Plasmid-Free mRNA Synthesis on a Reusable Solid-Phase IVT Platform

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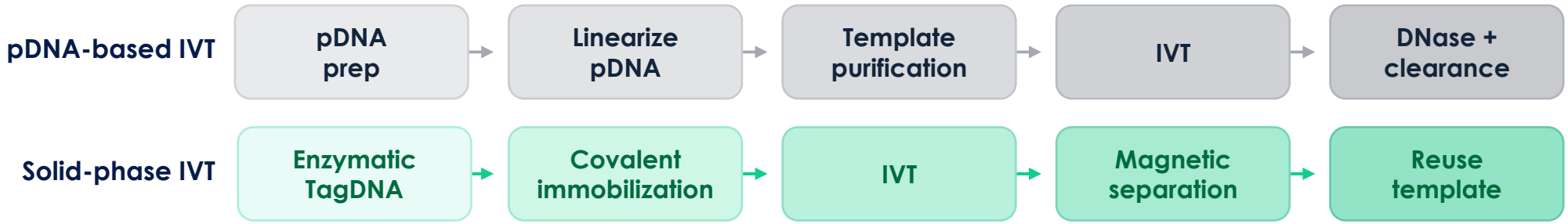
Why move beyond pDNA-based IVT?

The platform shifts template DNA from a soluble contaminant to a reusable solid-phase reagent.



pDNA-based IVT

1. **pDNA**
   - Analytics load: plasmid isoforms (supercoiled/linear/open-circular)
   - Safety optics around antibiotic-resistance sequences
   - Bacterial-origin impurities
2. **Linearized pDNA (template)**
   - Linearization dependence & efficiency
   - Template-end–driven dsRNA
3. **Residual DNA**
   - Clearance burden
   - Incomplete DNase digestion

Solid-phase IVT*

1. **Plasmid-free**
   - Enzymatic amplification
   - No extraneous sequences
   - No antibiotic-resistance sequences
2. **Linear, double stranded TagDNA (template)**
   - No linearization step
   - Immobilized DNA → Reduced dsRNA
3. **Cleaner reaction matrix**
   - TagDNA stays on solid-support

✖ No DNase step, reduce risks of DNA fragments

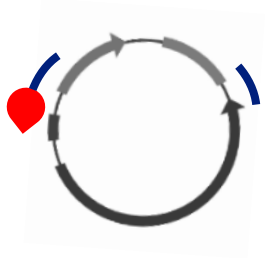
✓ Simplify separation

* Patent published WO2026/072628 A1

Solid-phase IVT step to help accelerate mRNA process development

A reusable bead-DNA complex enables repeat IVT cycles and built-in template separation.

pDNA or synthetic DNA



OR

TagOligo™

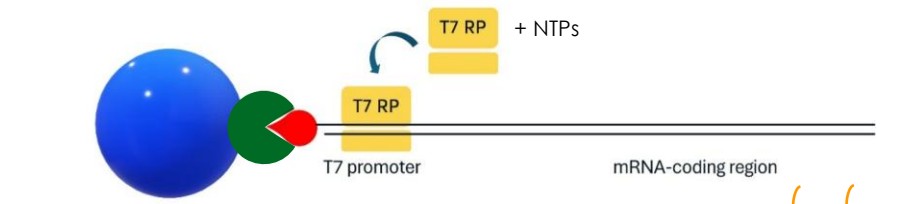
PCR amplification

TagDNA (template for IVT)

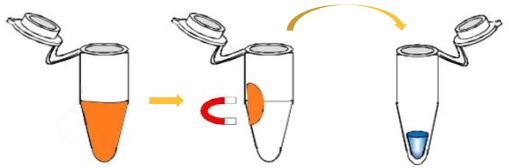
DNA immobilization by covalent attachment of DNA to magnetic beads

