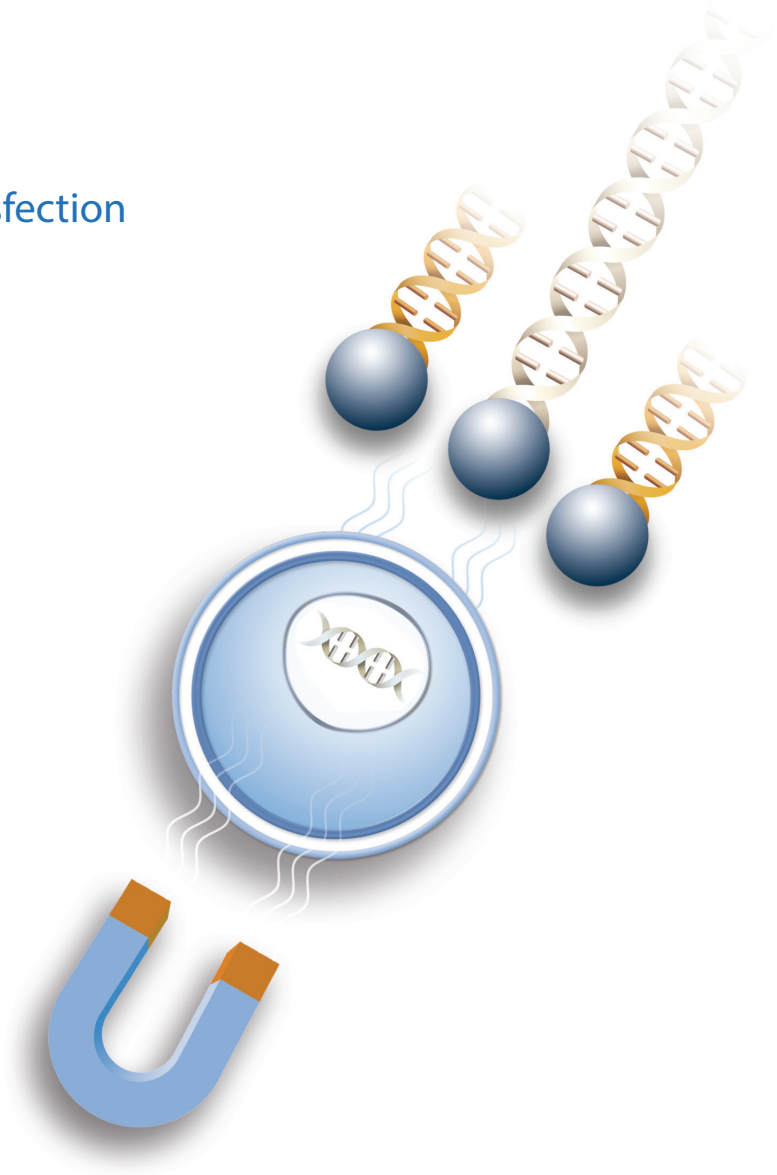
OZBIOSCIENCES
The art of delivery systems

Magnetofection™

For Primary and Hard-to-Transfect Cells

Magnetic-Assisted Transfection



Enhance Transfection Efficiency

Gene Expression - Gene Silencing
CRISPR/Cas9 Genome Editing
In vivo & *Ex vivo* Transfection

Ideal for Primary & Hard-to-Transfect Cells

MAGNETOFECTION TECHNOLOGY

Magnetofection™ is a simple and highly efficient method to transfect cells. This technology was developed to gather in one convenient system the advantages of the popular biochemical (*cationic lipids or polymers*) and physical transfection methods (*electroporation, gene gun*) while overcoming their respective limitations.

Magnetofection Benefits

- High transfection efficiency with any nucleic acids - increase efficiency from 30 to 500%
- Powerful on hard-to-transfect and primary cells
- High performance even with low dose of nucleic acids (enables to use 10 to 100 times less nucleic acids)
- Concentration of genetic material onto cells / acceleration of kinetics
- Biodegradable iron oxyde nanoparticles, safe and universal

How does it work?

