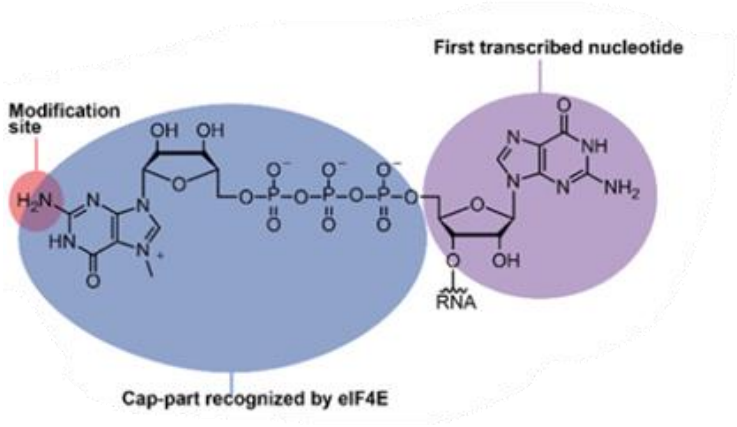
Photocage Cap for mRNAs

Cap analogue for the 5'-end of eukaryotic messenger RNAs

Invention

Almost all eukaryotic messenger RNAs (mRNAs) are modified at their 5'-ends by a cap that is synthesised by addition of a 7-methylguanosine attached via a 5'-5' triphosphate bridge to the first transcribed nucleotide of the mRNA chain. The cap structure plays a pivotal role in mRNA metabolism, mRNAs that carry a cap structure are efficiently translated (i.e. serve as template for protein synthesis).



Cap analogues with different modifications have been developed. Modified caps and capped mRNAs can be employed to alter production of proteins in various eukaryotic in vitro translations systems and in cultured cells.

Alternative strategies to further allow control of location and time of translation via caged nucleic acids have been developed. For this, numerous positions on nucleobases have been targeted, involving formal substitution of a hydrogen atom with a photocaging group. Such photo-caged caps, however, are an artificial compound in mRNA metabolism and will not yield the native nucleoside.

The N7 position of guanosine and the N1 position of adenosine were also used for chemical modification with a photolabile caging group. However, photocaging groups derived from the ortho-nitrobenzyl moiety were not suitable and did not yield the desired photocleavage to release guanosine. Additionally, the N7 position requires remethylation reducing the precision of time controlled translation.

Therefore, it is an object of the present invention to provide a photocontrollable 5'-cap analogue, particularly a photocleavable 5'-cap analogue that allows for a regeneration of the native cap. The object is solved by a photocleavable-cap as shown in the Figure.

The 5'-cap analogue consequently enables a photocontrollable translation with efficiencies similar to the natural process and has been shown in vitro, in cells and in vivo (Zebrafish).

Commercial Opportunities

The present invention allows for new strategies in the semi-synthetic synthesis of mRNAs and a controlled release of the cap. On behalf of University of Münster, PROvendis offers a patent license as well as a research collaboration with licensing option to innovative companies.

Current Status

In case of interest, we will be pleased to inform you about the patent status.

Relevant Publications

N. Klöckner, F.P. Weissenboeck, M.van Dülmen, P. Spacek, S. Hüwel, A. Rentmeister; 2022; Photocaged 5′ cap analogues for optical control of mRNA translation in cells. Nature Chemistry; Vol 14, 905-913.

An invention of University of Münster.

Competitive Advantages

- High efficiency
- Low toxicity
- Novel access via conjugation of new photoactive cap
- Compatible with normal IVT reaction

Technology Readiness Level

1 2 3 4 5 6 7 8 9

Technology validated in lab

Industries

- Biotechnology Industry
- Pharmaceutical Industry

Ref. No.

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