

Supporting Information

Lipid Nanoparticles – From Liposomes to mRNA Vaccine Delivery, a Landscape of Research Diversity and Advancement

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Table S1. Clinically approved LNP formulations^{1-8,*}

Trade Name	Approval	Administration	Active ingredient	Composition	LNP carrier	Indication for use	Manufacturing company
Abelcet	1995	IV	Amphotericin B	DMPC:DMPG	liposomes	Severe fungal infections	Sigma-Tau Pharmaceuticals
Ambisome	1997	IV	Amphotericin B	HSPC:DSPG:Chol	liposomes	Fungal infections	Astellas Pharma
Amphotec	1996	IV	Amphotericin B	Cholesteryl sulfate	liposomes	Severe fungal infections	Ben Venue Laboratories Inc.
Caelyx	1996	IV	Doxorubicin	PEG 2000-DSPE:HSPC:Chol (5:56:39)	PEGylated liposomes	Ovarian cancer, Kaposi's sarcoma, breast cancer	Sequus (formerly Liposome Technology Inc.)
Curosurf	1999	Intra-tracheal	Poractant alfa	pulmonary surfactant (mainly DPPC)	suspension	Respiratory distress syndrome	Chiesi Farmaceutici
DaunoXome	1996	IV	Daunorubicin	DSPC:Chol (2:1)	liposomes	AIDS-related Kaposi's sarcoma	NeXstar Pharmaceuticals
Depocyt	1999	Spinal	Cytarabine/Ara-C	DOPC, DPPG, Chol, triolein	liposomes	Neoplastic meningitis	SkyPharma Inc.

DepoDur	2004	Epidural	Morphine sulfate	DOPC, DPPG, Chol, triolein	liposomes	Pain management	SkyPharma Inc.
Diprivan	1989	IV	propofol	Soybean oil, egg lecithin	liposomes	Sedation or anesthesia	Fresenius Kabi
Doxil	1995	IV	Doxorubicin	HSPC:Chol:PEG2000-DSPE (56:39:5)	PEGylated liposomes	Ovarian, breast cancer, Kaposi's sarcoma	Sequus Pharmaceuticals
Epaxal	1993	IM	Inactivated hepatitis A virus (strain RGSB)	DOPC:DOPE (75:25)	liposomes	Hepatitis A	Crucell, Berna Biotech
Estrasorb	2003	Trans-dermal	Estradiol	Soybean oil	micelles	Menopause therapy	Novavax
Exparel	2011	IV	Bupivacaine	DEPC, DPPG, Chol, tricaprylin	liposomes	Pain management	Pacira Pharmaceuticals, Inc.
Fungizone	1997	IV	Amphotericin B	DMPC:DMPG	liposomes	Systemic fungal infections	Bristol-Myers Squibb
Ikervis	2014	Ocular (eye drops)	Cyclosporine A	Medium-chain triglycerides	emulsion	Keratitis in patients with dry eye disease	Santen Pharmaceutical Co.
Inflexal V	1997	IM	Inactivated hemagglutinin of influenza virus strains A and B	DOPC:DOPE (75:25)	liposomes	Influenza	Crucell, Berna Biotech

Lipusu	2020	IV	Paclitaxel	N/A	liposomes	Squamous non-small-cell lung cancer, esophageal cancer	Luye Pharmaceuticals
Marqibo	2012	IV	Vincristine	SM:Chol (60:40)	liposomes	Acute lymphoblastic leukemia	Talon Therapeutics, Inc.
Mepact	2004	IV	Mifamurtide	DOPS:POPC (3:7)	liposomes	High-grade, resectable, nonmetastatic osteosarcoma	Takeda Pharmaceutical Limited
Myocet	2000	IV	Doxorubicin	EPC:Chol (55:45)	liposomes	Combination therapy with cyclophosphamide in metastatic breast cancer	Elan Pharmaceuticals
Octocog alfa (Advate)	2009	IV	Factor VIII	PEG lipid	PEGylated liposomes	haemophilia A, uncontrolled bleeding	Bayer Pharma AG
Onivyde	2015	IV	Irinotecan	DSPC:MPEG-2000:DSPE (3:2:0.015)	liposomes	Combination therapy with fluorouracil and leucovorin in metastatic pancreatic adenocarcinoma	Merrimack Pharmaceuticals Inc.
Onpattro (patisiran)	2018	IV	RNAi therapeutic, transthyretin-directed siRNA	DLin-MC3-DMA, PEG2000-C-DMG, DSPC, Chol	lipid nanoparticle	Polyneuropathy caused by hereditary transthyretin-mediated	Alnylam Pharmaceuticals

						amyloidosis (hATTR amyloidosis)	
Rapamune	2002	Oral	Rapamycin (sirolimus)	PC, propylene glycol, glycerides, ethanol, soy fatty acids, ascorbyl palmitate	liposomes	Immuno-suppressant	Pfizer
ThermoDox	2014	IV	Doxorubicin	DPPC, MSPC, PEG 2000-DSPE	PEGylated liposomes	Hepatocellular carcinoma	Celsion Corporation
Visudyne	2000	IV	Verteporfin	DMPC, EPG	liposomes	Choroidal neovascularization	Novartis
Vyxeos	2017	IV	Daunorubicin / Cytarabine (1:5)	DSPC:DSPG:Chol (7:2:1)	liposomes	Acute myeloid leukemia	Jazz Pharmaceuticals

