

- ✦ Successful *in vivo* delivery of DNA, siRNA and oligonucleotides
- ✦ Multiple modes of administration in many species
- ✦ No detectable inflammatory response
- ✦ Reproducible results

In vivo-jetPEI™ reagent provides versatile, reproducible and reliable nucleic acid delivery in animals. This linear polyethylenimine reagent is used for:

- gene therapy^{1,2}
- RNA Interference^{3,4}
- protein function studies⁵
- genetic vaccination⁶

In vivo-jetPEI™ is currently used in human clinical trials as a delivery vector for cancer gene therapy¹.

✦ Successful *in vivo* delivery of DNA, siRNA and oligonucleotides

In vivo-jetPEI™ is able to deliver DNA and to mediate gene expression in various tissues. For example, the highest level of luciferase expression is detected in the lung following intravenous injection in mice (Fig. 1).

Depending on the route of administration, *in vivo-jetPEI™*-mediated gene expression is also observed in the brain, liver, pancreas, spleen, kidney, heart, bladder, skin and artery.

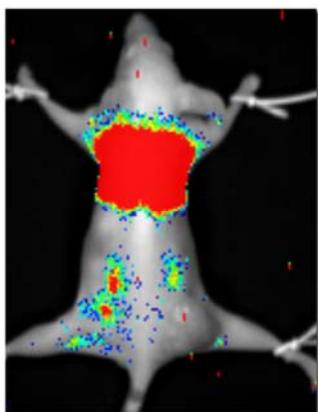


Fig. 1. Systemic delivery using *in vivo-jetPEI™*. Bioluminescent imaging of luciferase expression in living Balb/C mouse using a cooled camera 24 h after gene delivery. pCMVLuc (50 µg) was complexed with *in vivo-jetPEI™* in 400 µl of 5% glucose solution and injected into the tail vein. Courtesy J.L. Coll.

Specific inhibition of protein synthesis can be achieved by delivering small oligonucleotides such as siRNA, antisense or ribozyme with *in vivo-jetPEI™* in animal models (Fig. 2). Recently, an *in vivo-jetPEI™* derivative was successfully used as delivery reagent for anti-cancer therapy by RNA interference³⁻⁴.

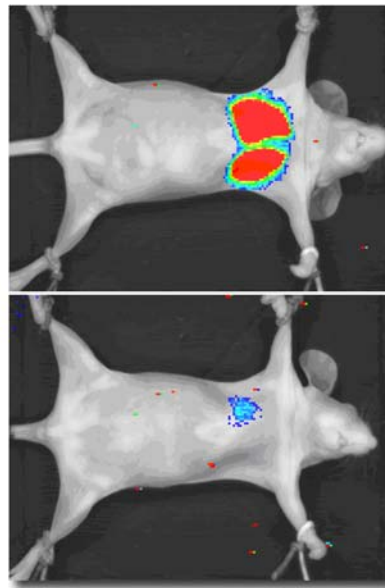


Fig. 2: RNA interference in the lung with *in vivo-jetPEI™*. pCMVLuc (40µg) was co-transfected with 10 µg of specific anti-Luc siRNA (upper) or with a control siRNA (lower). The complexes were injected into the tail vein of nude mice. Luciferase gene expression was monitored in living mice 24 h later by bioluminescence imaging using a cooled CCD camera.

✦ Multiple modes of administration in many species

Numerous delivery routes of administration have been tested using *in vivo-jetPEI™* (Fig. 3). Literature references are available on the Polyplus website (Product Citation Database).

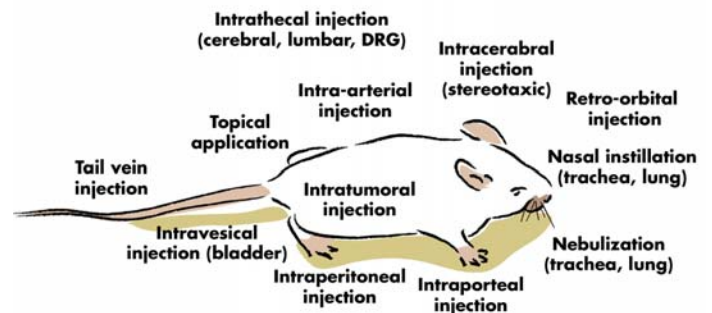


Fig. 3. Successfully delivery routes in mouse.