- Magnetic nanoparticles are associated with nucleic acids (naked or pre-complexed with a transfection reagent or viruses) by salt-induced aggregation and electrostatic interactions
- Magnetic force drives these complexes towards the target cells, allowing a rapid concentration of the vector dose onto cells
- The cellular uptake of the genetic materials is accomplished by endocytosis and pinocytosis
- Nucleic acids are released in the cytoplasm by flip-flop mechanism or proton sponge effect*

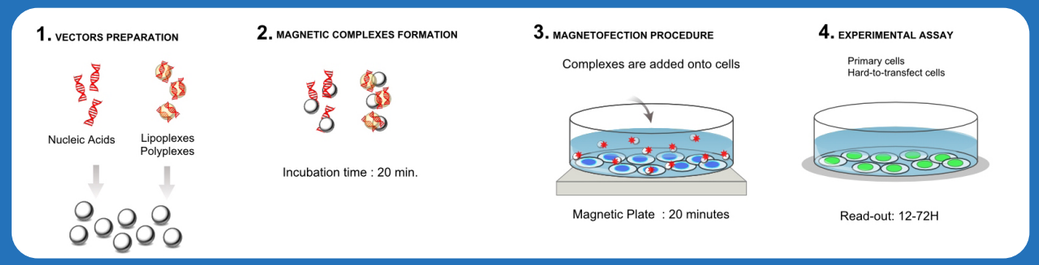


Figure 1: Magnetofection Protocol

Magnetofection reagents need to be used with an appropriate magnetic plate

Magnetic Plates for Magnetofection

Specific magnetic plates with optimal properties have been developed to reach the best transfection levels. For your convenience, we offer 2 magnetic plate sizes, suitable for all cell culture dishes:

- Super Magnetic plate (8 x 12 cm)
- Mega Magnetic plate (20 x 26 cm)

Plates can be used with incubators and robots.

* Plank *et al*, Adv. Drug Deliv. Rev. (2011), 63(14-15):1300-31

Magnetofection™ is the only versatile and universal technology adapted to *in vitro* or *in vivo* applications, to all types of nucleic acids (DNA, siRNA, dsRNA, shRNA, mRNA, ODN...) and to viral and non-viral transfection systems. Consequently, several optimized reagents have been designed according to defined applications.

Magnetofection Reagent Selection Guide

	Product	DNA	mRNA	siRNA/miRNA	Applications
***in vitro* Magnetofection** Primary and Hard-to-transfect Cells	CombiMag	V	V	V	Boost all transfection reagents efficiency
	Magnetofectamine O2	V			Ideal system for gene expression
	PolyMag Neo	V	V	V	Polymer-based magnetofection reagent
	NeuroMag	V	V	V	Powerful transfection reagent for neurons
	Glial-Mag	V	V	V	The solution for glial cells transfection
	SilenceMag			V	The bright idea for siRNA delivery
***in vivo* & *ex vivo* Magnetofection**	*in vivo* DogtorMag	V	V		*in vivo* lipid-based transfection reagent
	in vivo PolyMag	V			*in vivo* polymer-based transfection reagent
	in vivo SilenceMag			V	For *in vivo* gene silencing applications
	XPMag	V	V	V	Explant transfection reagent

*We also developed reagents dedicated to CRISPR/Cas9 Genome Editing and Viral Applications. For more information, please refer to the end of this document.

CombiMag

TRANSFECTION ENHANCER

CombiMag is a magnetic nanoparticle formulation that enables to improve transfection efficiency of any commercial transfection reagent. It can be used with all types of nucleic acids.

- Improves transfection efficiency without changing your standard protocol
- Allows creating your own optimal delivery system with an improved efficiency from 30% to 500%
- Save materials and time

«Discover how to use CombiMag to efficiently transfect primary cultures of bovine endometrial cells (fibroblasts & epithelial) with DNA.»
Lesage-Padilla A. et al, PLoS One. 2017.

