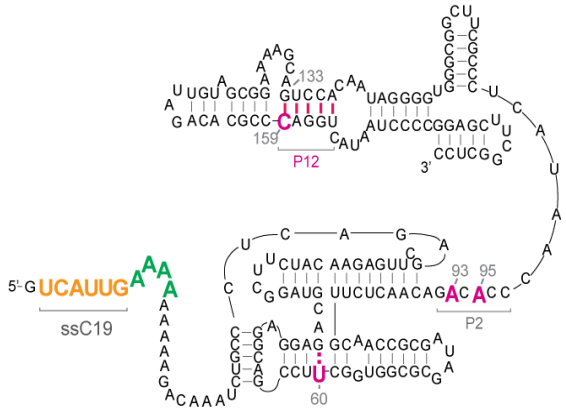
THE RNA WORLD: A RECONSTRUCTIVE APPROACH. James Attwater, Hannes Mutschler, Aniela Wochner, Alan Coulson and Philipp Holliger. MRC Laboratory of Molecular Biology, Francis Crick Avenue, Cambridge Biomedical Campus, Cambridge CB2 0QH, UK (Email: ph1@mrc-lmb.cam.ac.uk)

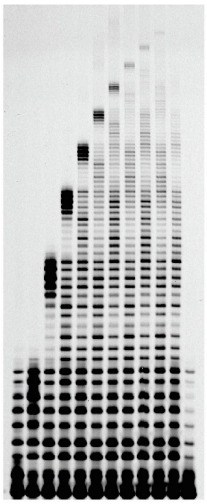
Introduction: A critical event in the origin of life is thought to have been the emergence of an RNA molecule capable of self-replication as well as mutation, and hence evolution towards ever more efficient replication.

Although the ancestral replicase appears to have been lost, key functional aspects of RNA-catalyzed RNA replication can be studied "by proxy" with the use of modern RNA enzymes (ribozymes) generated by *in vitro* selection.



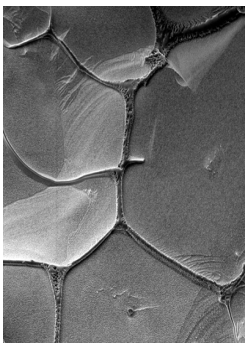
Starting from the R18 RNA polymerase ribozyme [1], a descendant of the the class I ligase ribozyme that was derived directly from a random RNA sequence pool, we have used both RNA evolution and engineering to generate new RNA polymerase ribozymes with improved polymerase activity and sequence generality.

I'll be presenting our progress in the engineering and evolution of RNA polymerase ribozymes towards a general polymerase and self-replication capacity.



We have discovered RNA polymerase ribozymes that are capable of the templated synthesis (i.e. transcription) of another simple ribozyme (a Hammerhead endonuclease ribozyme) [2] or RNA oligomers exceeding its own size (>200 nts) [3], a key milestone on the road to self-replication, although the synthetic power of these RPRs is currently restricted to favourable template sequences.

I'll also be presenting our work on the potential role that structured media such as the eutectic phase of water ice [4] may have played in early RNA evolution and catalysis [5] and the emergence of RNA self-replication.



References: [1] Johnston, W. K. *et al* (2001) *Science 292*, 1319-1325. [2] Wochner, A. *et al* (2011) *Science 332*, 209-212. [3] Attwater, J. *et al* (2013) *Nature Chem* **5**, 1011-1018. [4] Attwater, J. *et al* (2010) *Nat Commun 1*, 76. [5] Mutschler H. and Holliger P. (2014) *JACS, 136*, 5193-5196