In vivo-jetPEI™ was successfully used to deliver nucleic acid in many species including mouse, rat, guinea pig, duck, rabbit, monkey, goat, sheep, chicken, quail, hamster cow, tadpole, shrimp and fish.

+ No detectable inflammatory response

Linear PEI does not induce any pro-inflammatory response after systemic injection, especially when compared to highly immunogenic compounds such as lipid transfection reagents or branched PEI⁷. Additionally, linear PEI does not generate neutralizing antibodies, permitting repeated administrations⁶.

+ Unique properties of *in vivo-jetPEI*™

in vivo-jetPEI™ condenses nucleic acids into approximately 50 nm nanoparticles⁸ that are stable for several hours. As a result of this unique protection mechanism, aggregation of blood cells following injection is reduced compared to other reagents⁹, thereby preventing restricted diffusion within a tissue, erythrocyte aggregation and microembolism.

These nanoparticles are sufficiently small to diffuse into the tissues and enter the cells by endocytosis. *in vivo-jetPEI*™ favors nucleic acids release from the endosome and transfer across of the nuclear membrane.

+ Reproducible results

Gene delivery using *in vivo-jetPEI*™ is reliable and provides reproducible data experiment after experiment (Fig. 4), without any noticeable toxic side effects observed using other methods.

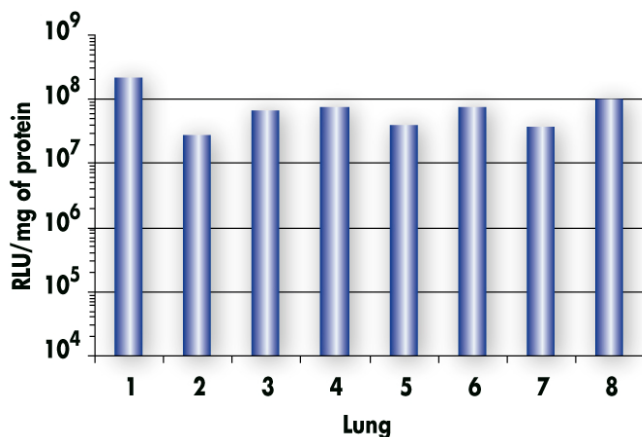


Fig. 4. Systemic delivery using *in vivo-jetPEI*™. pCMVLuc (50 µg) was complexed with *in vivo-jetPEI*™ in 5% glucose and injected retro-orbitally. After 24 h, luciferase gene expression was assessed in the lung (n=8). Viability of mice was 100%.

Product	Cat N°	Reagent	Glucose solution
<i>in vivo-jetPEI</i> ™	201-10G	0.1 ml	10 ml
	201-50G	0.5 ml	2 x 10 ml

0.1 ml of *in vivo-jetPEI*™ is sufficient to perform up to 20 intravenous injections in mouse (50 µg of DNA per injection).

Bulk quantities available upon request.

QC reports and cGMP-*in vivo-jetPEI*™ are available upon request for clinical trials.

INTELLECTUAL PROPERTY

The use of polyethylenimine (PEI) or polypropylenimine (PPI) or cationic polymers similar in structure thereto for transfecting cells, as well as compositions comprising these cationic polymers and at least one nucleic acid, are the subject matter of U.S. Patent No. 6,013,240, EP Patent No. 0770140 and foreign equivalents, for which Polyplus-transfection™ is the worldwide exclusive licensee.

For additional information, please contact our technical support at www.polyplus-transfection.com.

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- Ohana et al., 2004. *Gene Ther Mol Bio* 8:181-192.
- Vernejoul et al., 2002. *Cancer Research* 62:6124-31.
- Urbain-Klein et al., 2004. *Gene therapy* 23:1-6.
- Grzelinski et al., 2006. *Human Gene Therapy* 17:751-66.
- Lemkine et al., 2002. *Mol. Cell. Neurosci.* 19:165-174.
- Garzon et al., 2005. *Vaccine* 23:1384-92.
- Kawakami et al., 2006. *J Pharmacol Exp Ther* 317:1382-90.
- Goula et al., 1998. *Gene Therapy* 5:712-717.
- Kirchheis et al., 2001. *Gene Therapy* 8:28-40.