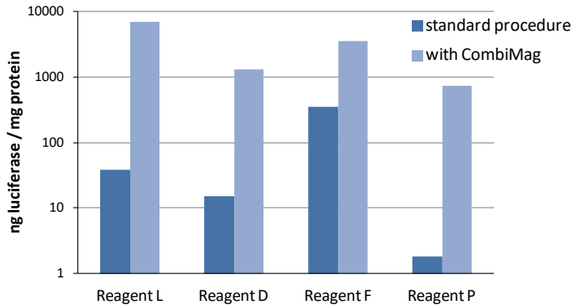


Figure 2: Luciferase expression in primary rabbit articular chondrocytes transfected with various commercial reagents without or with CombiMag. We are grateful to Dr. U. Schillinger (Technical University, Munich) for kindly providing these data.

*For an optimized delivery system, use Combimag in association with MTX reagent (Magnetofectamine O2) or DreamFect Gold reagent (LipoMag Kit).

Exceed your Transgene Expression by Using Magnetofection

PRIMARY CELLS

Magnetofectamine O2

The alliance of MTX transfection reagent and CombiMag reagent is the perfect one to lead to increased transfection efficiency, minimized toxicity and enhanced gene expression.

- Boost transfection efficiency
- Low amount of nucleic acids - minimized toxicity
- No need to change your standard protocol
- Serum compatible

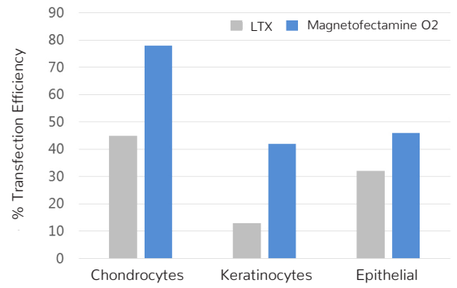


Figure 3: Various primary cells were transfected with LTX or Magnetofectamine O2 (MTX-O2). Results showed that Magnetofectamine O2 outperforms LTX transfection efficiency.

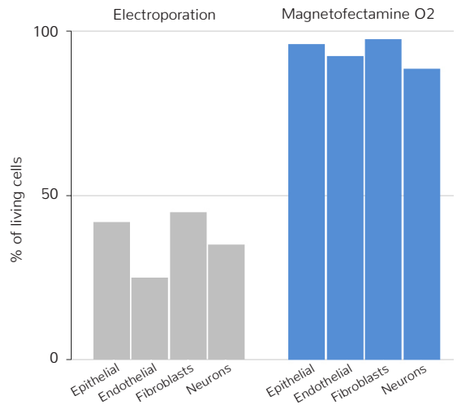


Figure 4: Cytotoxicity comparison on primary cells between 2 transfection methods: Electroporation and MTX02.

PolyMag Neo

PolyMag Neo, a versatile polymer-based transfection reagent, is composed of magnetic nanoparticles coated with specific cationic molecules. It enhances transfection efficiency on primary cells and hard-to-transfect cells.

- High transgene expression
- High transfection efficiency on primary cells
- Multipurposes: successfully tested with with various cells and nucleic acids
- High performance even with low doses of nucleic acids

Over 120 cells tested!

«Primary human neonatal cardiomyocytes successfully transfected with plasmid DNA using Polymag.»
Bittel DC. et al, Cells. 2014.

«DNA Transfection, gene silencing & cotransfection (DNA + siRNA) in HUVEC using PolyMag.»
Acosta MI. et al, Scientific Rep. 2018.

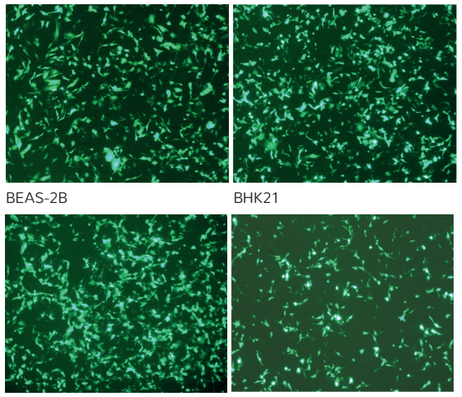


Figure 5: 1x10^5 cells were transfected with PolyMag Neo reagent in 24-well plates. EGFP expression was monitored 24h after transfection by fluorescence microscopy.

DNA/RNA/ODN...

