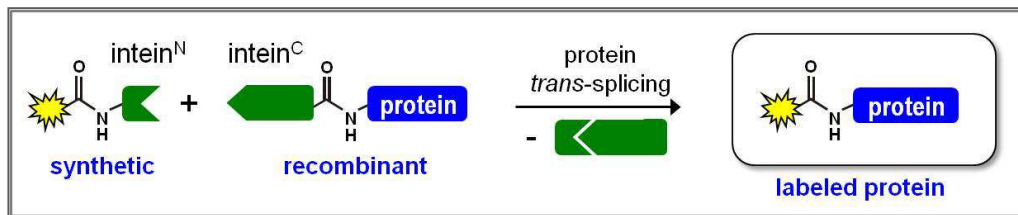


# Short N terminus Split Inteins

## Novel Split Inteins for protein semisynthesis and protein coupling

### Invention

Protein trans-splicing catalyzed by split inteins is a powerful technique for assembling a polypeptide backbone from two separate parts. As shown in the figure, the N and C terminal intein fragments associate and fold into the active domain thereby linking the flanking sequences with a peptide bond.



However, split inteins with robust efficiencies and short fragments suitable for peptide synthesis are rare and have mostly been artificially created exhibiting poor to moderate coupling efficiencies only.

The present invention provides naturally split inteins characterized for protein labeling with an N terminus as short as 25 amino acids and even shorter.

The N terminal fragments were easily amenable to chemical synthesis with a fluorescent label. Optimal protein trans-splicing activity was observed at low temperatures. Further improved mutants were selected by directed protein evolution. The engineered intein variants with up to 50-fold increased rates showed unprecedented efficiency in chemically labeling of a diverse set of proteins.

### Commercial Opportunities

The present invention allows for new strategies in the semisynthetic synthesis of proteins and in biotechnology.

On behalf of University of Muenster and Yeda, PROvendis offers a patent license as well as a research collaboration with licensing option to innovative companies.

### Current Status

A European patent application has been filed and is within the priority year.

### Relevant Publication

Thiel, I. V., Volkmann, G., Pietrokovski, S. and Mootz, H. D. (2014): An Atypical Naturally Split Intein Engineered for Highly Efficient Protein Labeling. *Angew. Chem. Int. Ed. Engl.* 53 (5):1306-10.

An invention of Westfaelische Wilhelms-University Muenster (UniMuenster) and Weizmann Institute of Science.

### Competitive Advantages

- **Inteins featuring a short N terminus**
  - N terminus of 25 AAs and shorter
  - Naturally occurring, thus, providing high yields
  - Engineered variants available
- **N terminus readily synthesized and modified by solid support synthesis**
- **Novel access to protein semisynthesis and protein modification**

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