

# RCB – Colloquium

Donnerstag, 9. November 2023 14.00 Uhr  
Neubau Biologie H 53



## Prof. Dr. Andrea Rentmeister

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*Harnessing the Power of Click Chemistry and Light  
to Unlock the Secrets of mRNA*

Messenger RNAs (mRNAs) enable the production of almost any functional protein/peptide in the human body as a vaccine or therapeutic agent. The translation of mRNA is a fundamental process in gene expression, and controlling translation is crucial for regulating the production of proteins in cells. In addition, internal modifications of mRNA have emerged as widespread and versatile regulatory mechanism to control gene expression at the post-transcriptional level. Most of these modifications are methyl groups, making S-adenosyl-L-methionine (SAM) a central metabolic hub. We established metabolic labeling with a clickable metabolic precursor of SAM that enables detection and identification of various methylation sites.<sup>1,2</sup> Integration into next generation sequencing enabled mapping of N<sup>6</sup>-methyladenosine (m<sup>6</sup>A) and 5-methylcytidine (m<sup>5</sup>C) sites in mRNA with single nucleotide precision and independent of antibodies. In a different project, we aimed to control translation of mRNA by light as external stimulus. We synthesized 5' cap analogues with photo-cleavable groups (FlashCaps) that prohibit binding to the eukaryotic translation initiation factor eIF4E. These compounds are compatible with the general and efficient production of mRNAs by *in vitro* transcription.<sup>3,4</sup> FlashCaps offer a route to regulate the expression of any given mRNA *in vitro* and in cells and may provide an approach to dose mRNA therapeutics with spatio-temporal control.

### References

- [1] K. Hartstock, B. S. Nilges, A. Ovcharenko, N. V. Cornelissen, N. Püllen, A. M. Lawrence-Dörner, S. A. Leidel and A. Rentmeister, *Angew Chem Int Ed* **2018**, *57*, 6342-6346.
- [2] K. Hartstock, A. Ovcharenko, N. A. Kueck, P. Spacek, N. V. Cornelissen, S. Hüwel, C. Dieterich and A. Rentmeister, *bioRxiv* **2022**, 2022.2003.2016.484494.
- [3] N. Klocker, F. P. Weissenboeck, M. van Dulmen, P. Spacek, S. Huwel and A. Rentmeister, *Nat Chem* **2022**, *14*, 905-913.
- [4] A. Bollu, N. Klöcker, P. Špaček, F. P. Weissenboeck, S. Hüwel and A. Rentmeister, *Angew Chem Int Ed* **2023**, *62*, e202209975.

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