

Eukaryotic *In Vivo* Reaction Compartments

Problem to be solved

Biotechnological expression of highly active proteins or small chemical compounds of pharmaceutical relevance is often difficult. Many proteins or molecules of interest (POIs/MOIs) have cytotoxic side effects and interfere with the host's metabolism. A common problem in the production of POIs is also often the incorrect posttranslational modification (PTM) in expression hosts such as bacteria, yeast, and mammalian cells. Besides that, the full or partial synthesis of many bioactive MOIs is far from being solved and reconstituted in the lab or chemical plant. Therefore, for the manufacture of high value products, both a powerful eukaryotic protein production system with a tight expression control in a spatial and time-dependent manner and delivering proper PTMs and new strategies in synthetic biology are of particular interest in biotechnological applications upstream of industrial production.

Novel solutions

Protein production. The new approach uses a versatile tool based on a low-temperature inducible protein accumulation system (It-degron) that allows to switch the function of POIs ON/OFF. Remarkably, this switchable/conditional protein accumulation is achieved by a simple temperature shift within the physiological range. It is applicable to various eukaryotic hosts. For the first time, it does not only work in single celled organisms such as yeasts, but also in multicellular ones like insects and intact plants *in vivo*. It has been demonstrated to work for various target POIs among them transcription factors and enzymes like kinases, proteases and hydrolases but also toxic proteins (Fig. 1a).

Secondly, conditional expression of POIs can be used to create reaction compartments such as leaf hairs (trichomes; Fig. 1b). These comprise a highly bioactive environment with respect to the formation of metabolites and small bioactive molecules.

Production of small molecules. On top, these 'switchable' cells can be equipped with further regulators and enzymes needed to build up a biosynthetic pathway for the production of MOIs *in situ*. This is an example for the engineering of morphologically separated cell- or tissue-based bioreactors. In these specific compartments, POIs and MOIs can be produced on demand. The system is suitable for products, which otherwise lead to adverse effects in the expression host and are therefore difficult to be produced heterologously in regularly used organisms.

The invention provides tools and methods to generate so-called '**phenotypes on demand**' for the production of POIs/MOIs in a spatial and time-dependent manner ensuring proper PTMs.

Applications

Establishment of the production of POIs or MOIs, which are difficult to be produced by common systems.

Commercialization

We are seeking collaboration partners and licensing relationships to develop this exciting synthetic biotechnology further. We also provide the possibility to obtain a license for use of the tools.

Patent situation

A patent application has been filed claiming both the tools and the methods.

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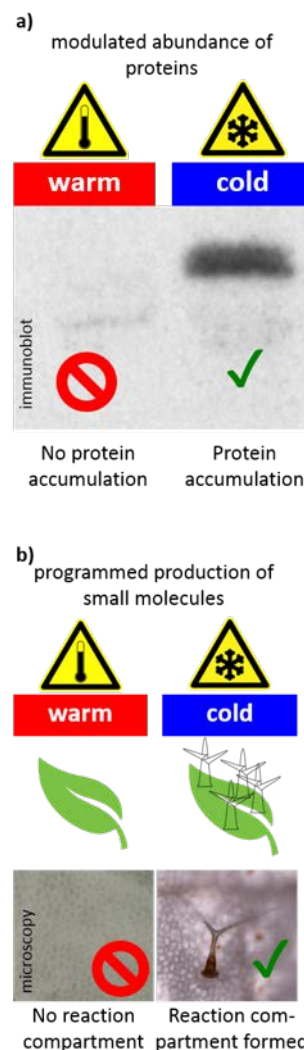


Figure 1. Biotechnological application of the It-degron system. a) Production of proteins and b) establishment of reaction compartments *in vivo* used for the production of small molecules.

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