



Max-Planck-Innovation

## Technology Offer

### Do you need to shut down protein synthesis reversibly and in a cell-type specific manner?

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**Max-Planck-Innovation GmbH**  
Amalienstr. 33  
80799 Munich  
Germany

Phone: +49 (89) 29 09 19 - 0  
Fax: +49 (89) 29 09 19 - 99  
info@max-planck-innovation.de  
www.max-planck-innovation.de

**Contact:**  
Dr. Dieter Link  
Tel.: 089 / 290919-28  
link@max-planck-innovation.de

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## Background

Proteins are the main functional units within cells. Their regulated synthesis and degradation are crucial for controlling biological processes. In all cells, protein synthesis is used to respond to extra- and/or intracellular cues to remodel cellular function. In the brain protein synthesis is crucial for some forms and specific temporal phases of synaptic plasticity and learning and memory. Previous studies probing the role of protein synthesis have used chemical inhibitors, often common antibiotics, which are effective but lack functional and cell-type specificity.

## Technology

Scientists from the Max-Planck Institute for Brain Research in Frankfurt/Main designed a very precise and genetically encoded Protein Synthesis Inhibitor (gePSI) (1). In contrast to the classical chemical approach, the gePSI allows for a cell-type selective, inducible and reversible inhibition of protein synthesis.

The basis for the gePSI system is a class of bacterial and plant toxins from the Shiga and Ricin families that are also known as ribosome inactivating proteins (RIPs). These highly potent proteins trigger a complete shutdown of protein synthesis by depurinating a specific adenine on the ribosomal 28S-rRNA. The scientists harnessed the toxicity by splitting the protein in two parts, each part being inactive in isolation. In the gePSI tool, both parts are expressed in a cell-type specific manner from an inducible promoter allowing for spatial and temporal control of the holo-enzyme formation.

The system was tested in neurons and was shown to interfere with protein synthesis in a cell-autonomous manner. Neighboring cells in direct physical contact with the gePSI-expressing cells showed no change in protein synthesis. The time-controlled expression of the gePSI in neurons was able to block a form of synaptic change that is a correlate of learning and memory. Furthermore, effective protein synthesis inhibition was achieved after 2-4 hrs and following the removal of the inducing agent the cells exhibited functional recovery of protein synthesis capabilities.

In summary, the gePSI is highly effective tool to analyze protein synthesis inhibition in a subset of cells in a complex mixture or tissue (e.g. cell cultures, organoids, tissue- or animal models).

We are currently seeking licensing partners for this technology.

**Patent Information:** A European priority application has been filed in May 2019.

**Reference:** (1) Heumüller M. et al., Nature Methods 2019, doi: 10.1038/s41592-019-0468-x