NEURONS

NeuroMag

NeuroMag is the first dedicated transfection reagent for neurons. It is perfect for primary neurons but also for neural cells. Due to its unique properties, NeuroMag allows to follow the maturation of transfected neurons during several days after transfection.

- Highly efficient on primary neurons: hippocampal, cortical, motor and dopaminergic neurons, glioblastoma, neuroblastoma, DRG, oligodendrocytes, neural stem cells...
- Efficient from 1 DIV to 21 DIV
- Non toxic and completely biodegradable: high transfected neurons viability
- Long transgene expression (up to 7 days)
- Suitable for all types of nucleic acids

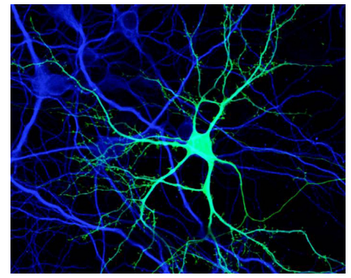


Figure 6: Primary rat hippocampal neurons 6 days after transfection with NeuroMag.

«Transfection of small RNAs (siRNAs, siPOOLs or sgRNAs) in primary Retinal Ganglion Cells using NeuroMag.»
Welsbie DS et al, Neuron. 2017.

«Transfection efficiency of primary cortical neurons was in the range of 20–30% for overexpression, and 10–15% for TDP-43 knockdown experiments.»
Chou C.C. et al, Nature Neuroscience. 2018.

GLIAL CELLS

Glial-Mag

Glial-Mag transfection reagent is a new powerful formulation for delivery of nucleic acids into microglial cell lines and primary microglia. This kit is the association of a specific magnetic nanoparticles formulation (Glial-Mag reagent) and a booster (Glial-Boost) designed to enhance transfection efficiency.

- For transfection of microglial cells line such as BV2, N9, N13, HMO6, MG-5, SIM-A9 and primary microglia
- Low nucleic acid amount - minimized toxicity
- High level of nucleic acid compaction

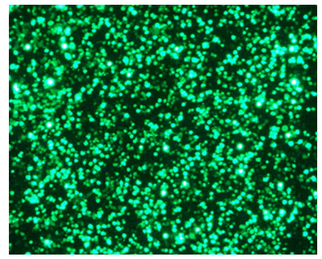


Figure 8: BV2 transfected with pVectOZ-GFP using Glial-Mag.

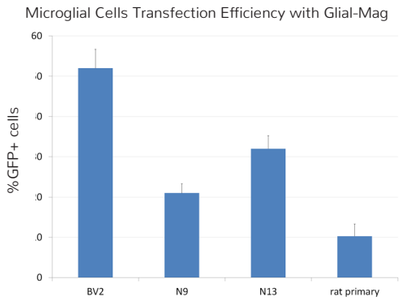


Figure 7: BV2, Rat Primary, N9 and N13 cells were transfected with Glial-Mag. After 24h, GFP+ cells were analyzed by Flow cytometry.

«Magnetofection is superior to other chemical transfection methods in a microglial cell line.»
Smolders S. et al, Journal Neuroscience Methods. 2018.

Efficiency Proven in More than 2000 Publications

Successfully tested and published!

SilenceMag

SilenceMag uses the magnetic force to enhance transfection efficiency on primary and hard-to-transfect cells or target silencing into tissues. Based on the Magnetofection technology, SilenceMag reagent gives high protein knockdown at very low doses of siRNA in numerous cell types and tissues.

- Increased silencing efficiency
- Minimized toxicity and off-target effects
- Low siRNA/miRNA doses required
- Targeted silencing (magnetically-driven)

«90% gene silencing in primary human endothelial colony forming cells.»
Hubert L. et al, J Thromb Haemost. 2014.

«Gene Silencing in Endothelial Colony Forming Cells (ECFC) using magnetofection SilenceMag - Approximatively 85-90% ECFC transfection efficiency was achieved.»
Essaadi K. et al, Scientific Reports. 2018.

«siRNA transfection on THP-1 cells and RAW 264.7 was performed by using Magnetofection SilenceMag.»
Iwata H. et al, Nat. Commun. 2016.