* The LNP-based mRNA COVID-19 vaccines BNT162b2 and mRNA-1273 are not included in the table, because they have received only Emergency Use Authorization (EUA) in 2020.

Abbreviations: Chol, cholesterol; PC, phosphatidylcholine; PG, phosphatidylglycerol; PE, phosphatidylethanolamine; PS, phosphatidylserine; DEPC, Dierucoyl PC; DMPC, dimyristoyl PC; DMPG, dimyristoyl PG; DOPC, dioleoyl PC; DOPE, dioleoyl PE; DOPS, dioleoyl PS; DPPG, dipalmitoyl PG; DSPC, distearoyl PC; DSPE, distearoyl PE; DSPG, distearoyl PG; EPC, egg PC; HSPC, hydrogenated soy PC; MSPC, monostearoyl PC; IM, intramuscular; IV, intravenous; PEG, polyethylene glycol; MPEG, methoxy PEG; POPC, palmitoyloleoyl PC; SM, sphingomyelin.

Table S2. Marketed LNP cosmetic preparations ⁹⁻¹²

Type of Delivery system	Product Name	Producer	Activity
SLN	Cutanova Cream Nano Repair Q10	Dr. Rimpler	Antiaging and skin repair
	Intensive Serum NanoRepair Q10	Dr. Rimpler	Skin repair
	Cutanova Cream NanoVital Q10	Dr. Rimpler	Antiaging and skin repair
	Lipopearl	Adina	Skin emollient (pearlescent beads, oils and vitamins)
	Swiss Cellular White Illuminating Eye Essence	La Prairie	Brightening skin care
	Olivenöl Anti Falten Pflege	Medipharma Cosmetics	Anti-wrinkle
	Super Vital Cream	IOPE	Antiaging cream
	SURMER Creme Legere	Isabelle Lancray	Face moisturizer
	Eusolex 4360	Merck	Sunscreen
	Allure Body Cream	Chanel	Body moisturizer
	Allure Parfum Bottle	Chanel	Perfume
	Allure Eau Parfum Spray	Chanel	Perfume
	Soosion Facial Lifting Cream	Soosion	Anti-wrinkle cream
Phyto NLC Active Cell Repair	Sireh Emas	Skin rejuvenation, moisturizing & skin firming	
NLC	Nanopearl	PharmaSol	Cosmetic creams, gels, lotions
Ethosomes	Nanominox	Sinere, Gernay	Hair growth stimulant
	Supravir Cream	Trima Israel	Antiaging and skin repair
	Cellulite EF	Hampden Health, USA	Anti-cellulite
	Decorin Cream	Genome Cosmetics, U.S.	Antiaging and skin repair

	Noicellex	Novel Therapeutic Technologies, Israel	Anti-cellulite cream
	Skin Genuity	Physonics, Nottingham, UK	Anti-cellulite
	Lipoduction	Osmotics, Israel	Anti-cellulite
Liposomes	Celadrin	Pharmaceutical Grade (USP)	Topical liposome lotion
	Capture Totale	Christian Dior	Antiaging and skin repair
	Efect du Soleil	L'Oréal	Tanning agents
	Future Perfect Skin Gel	Estée Lauder	Anti-wrinkle cream
	Aquasome LA	Nikko Chemical Co	Skin humectant
	Eye Perfection	Avon	Soothing cream for eye irritation
	Flawless Finish	Elisabeth Arden	Liquid make-up
	Revitalift	L'Oréal	Anti-wrinkle, skin firming
	Lyphazome	Kara Vita	Skin emollient
	Celazome	Celazome	Skin moisturizer
	Psorinel Lotion	DERMAVIDUALS	Skin lotion
	Hydra Zen	Lancôme	Skin moisturizer
	Dermosome	Microfluidics	Skin moisturizer
	Decorte Moisture Liposome Face Cream	Decorte	Skin moisturizer
	Decorte Moisture Liposome Eye Cream	Decorte	Skin moisturizer, conditioner
	Natural Progesterone Liposomal Skin Cream	NOW Solutions	Skin conditioner
	C-Vit Liposomal Serum	Sesderma	Skin moisturizer, conditioner
Advanced Night Repair Protective Recovery Complex	Estée Lauder	Skin repair	

