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Molecular reagents that bind to specific proteins with high affinity are valuable tools in the endeavour to understand protein function. In the Early Edition of Proceedings of the National Academy of Science, Wilson *et al.* describe how a method based on mRNA display can be used to identify ligands with higher affinity than those selected using the phage display technique. The new technique generates polypeptides that are linked via a puromycin moiety to their encoding mRNAs. Wilson *et al.* demonstrate that the limitations of non-constrained linear peptide libraries can be overcome by increasing the complexity (the diversity) of the library and the length of the polypeptides. Using an ultra-high complexity library of 1013 random peptides, each 88 amino acids long, they selected 20 different aptamers which bound to a protein target with dissociation constants as low as 5 nM. Such an approach therefore has advantages over antibody production or phage display techniques to screen for high-affinity protein-binding reagents.

## References

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