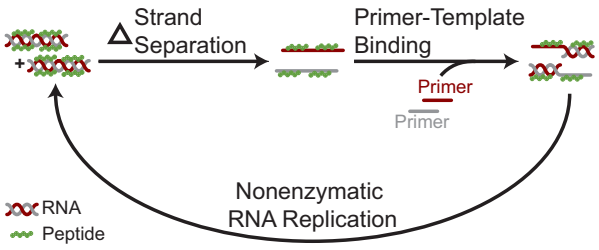
NONENZYMATIC RNA REPLICATION THROUGH PEPTIDE-ASSISTED STRAND ANNEALING INHIBITION.

T. Z. Jia[1,2,*], A. C. Fahrenbach[1,3], N. P. Kamat[1,†], K. P. Adamala[1,‡], and J. W. Szostak[1,2,3,4]; [1]Howard Hughes Medical Institute, Department of Molecular Biology, and Center for Computational and Integrative Biology, Massachusetts General Hospital, 185 Cambridge Street, Boston, Massachusetts, 02114, USA; [2]Department of Chemistry and Chemical Biology, Harvard University, 12 Oxford St., Cambridge, Massachusetts, 02138, USA; [3]Earth-Life Science Institute, Tokyo Institute of Technology, 2-12-1-IE-1 Ookayama, Meguro-ku, Tokyo 152-8550, Japan; [4]Department of Genetics, Harvard Medical School, 77 Avenue Louis Pasteur, Boston, Massachusetts, 02115, USA; [*]Current Affiliation: Earth-Life Science Institute, Tokyo Institute of Technology, 2-12-1-IE-1 Ookayama, Meguro-ku, Tokyo 152-8550, Japan; [†]Current Affiliation: McCormick School of Engineering, Department of Bio-engineering, Northwestern University, Evanston, Illinois, 60208, USA; [‡]Current Affiliation: Department of Genetics, Cell Biology, and Development, University of Minnesota, Minneapolis, Minnesota, 55455, USA

The nonenzymatic replication of RNA is thought to have been a critical aspect of the chemistry of the origin of life [1]. One unsolved difficulty with nonenzymatic RNA replication is that template-directed copying of RNA results in a double-stranded product; following strand separation, rapid strand reannealing outcompetes slow nonenzymatic template copying, rendering multiple rounds of RNA replication impossible [2]. Here we show that oligoarginine peptides slow annealing of complementary oligoribonucleotides by up to several thousand-fold; however, short primers and activated monomers can still bind to template strands, and template-directed primer extension can still occur within a phase-separated condensed state, or coacervate. Furthermore, we show that within this phase, partial template copying occurs even in the presence of full-length complementary strands. This method for enabling further rounds of replication suggests one mechanism by which short, non-coded peptides could have enhanced early cellular fitness, potentially explaining how longer, coded peptides, i.e. proteins, came to prominence in modern biology [3].



References: [1] Robertson M. P. and Joyce G. F. (2012) *Cold Spring Harb. Perspect. Biol.*, 4, a003608. [2] Szostak J. W. (2012) *J. Sys. Chem.*, 3, 2. [3] Jia T. Z. *et al.* (2016) *Nature Chem.*, 8, 915-921.