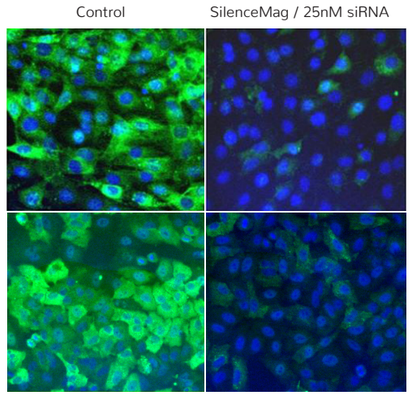


Figure 9: NIH-3T3 (A) and A549 (B) cells were treated with 5 µL SilenceMag and 25nM siRNA targeting GAPDH gene. GAPDH expression was monitored 72h after transfection.

siRNA

in vivo & ex vivo Magnetofection

In vivo Magnetofection has been designed for *in vivo* targeted transfection and transduction. This original system combines magnetic nanoparticles & nucleic acid vectors that are retained after injection at the magnetically targeted site. In this way, systemic distribution is minimized and toxicity is reduced. DNA complexes can be easily administrated through various injection routes such as systemic administration (intravenous, intra-artery) or local administration (intratumoral, intracerebroventricular).

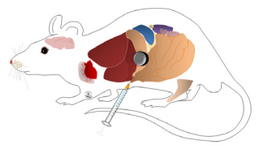


Figure 10: Targeted transfection in stomach.

«Kidney-specific *Csf2* knockdown. *In vivo* gene silencing achieved by transfecting siRNA using *in vivo* SilenceMag.»
Fujiu K et al, Nature Medicine. 2017

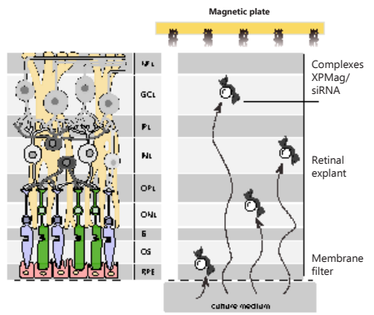


Figure 11: Transfection by «Reverse Magnetofection in sections of the central retina.

- *in vivo* PolyMag, a cationic polymer-based magnetic nanoparticles formulation, designed for *in vivo* transfection of nucleic acids.
- *in vivo* DogtorMag, a cationic lipid-based magnetic nanoparticles formulation, designed for *in vivo* transfection of nucleic acids.
- *in vivo* SilenceMag, a cationic lipid-based magnetic nanoparticles formulation, designed to transfect siRNA/miRNA, into target cell/ tissue *in vivo.*
- XPMag, a novel magnetic nanoparticles formulation dedicated to gene transfection in organotypic cultures of explant by "Reverse Magnetofection".

