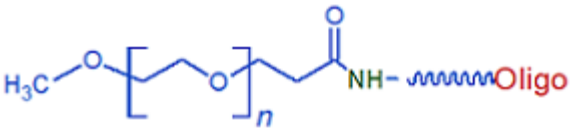
mPEG 20kDa Oligo

Category	Antisense & siRNA
Modification Code	mPEG-20kDa-N
Reference Catalog Number	26-6793
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	20000



mPEG-2kDa-Oligo; [26-6790-XX]

mPEG-5kDa-Oligo; [26-6791-XX]

mPEG-10kDa-Oligo; [26-6792-XX]

mPEG-20kDa-Oligo; [26-6793-XX]

mPEG-40kDa-Oligo; [26-6894-XX]

Oligonucleotide PEGylation : Spacers vs. PEGylation Gene Link offers short PEG3 and PEG6 as direct coupling using automated chemistry. The PEG3 is termed as Spacer 9 and PEG6 as spacer 18. These are also used to introduce space between adjacent sequence and modifications. These can be inserted multiple times to increase the PEG units.
Larger 2, 5, 10 and 20 kDa PEGylation of oligonucleotides is inserted at any site of an oligonucleotide using a post synthesis amino group on the oligo with PEG-NHS.
PEGylation is the covalent attachment of polyethylene glycol (PEG) to oligonucleotides such as DNA, RNA, antisense, siRNA and aptamers. It improves pharmacokinetics, reduces renal clearance, increases nuclease stability, and decreases immunogenicity. (1) The way PEG shields its conjugated payload offers new challenges and opportunities for oligonucleotide PEGylation. Other than aptamers, the target of most oligonucleotides is a complementary sequence.

Solubility Note: solubility decreases as the PEGylation size increases. PEG larger than 10 KDa are completely soluble in water and DMSO at 10 mg/ml. Higher concentration solution will be turbid suspension.
Comparison of PEGylation Size & Biological Outcome

PEG Size (Ethylene Glycol Units)

Hydrodynamic Effect

Typical Outcome 2 kDa (~44) Minimal Slight stability increase 5 kDa (~114) Moderate Partial half-life improvement 10 kDa (~227) Strong Reduced renal clearance 20 kDa (~455) Very strong Long circulation 40 kDa (~910) Extreme Depot-like behavior Pharmacokinetics depend on hydrodynamic diameter, not molecular weight of the oligo. Unmodified 20-mer oligo ≈ ~7 kDa. Kidney filtration cutoff ≈ 40-60 kDa hydrodynamic equivalent Oligo PEG size controls circulation time versus tissue penetration.

Optimal design balances exposure and activity

Messenger RNA (mRNA) delivery strategies are required to protect biologically fragile mRNA from ribonuclease (RNase) attacks to achieve efficient therapeutic protein expression. To tackle this issue, most mRNA delivery systems have used cationic components.

A cation-free delivery strategy by hybridization of PEGylated RNA oligonucleotides with mRNA. The PEG strands on the mRNA sterically and electrostatically shields the mRNA, improving mRNA nuclease stability 15-fold and the PEGylated mRNA induced nearly 20-fold higher efficiency of reporter protein expression than unhybridized mRNA in cultured cells (2). PEGylation has been used to improve the biopharmaceutical properties of protein drugs since the 1990s, and over a dozen PEGylated pharmaceuticals are currently on the market (2). PEG creates a large hydration shell, which sterically blocks other biomacromolecules from penetrating through the polymer layer and binding with the interior substrate (3, 4). Binding requires displacing the PEG by the incoming molecule, generally making such binding less thermodynamically favorable. These properties usually result in weaker interactions between the receptor and the conjugated molecule, but increased drug solubility, prolonged blood circulation, and increased drug stability often offset by the reduced binding affinity. PEGylated oligonucleotides can be an exception to this generalization, with increased binding to a complementary sequence compared to unmodified ONs. The effect is attributed to macromolecular volume exclusion (6).

References

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Spacers

Spacer 18 also known as PEG6 is a hexaethylene glycol chain that is 18 atoms long (12 carbons + 6 oxygen's), and is used to incorporate a long spacer arm into an oligonucleotide. Spacer 18 can be incorporated in consecutive additions whenever a longer spacer is required. Spacer 18 had been used to form bold folds and hairpin loops in oligonucleotides (1,2), and for solid-phase immobilization of hybridization probes (3). Spacer 18 has also been used to modify random primers used in whole genome amplification (WGA)-based applications, as a way to eliminate self-priming events that form spurious DNA products (that is, false-positive amplification) in the PCR reactions (4).

Gene Link offers spacers of various length, examples C2, C3, C6, C12 and Spacer 9 and 18. These can be inserted multiple times to yield a total much longer spacer length. **References**

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