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# Liquid Crystal Self-Assembly of Short RNA/DNA Oligomers as Autocatalytic Pathway for Ribozymes Formation

T. P. Fraccia[1,3]*, G. P. Smith[2], M. Todisco[1], G. Zanchetta[1], N. A. Clark[2] and T. Bellini[1]
[1]Biotechnology and Translational Medicine Dept. Università degli Studi di Milano, IT;
[2]Soft Material Research Center, Physics Dept. University of Colorado, Boulder (CO), USA;
[3]Promotion of Human Sciences and Life Quality Dept., Università San Raffaele, Roma, IT

*Correspondence Author: tommaso.fraccia@unisanraffaele.gov.it

Based on a broad experimental exploration of the collective behavior of short DNA and RNA oligomer (oligoNA), we will report recent progresses in the investigation of a pathway by which linear self-assembly and spontaneous Liquid Crystal (LC) ordering might have enhanced the prebiotic formation of long and potentially active RNA polymers. The key features of this auto-catalytic pathway are reported in figure. A hierarchy of base pairing and stacking, linear aggregation, phase separation of sequences and structures, and LC ordering can select oligoNA and guide their polymerization inside compact, ordered yet fluid micro-domains (colored domains inlet picture). Here in, oligoNA are held in end-to-end contact to form chemically discontinuous but physically continuous double strands. Minimal conditions for LC phases to emerge have been recently successfully tested, as DNA 4mer assembling in running-bond type chains [1], and remarkably, mononucleotide triphosphates (dNTPs), which ordering is led by the interplay of Watson-Crick base pairing and chromonic type stacking [2]. LC catalytically promotes non-enzymatic chemical ligation of oligoNA, with more than 10-fold elongation [3, 4]: the LC droplets act as fluid, permeable micro-reactors in which linear oligomers are selected and ligated. Our current investigation is aimed in testing concentration and temperature cycles as promoters of the evolution of a starting random oligoNA-monomer distribution, wherein potentially formed folding sequences would be selected from the LC phase. Lastly, in presence of lipids, hybrid assemblies can form, as vesicles or lamellar phases, stabilized by the tendency for rigid and flexible layers to spatially segregate either in hydrated or dry conditions.

**References:** [1] Fraccia TP et al. (2016) Liquid Crystal Ordering and Isotropic Gelation in Solutions of 4-base-long DNA Oligomers. *ACS Nano* 10:8508. [2] Smith GP, Fraccia TP et al. (2017) Liquid Crystal Formation of Mononucleotide Triphosphates by Base-Pairing and Duplex Stacking in Aqueous Solution. *Under submission.* [3] Fraccia TP et al. (2015) Abiotic Ligation of DNA Oligomers Templated by their Liquid Crystal Ordering. *Nat. Commun.* 6:6424. [4] Todisco M, Fraccia TP et al. (2017) Non-enzymatic Ligation of RNA Oligomers Enhanced by their Liquid Crystal Ordering. *Under Submission.*