Hongene Biotech

BRING YOUR RNA TO LIFE

Established in 1998, Hongene Biotech has been specialized in the production of nucleic acid raw materials for more than 25 years, covering nucleosides and modified nucleosides, nucleotides, phosphoramidite, GalNAc delivery molecules and enzymes. The annual capacity of phosphoramidite is 58 tons and nucleoside triphosphates is 54,000 litres (equivalent of 1.05 billion doses of mRNA vaccines).

To date, Hongene has over 1,600 employees globally with over 400 R&D staff. Hongene brand is highly recognised by major pharmaceutical companies and biotech companies developing mRNA and oligonucleotide drugs. Hongene's products have entered almost all nucleic acid drug pipelines worldwide. During the Covid-19 pandemic, Hongene was the largest supplier of raw materials used in billions of mRNA COVID-19 vaccines.

Currently, the company has established end-to-end mRNA CDMO capability, provide one-stop shopping from raw materials to final product, supporting clients from preclinical research to commercialization.

25
Years of Experience in the RNA Industry
Founded in 1998

1,600
Employees
R&D: ~380
US: ~50

2,000+
SKUs
Amidite
NTP/dNTP
Cap Analog
Cationic Lipid
GalNAc
Enzyme
Others

4
Manufacturing Sites
① Mfg. Facility No.1 (ISO)
② Mfg. Facility No.2 (GMP)
③ mRNA CDMO Facility (GMP)
④ mRNA DS/DP GMP Facility (under construction in Shanghai)

2
R&D Centers
San Francisco (US)
Shanghai (China)

5
Intl. Sales Offices
San Francisco (US), Boston (US), Hamburg (Germany), Tokyo (Japan), Shanghai (China)

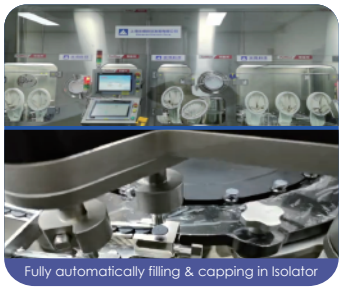
Comprehensive and fully-integrated platform for mRNA vaccine and therapy

01 One-pot reaction
- ✓ High purity
- ✓ High yield
- ✓ Reduced cost

02 State-of-the-art Facility
- ✓ GMP Facility
- ✓ Small-scale
- ✓ Mid-scale
- ✓ Analytical instrument

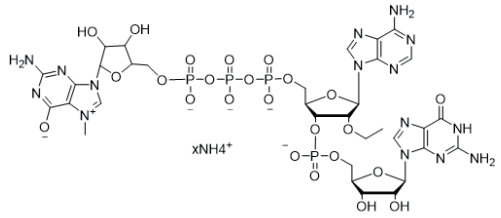
03 Vertical Integration
- ✓ Total solution from plasmid to mRNA DS to F&F

mRNA drug
NTP
Cap Analogs
Enzymes


Fully automatically filling & capping in Isolator

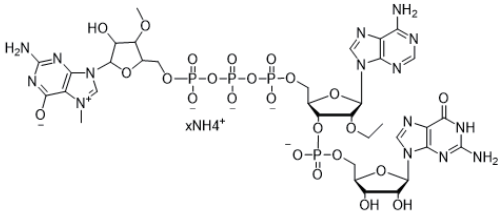
Novel mRNA Cap Analogue

Improve translation under immune stress conditions



m7G(5')pppA(2'-O-ethyl)mpG

$GA_{2'\text{-}OET}G$



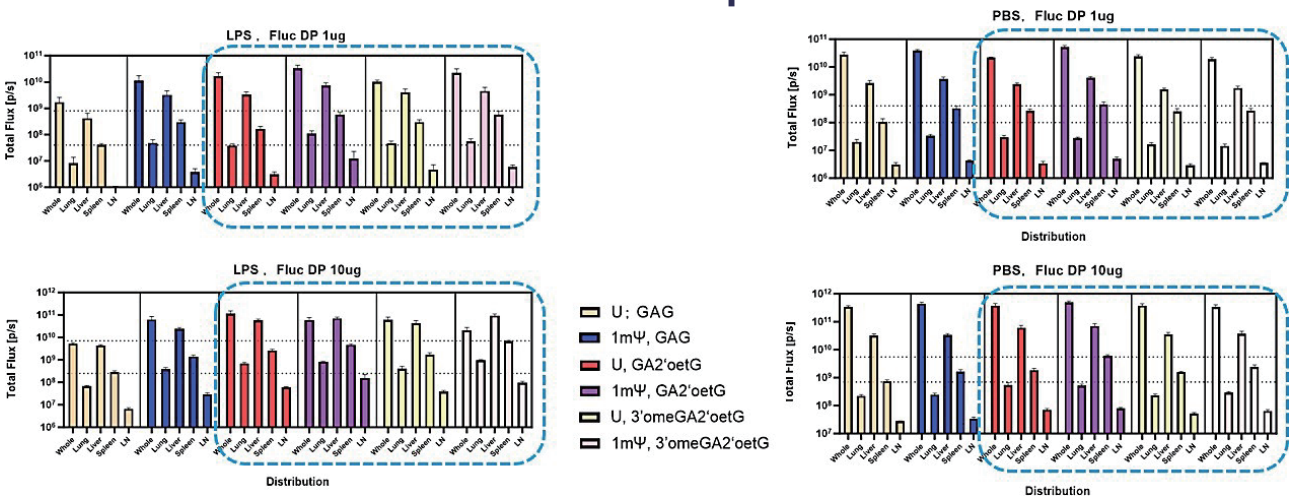
(3'-OMe-m7G)(5')pppA(2'-*O*-ethyl)pG

$^{3'OMe}GA_{2'\text{-}OET}G$

New cap features

- **Substitution of methyl for ethyl at the 2'-O position.**
- **Dramatically improves mRNA translation under immune stress conditions. Capping efficiency ranges from 94~99%.** (Vary based on reaction conditions, different sequences)
- **The translation effect of the new ethyl cap is better than that of the methyl cap.**
- **Compared with methyl cap, it has more efficient mRNA translation expression for mRNA infectious vaccine and mRNA neoantigen cancer vaccine.**

Fluc mRNA Mice Experiment



Experiment Result

- **LPS induces pro-inflammatory signaling through TLR4. Normally pro-inflammatory condition impacts mRNA translation, but mRNA with modified cap structure shows same translation even more under LPS model mice comparing to PBS model mice specially in spleen and lymph nodes. (Figure above)**
- **Fluc with new ethyl cap structure shows higher translation in the spleen and lymph nodes of PBS group. (Figure above)**
- **Fluc was injected at three-day intervals, the protein expression with the methyl cap decreased dramatically in the second injection, while that of the ethyl cap remained almost unchanged. (Figure on right)**