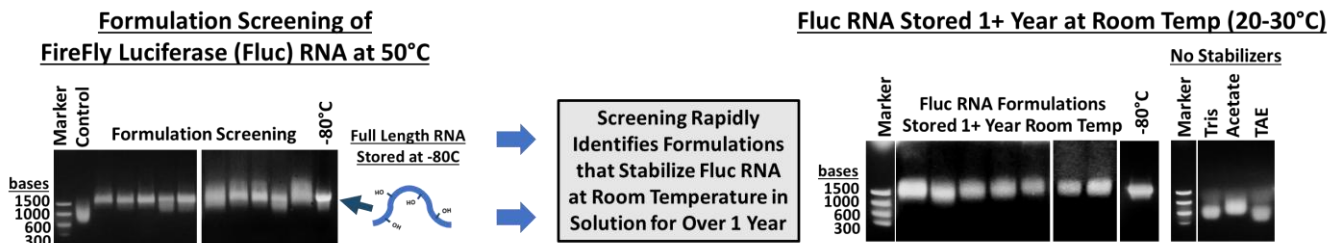


Hypothesis Behind Thermodynamic Approach Stabilizes RNA Through Multiple Mechanisms: Several classes of RNA stabilizing molecules work synergistically to dramatically improve RNA stability in solution.

Masking Agent	Ionic Suppressor	Molecular Chaperone	Hydration Coordinator	Base Coupler	Molecular Restraint
Prevent aggregation & reduce electrostatic interactions that promote RNA degradation	Reduce movement of protons & ions in solution, lowering catalytic potential of water	Protect free strands & unfolded regions of RNA that are more prone to hydrolysis	Order water structure & hydrogen bonding network of water molecules surrounding RNA	Interact with bases at hydrophobic hydrophilic interface to protect from chemical modifications	Restrict RNA movement in solution & limit flexibility to prevent self-cleavage

Combining multiple classes of RNA stabilizing compounds improves stability beyond any single stabilizer.

Alpine Med Tech has spent years creating a library of RNA stabilizing compounds capable of improving RNA stability independent of RNA sequence and without modifications or complex treatments.



Take your RNA to the next level with Alpine Med Tech's proprietary RNA stabilizing technology!

Multiple Patents Pending

Tailored Solutions and Custom Formulations also available - Contact Kyle Heim: Kyle@AlpineMed.Tech