Technology Offer

TLB
Technologie-Lizenz-Büro
der Baden-Württembergischen Hochschulen GmbH

Reverse solid phase transfection of proteins and other macromolecules into living eukaryotic cells

Abstract

Cell-friendly universal tool for transfection of numerous types of molecules into all common cells and cell lines. High throughput due to automatable sample preparation, simple storage conditions and user-friendly sample preparation.

Background

For basic research, diagnostics and therapy, there is a need for a simple method to introduce macromolecules, such as antibodies, into living eukaryotic cells. The new method enables an accelerated and cost-efficient search for new biopharmaceuticals, the identification of intracellular drug targets, the optimisation of already existing drugs and the establishment of novel cellular assays.

Problem

The decisive factors for the success or failure of a transfection are above all the cell type used and the properties of the cargo molecule to be introduced. Established transfection technologies exist for immortalised cell lines (e.g. HeLa or CHO) as well as some primary cells, but always in combination with nucleic acids in order to specifically intervene in the gene expression of the cell. For all other classes of molecules, however, there are currently only a few solutions, just as for other cell types (stem cells, immune cells, neuronal cells as well as fully differentiated cells).

Solution

A novel technology for the reverse transfection of proteins and other macromolecules into eukaryotic cells has been developed at the BioQuant Research Institute at Heidelberg University. The new method, called TOP-fase (transfection of proteins from the solid phase), allows the gentle introduction of very different classes of macromolecules, functionally active proteins (e.g. antibodies), peptides, metabolites or membrane-impermeable active substances. In addition, the method according to the invention can also be used to introduce more exotic cargoes, such as exogenous organelles, molecular probes or nanoparticles into the cell. TOP-fase here stands for reverse solid-phase transfection technology, in which multi-well plates are coated with a special complexation of cargo and transfection reagents. In this process, the molecules to be introduced into living cells are complexed with carrier molecules and mixed with additives and coating molecules. The solution is then applied to the surface of the substrate carrier and allowed to dry. In the "reverse" step, the living cells are only added to this solid substrate at the end. The molecules to be transported are taken up by means of endocytosis and thus in a much gentler way than with conventional methods for introducing molecules into cells. The functional principle of TOP-fase has been repeatedly experimentally validated and is applicable to all common cells and cell lines.

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Development Status

TRL 4 – technology validated in the lab

Patent Situation

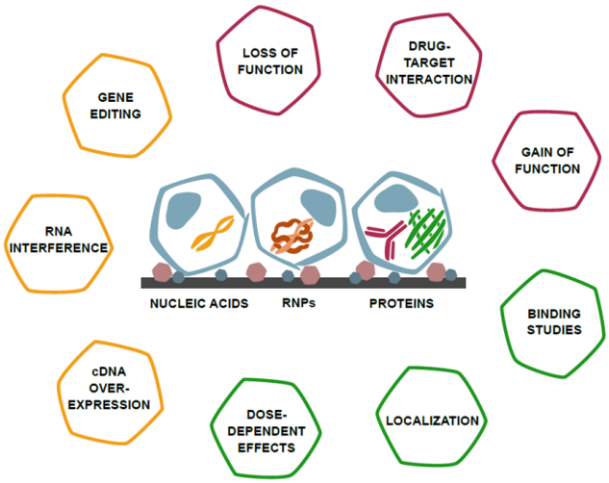
EP2981616B1 granted
DE, FR,GB, LTU, EST, LVA validated
Unionsmarke „TOP-fase“
EUTM 018024529 registered

Reference ID

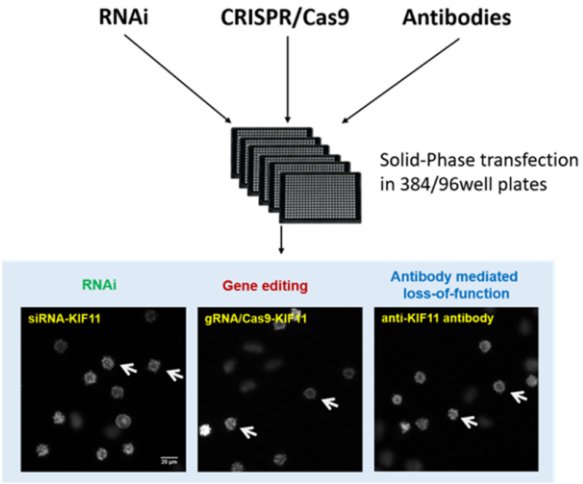
13/017TLB

Service

The Technologie-Lizenz-Büro GmbH is in charge of the exploitation of this technology and assists companies in obtaining a license.



By solid phase transfection, it is possible to introduce any molecules into cells. In addition to the (well-established) transfection of nucleic acids, the method allows the introduction of large biomolecules such as ribonucleoproteins or even functional proteins (e.g. antibodies). The potential applications are therefore manifold, ranging from gene editing, RNA interference to overexpression, in order to identify, enhance or suppress specific cellular functions and interactions. [Fig: Dr. H. Erfle, University of Heidelberg, BIOQUANT]



Solid phase transfection in multiwell plates and cell arrays for DNA knock-out by CRISPR, protein knock-down by antibodies or gene silencing by RNAi. Arrows: Nuclei of cells in the expected phenotype (e.g. cell cycle arrest) after transfection. [Fig: Dr. H. Erfle, University of Heidelberg, BIOQUANT]

Advantages

- applicable to numerous molecules to be transported
- can be used for common cells and cell lines
- particularly gentle on cells due to natural uptake process

- simple sample preparation and conversion
- high throughput: can be automated without problems and stored for a long time

Fields of application

From "target identification" to "lead optimisation" in target-based drug discovery, from the first screen to target deconvolution in phenotypic drug discovery - the variety of possible applications at all stages of the drug discovery process is enormous. Possible areas of application are, for example, point-of-care diagnostics, protein knock-downs or knock-ins as well as the determination of the localisation of intracellular proteins.

Literature and links

R. Bulkescher et al., *Solid-phase reverse transfection for intracellular delivery of functionally active proteins*, Genome Research, 2017