Avantor developed TagOligo™ and magnetic beads

Solid-phase *in vitro* transcription*



DNA template can be reused



Immobilized template + IVT mix

Magnetic separation of immobilized template

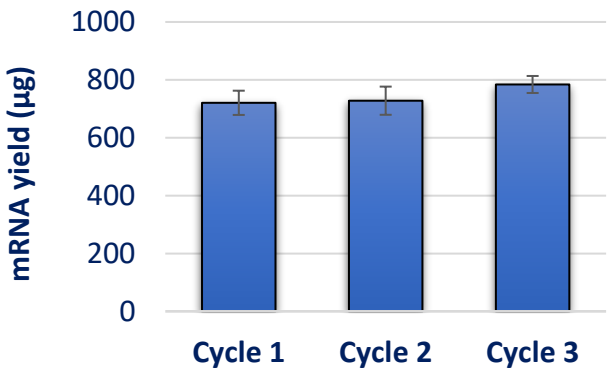
Crude *in vitro* transcript

* Patent published WO2026/072628 A1

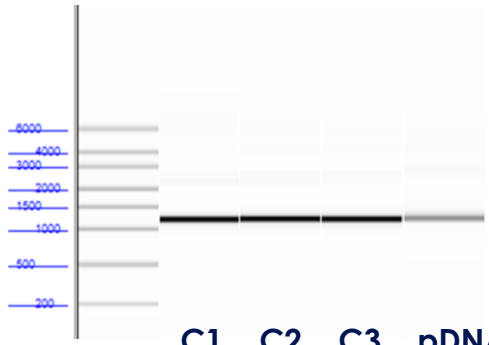
Data snapshot: mRNA output maintained, dsRNA reduced

Across reuse cycles, the platform preserves mRNA output while reducing impurity burden.

Reusable TagDNA output

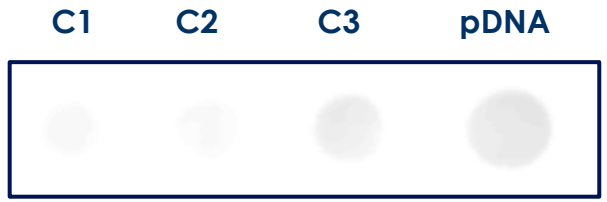


Integrity and purity of mRNA



	C1	C2	C3	pDNA
Purity (%)	92.2	91	91.5	86.1

dsRNA reduction



	C1	C2	C3	pDNA
% dsRNA of mRNA	0.009	0.026	0.037	0.103

9.2 g/L
2.2 mg total mRNA from 2 ug TagDNA over 3 IVT cycles

91-92% Purity
High mRNA purity across cycles (*c.f.* pDNA: 86.1%)

3 to 11x lower
Significant reduction of dsRNA impurity

1.2 to 4.6 kb
Transcript length diversity

Co-transcriptional: 92-99%
Post-transcriptional: 85-88%
Compatibility with 5' capping of RNA and good capping efficiency

< 0.0006%
Low template leaching from beads during IVT cycles

* Patent published WO2026/072628 A1

Plasmid-free solid-phase IVT platform

Key Features

Cost-effective and Speed

Reduced pDNA consumption:
13,750x less

- Template for IVT is generated using enzymatic methods
- Fewer unit operations
- Smaller upstream footprints
- Reduce fermentation process volumes and material e.g., antibiotics

Improved Purity and Yield

Higher RNA yield per DNA template unit:
2.75x more

- Template immobilization enables reuse for multiple IVT cycles
- **Lower dsRNA impurities**
- Eliminate DNA fragments

Flexibility of Scale

Suitable for rapid multi-construct screening

- Supports scale-down models for rapid DoE and comparability
- Can be scaled out depending on demand

Streamlined workflow

Elimination of certain steps required for conventional workflow

- Linearization step is omitted since pDNA is not used
- TagDNA purification step is not required
- Built-in DNA template removal via magnetic separation eliminates DNase digestion step

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