	Fillderma Lips Lip Volumizer	Sesderma	Lip volumizer, wrinkles repair, skin moisturizer
	Lumessence Eye Cream	Aubrey Organics	Anti-wrinkle & firming
	Russell Organics Liposome Concentrate	Russell Organics	Skin moisturizer & rejuvenator
	Clinicians Complex Liposome Face & Neck Lotion	Clinicians Complex	Skin conditioner, sunscreen
	Kerstin Florian Rehydrating Liposome Day Crème	Kerstin Florian	Skin moisturizer

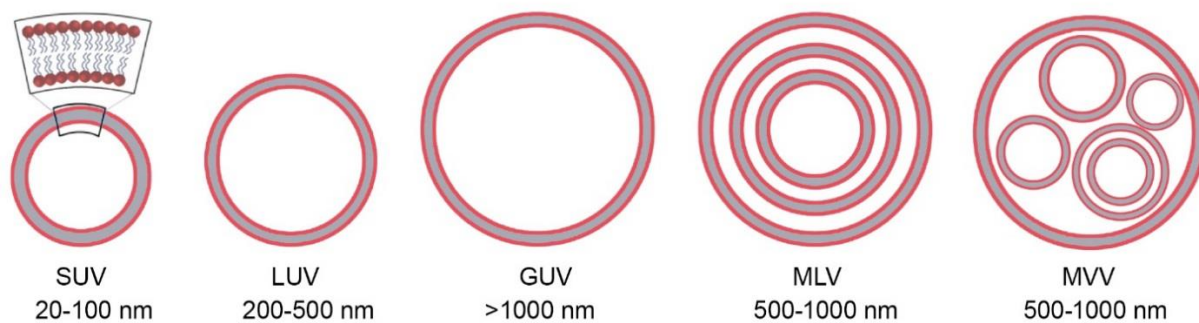


Figure S1. Classification of liposomes according to their size and lamellarity: small unilamellar vesicles (SUV); large unilamellar vesicles (LUV); giant unilamellar vesicles (GUV); multilamellar vesicles (MLV); multivesicular vesicles (MVV).

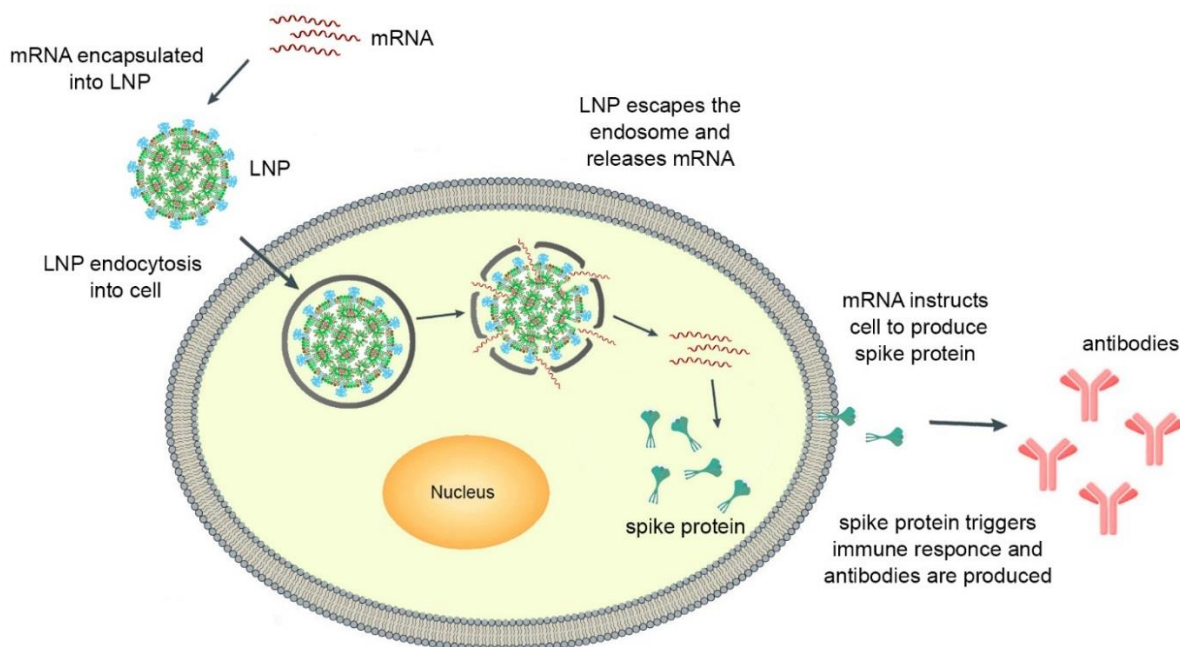


Figure S2. Mechanism of action of mRNA mediated vaccination.

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