c-diGMP (aka cyclic diguanylate or cyclic bis(3′→5′)diguanylic acid) was first described in the 1980s as a modulator of cellulose synthesis in the fruit-degrading bacterium *Glucanacetobacter xylinus*. Subsequently, the c-diGMP-metabolizing enzymes were identified to be diguanylate cyclases carrying GGDEF domains and specific phosphodiesterases that carry EAL or HD-GYP domains. EAL and HD-GYP domain proteins linearize c-diGMP to pGpG, which is then further degraded to 5′-GMP (Fig. 1).

Based on the near ubiquitous presence of the GGDEF and EAL domains in bacteria, c-diGMP is currently believed to be a universal bacterial second messenger involved in the regulation of many complex and diverse physiological processes including bacterial motility, adhesion, cell-to-cell communication (quorum sensing) and exopolysaccharide synthesis. It was also found to exhibit immunostimulatory action in mice and to play a role in virulence and in the formation of biofilms, thus identifying the c-diGMP signalling system to be an important target in medical research and health care. However, many aspects of the complex c-diGMP signalling system such as the integration of external signals are not yet fully understood and need to be further investigated.

Another second messenger candidate in bacteria was recently discovered: c-diAMP (Fig. 2) is considered to be a messenger molecule that signals DNA integrity in *Bacillus subtilis* during sporulation. A *Bacillus subtilis* protein exhibiting phosphodiesterase activity towards c-diAMP and generating the linear pApA has also been described. However, the occurrence of c-diAMP in bacteria, the mechanisms controlling its production and breakdown, as well as its role in bacterial signalling remain to be discovered.

**The cyclic dinucleotide c-diGMP is an essential signalling molecule in bacteria**

**c-diGMP / Metabolite of c-diGMP**

- **c-diGMP** is a near ubiquitous bacterial second messenger that was found to be involved in a wide variety of physiological processes in bacteria.
- **pGpG** is the first physiological metabolic degradation product of the bacterial signalling nucleotide c-diGMP.

**c-diAMP / Metabolite of c-diAMP**

- **c-diAMP** is considered to be an additional purine-based signalling nucleotide in prokaryotes.
- **pApA** is a potential metabolic degradation product of the second messenger candidate c-diAMP.

See back page for analogues of c-diGMP and c-diAMP.
Biotinylated Analogues of c-diGMP

Biotin connected to one of the two ribose 2'-hydroxy groups in c-diGMP via a 16 atom spacer.

2'-[Biotin]-AHC-c-diGMP
B 098-001, 0.1 µmol/~0.1 mg
B 098-005, 5 x 0.1 µmol

2',2''-Di-[Biotin]-AHC-c-diGMP
D 111-001, 0.1 µmol/~0.2 mg
D 111-005, 5 x 0.1 µmol

2'-AHC-c-diGMP immobilized on free beads.

Fluorescent Analogues of c-diGMP and c-diAMP

The MANT fluorophore (λex 355 nm, λem 448 nm) is sensitive to its environment.

Di-MANT-c-diGMP
D 101-001, 0.1 µmol/~0.1 mg
D 101-005, 5 x 0.1 µmol

2'-Fluo-AHC-c-diGMP
F 009-001, 0.1 µmol/~0.1 mg
F 009-005, 5 x 0.1 µmol

DY-547 (λex 557 nm, λem 574 nm) connected to one of the two 2'-hydroxy groups in c-diGMP.

Biotinylated Analogues of c-diAMP

Biotin connected to both ribose 2'-hydroxy groups in c-diAMP via 16 atom spacers.

2'-[Biotin]-AHC-c-diAMP
B 106-001, 0.1 µmol/~0.1 mg
B 106-005, 5 x 0.1 µmol

2',2''-Di-[Biotin]-AHC-c-diAMP
D 122-001, 0.1 µmol/~0.2 mg
D 122-005, 5 x 0.1 µmol

Biotin connected to both ribose 2'-hydroxy groups in c-diAMP via 16 atom spacers.

Fluorescent Analogues of c-diGMP and c-diAMP

Fluorescein (λex 494 nm, λem 517 nm) connected to one of the two 2'-hydroxy groups in c-diGMP.

DY-547 (λex 557 nm, λem 574 nm) connected to one of the two 2'-hydroxy groups in c-diAMP.

CDiamp-based Ligands

Suitable as a ligand in affinity chromatography or for coupling of various labelling structures.

2'-AHC-c-diGMP
A 151-001, 0.1 µmol/~83 µg
A 151-005, 5 x 0.1 µmol

2',2''-Di-AHC-c-diGMP
D 112-001, 0.1 µmol/~97 µg
D 112-005, 5 x 0.1 µmol

Suitable as a ligand in affinity chromatography or for coupling of various labelling structures.

2'-AHC-c-diAMP
A 182-001, 0.1 µmol/~80 µg
A 182-005, 5 x 0.1 µmol

2',2''-Di-AHC-c-diAMP
D 121-001, 0.1 µmol/~94 µg
D 121-005, 5 x 0.1 µmol

Suitable as a ligand in affinity chromatography or for coupling of various labelling structures.

Affinity Gels

c-diGMP immobilized on agarose gel. Available in pre-packed columns or as free beads.

2'-AHC-c-diGMP-Agarose
A 153-06, 0.6 mL
A 153-25, 2.5 mL
A 153-60, 6 mL

2'-AHC-c-diAMP-Agarose
A 183-06, 0.6 mL
A 183-25, 2.5 mL
A 183-60, 6 mL

Brominated Analogues of c-diGMP

Suitable as a ligand in position 8 of one of the two guanine nucleobases.

8-Br-c-diGMP
B 099 Please inquire!

8',8''-Di-Br-c-diGMP
D 113 Please inquire!

Suitable as a ligand in the 8-positions of both guanine nucleobases.

Brominated Analogues of c-diGMP


Bi-diIMP


C 105 Please inquire!