

July 16-21, 2017 at UC San Diego, CA, USA

## Lanthanide Cofactors for Triphosphorylation Ribozymes

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The RNA world hypothesis describes an early stage in the evolution of life in which RNA would have served as genome and the only genome-encoded catalyst. RNA world organisms would have required an energy source for the thermodynamically unfavorable polymerization of RNA. We previously showed that trimetaphosphate (Tmp), a prebiotically plausible energy source, can be used by ribozymes to triphosphorylate RNA 5'-hydroxyl groups, thereby generating chemically activated RNA 5'-phosphates that contain the thermodynamic driving force for RNA polymerization [1]. Analogous 5'-triphosphates could be seen as the precursors for ATP, the energy currency in every known form of life.

To test whether different metal ion cofactors could be used by triphosphorylation ribozymes we performed an in vitro selection in the absence of Mg<sup>2+</sup> and in the presence of the lanthanide Yb<sup>3+</sup>. Lanthanides are promising cofactors for triphosphorylation reactions because they activate Tmp for nucleophilic attack, modulated by the lanthanide's coordination status [2]. While the lanthanide's prebiotic relevance is debatable (they are highly enriched in pegmatites [3] but these minerals may be hard to mobilize) these experiments explore the chemical space accessible to RNA-catalyzed RNA triphosphorylation.

After eight rounds of selection from a pool with 150 randomized nucleotides several active ribozymes were recovered. Interestingly, different sequence clusters displayed very different responses to changes in pH and ion concentrations. This suggests that these lanthanide-using ribozymes employ different catalytic strategies.

### References

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