In vitro two hybrid system as a potential novel selection method for the DNA encoded libraries

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The DNA encoded libraries (DELs) technology is a hot topic interesting for many researchers in the field of drug discovery. A DEL consists of a pool of small molecules, each covalently attached to a DNA 'barcode' unique to the small molecule. Traditionally, these DEL pools are affinity enriched with a target protein, only leaving potential binders in solution. After PCR and sequencing, the identity of the small molecules can be determined. However, affinity enrichments come with limitations, and better selections methods are sought after. The goal of this project is to engineer a bacterial two hybrid in vitro transcription system1 as an alternative to affinity enrichments. When a DNA-bound ligand binds to the protein of interest, the transcription reaction will start, and the DNA encoding for the small molecule will be transcribed into multiple RNA copies, thus amplifying the signal. We hope that the amplification increases the sensitivity of the selection method, giving a better signal-to-noise ratio and reducing the amount of false-positive hits.

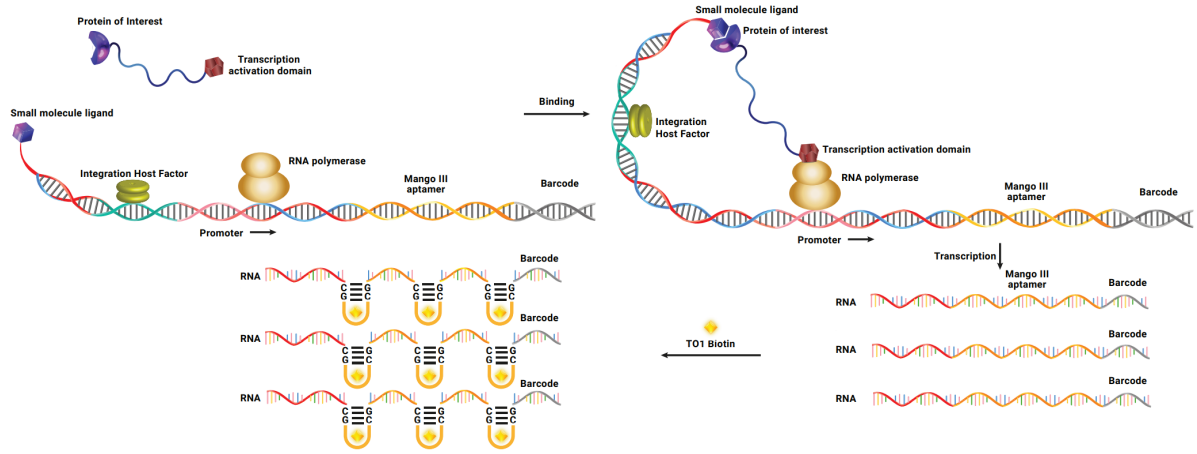

Figure 1. DNA bound ligand – protein two hybrid system in vitro transcription

[1] 1 Y. Zhou, H. Schneider, P. Dranchak, J. Inglese, *J Am Chem Soc*. **2014**, 136(40), 14031-8