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Non-Enzymatic Ligation of Short RNA Oligomers Enhanced by Supramolecular Self-Assembly and Liquid Crystal Ordering

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We have studied the effect of spontaneous self-assembly of short oligonucleotides of RNA (12nt and 6nt) on their non-enzymatic ligation, in light of its potential relevance in the formation of long RNA chains capable to show catalytic activity on the prebiotic Earth. This work is based on the observation that complementary oligoribonucleotides as short as 6nt are able to self-assemble and order into liquid crystal solutions when sufficiently concentrated¹.

In a recent work it has been shown that liquid crystal self-assembly in complementary DNA dodecamers enhances the yield of non-enzymatic polymerization². The close proximity between DNA terminals, held close inside the liquid crystalline structure, enhances the chance of the ligation to occur.

Since then, we have expanded these observations to short RNA oligomers³. We have shown that RNA self-assembles more easily than DNA and its supramolecular order enhances ligation efficiencies producing longer polymers (~6n) than the ones produced under the same conditions in a disordered solution (~2n) or when RNA is phase separated but not ordered (~2.5n). Moreover, our findings indicate that liquid crystal ordering favors the formation of linear polymers over circular polymers, which are instead dominant in isotropic solutions.

References:

- [1] Zanchetta G et al (2008) Physical Polymerization and Liquid Crystallization of RNA Oligomers. *Journal of the American Chemical Society* 130(39), 12864-65.
- [2] Fraccia TP et al (2015) Abiotic Ligation of DNA Oligomers Templated by their Liquid Crystal Ordering. *Nature Communications* 6:6424 doi: 10.1038/ncomms7424.
- [3] Todisco M et al (2017) Non-enzymatic Ligation of RNA Oligomers Enhanced by their Liquid Crystal Ordering. *Under Submission*.

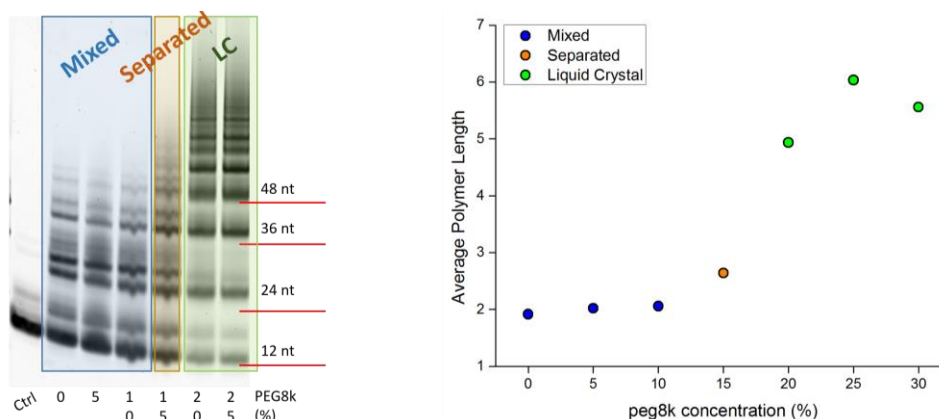


Figure 1 – On the left, PAGE analysis of non-enzymatic ligation reaction of RNA 12mers. On the right, average size of produced polymers in different conditions, extrapolated using flory analysis on the ligation products.