IN VIVO & EX VIVO MAGNETOFECTION

REFERENCES

Products	Primary Cells	Publications
CombiMag	LSK (Bone Marrow Hem. S.C.)	Naka K., Nat Commun. 2015;6:8039
	Bone Marrow derived macrophages	Iwata H., Nat Commun. 2016;7:12849
	Melanoma	Alvizo-Báez., J Nanopart Res. 2022;24:165
	Endometrial cells (Fibroblasts + Epithelial)	Lesage-Padilla A., PLoS One. 2017;12(12):e0189942
	Primary Human Endothelial cells	Hubert L., J Thromb Haemost. 2014;12(7):1170-81
	Hepatocellular carcinoma	Rong M., BMC Cancer. 2013;13:21
	Glioblastoma	Fukushima T., J Biol Chem. 2007;282(25):18634-44
	Lung (*in vivo*)	Ungureanu BS., J Gastrointestin Liver Dis. 2016;25(3):375-83.
Magnetofectamine O2	Lung carninoma	Shi Q., Genes Cancer. 2015;6(5-6):220-30
	Neuroblastoma	Long AN., BMC Neurol. 2015;15(1):272
	HUC-MSC	Schade A., Stem Cells International. 2014.197154
	Cortical neurons	Zemoura K., J Biol Chem. 2014;289(11)7738-46
	synovial fibroblasts	Frolov A., J Biol Chem. 2013;288(33):23696-703
	Hippocampal neurons	Tyagarajan SK., J Biol Chem. 2013;288(14):9634-47
	Mesenteric lymph node endothelium	François M., Nature. 2008;456(7222):643-7
PolyMag Neo	MDCK	Underhill SM., J Neurosci. 2015;35(13):5260-70
	Cardiomyocytes	Bittel DC., Cells. 2014;3(3):713-723
	Keratinocytes	Zhang SQ., Nat Genet. 2012;44(10):1156-60
	HUVEC	Acosta MI., Sci Rep. 2018;8(1):1410
	Trabecular Meshwork	Tellios N., Sci Rep. 2017;7(1):812.
	Left adductor muscle (*in vivo*)	Ohashi K., J Biol Chem. 2014;289(20)14132-44
SilenceMag	Cervical epithelial carcinoma	Mykhaylyk O., Methods Mol Biol. 2015;1218:53-106
	Endothelial colony forming	Essaadi A., Sci Rep. 2018;8(1):9387
	Monocytes	Lei Y., J Cardiovasc Dev Dis. 2015; 2:31-47
	Kelly cells	Kasim M., J Biol Chem. 2014;289(39):26973-88
	Myometrial cells	Lappas M., Biol Reprod. 2013;89(1):14
	Endothelial cells (*in vivo*)	Fujiu K., Nat Med. 2017;23(5):611-622
	Hepatocellular carcinoma, HepG2 (*in vivo*)	Chen J., BMC Cancer. 2014;14(1):114
NeuroMag	Motor neurons	Baron, D., Cell reports. 2022;110598
	Cortical neurons	Mendonça, P. R.., Nat Commun. 2022;13:3497
	Cortical neurons	Petrova, Nat Commun. 2020; 11(1):5614
	Cortical neurons	Asselin, L., Nat Commun. 2020;11(1):2441
	Cortical neurons	Courchet J., Cell. 2013;153(7):1510-25
	Cortical neurons + iPSC derived neurons	Wang W., Nat Med. 2016;22(8):869-78.
	Dopamine neurons	Underhill SM., Neuron. 2014;83(2):404-16
	Hippocampal neurons	Charrier C., Cell. 2012;149(4):923-35
	Hippocampal neurons	Alavian KN., Nat Cell Biol. 2011;13(10):1224-33
	Motor neurons derived from ES cells	Terenzio M., EMBO J. 2014;33(14):1582-98
Glial-Mag	Microglial	Grubman, A., Nat Commun. 2021;12:3015
	BV2	Smolders S., J Neurosci Methods. 2017;293:169-173
	Microglial	Carrillo-Jimenez A., Front. Cell. Neurosci. 2018;12:313
Magnetofection	Embryonic kidney	Choi, J., Nature. 2022;1-10
	Fibroblasts	Frolov A., J Biol Chem. 2013;288(33):23696-703
	LSK	Ikushima YM., Blood. 2013;121(11):1995-2007

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Viral Applications

Magnetofection is ideal for **enhancing viral transduction efficiency**. Tailored reagents are available: ViroMag, ViroMag RL & AdenoMag.

CRISPR/Cas9 Genome Editing

"**Genome editing**" or "**Genome engineering**" gives the ability to introduce a variety of genetic alterations (deletion, insertion...) into mammalians cells. Successful CRISPR/Cas9 genome editing can be performed through diverse approaches (plasmids, mRNA, nuclease, viral delivery). Accordingly, efficient nucleic acids delivery represents a critical step for genome editing experiments. **With more than 15 years of expertise in the development of transfection reagents**, OZ Biosciences offers specific solutions:

Product Name	Molecul vector	Technology	Application
Ⓜ PolyMag CRISPR	Plasmid DNA	Magnetofection	Primary and hard-to-transfect cells
Pro-DeliverIN CRISPR	Protein	Lipofection	All cells
RmesFect CRISPR	mRNA	Lipofection	All cells
Ⓜ ViroMag CRISPR	Virus	Magnetofection	All cells including primary and hard-to-transfect cells

Figure 12: Transfection Reagents for CRISPR/Cas9

Ⓜ These reagents are based on Magnetofection technology

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