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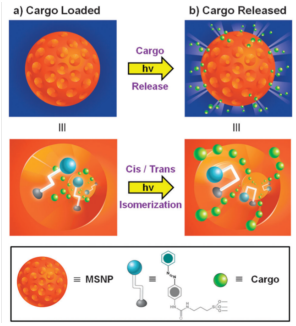


Mesoporous silica nanoparticles (MSNP)

Developer(s)

University of California

Originator

https://regents.universityofcalifornia.edu/

United States of America

The University of California (UC), established in 1868, is a renowned public research institution comprising 10 campuses, governed by the Board of Regents, which oversees its strategic direction. With a legacy of academic excellence and innovation, UC has pioneered advancements across diverse fields, including mesoporous nanoparticle technology for precision drug delivery and targeted therapies.

Sponsor(s)

No sponsor indicated

Partnerships

Merrimack Pharmaceuticals, Inc.
https://www.merrimack.com/

Washinton University in St.Louis
https://medicine.washu.edu/

National Health Research Institutes
https://nicr.nhri.edu.tw/en/

National Cheng Kung University Hospital
https://web.hosp.ncku.edu.tw/nckm/english/index.aspx

Technology information

Type of technology

Silica based nanoparticles

Administration route

Oral, Subcutaneous, Intramuscular, Intravenous, intraarterial, intracerebral, intrathecal, intranasal

Development state and regulatory approval

Active Pharmaceutical Ingredient (API)

irinotecan

Development Stage

Phase II

Regulatory Approval

Not provided

Description

The Mesoporous Silica Nanoparticle Platform Technology (MSNP) is composed of silicasomes (lipid-coated porous silica nanoparticle) , proton gradients, and a phospholipid bilayer (LB) coating. These components collectively function as a nanocarrier, enabling the delivery of multiple APIs to targeted site of action. These nanocarriers prolong the drug's circulatory half-life and deliver high doses at the site of action with reduced systemic toxicity compared to the free drug.

Technology highlight

1) Biocompatible 2) Cellular-level delivery of hydrophobic drugs 3) Nanocarriers encapsulate, covalently attach, and/or adsorb therapeutic agents to overcome drug solubility problems 4) Large surface area and porous interior to accommodate multiple API

Technology main components

The Mesoporous Silica Nanoparticle (MSNP) system comprises 'n' nanocarriers, each characterized by the following components: (i) API; (ii) a silicasome structure featuring a defined surface with a network of multiple pores; (iii) a phospholipid bilayer coating the silicasome surface; and (iv) a cargo-trapping agent (e.g., trimethylammonium salts, alpha- cyclodextrin sulfate, trim ethylammonium, beta-cyclodextrin phosphate, trimethyl ammonium citrate, and trimethylammonium acetate) and a targeting peptide (optional). These structural components are organized at the submicron scale.

Information on the raw materials sourcing, availability and anticipated price

Not provided

Delivery device(s)

No delivery device

APIs compatibility profile

API desired features

Water-insoluble molecules

Small molecules

MSNP-based drug delivery systems include a range of antifungal agents such as amphotericin B, anidulafungin, caspofungin, fluconazole, flucytosine, isavuconazole, itraconazole, micafungin, posaconazole, nocodazole, and voriconazole. Additionally, antiviral agents such as tenofovir disoproxil fumarate, antibiotics including ciprofloxacin and levofloxacin, and hydrophobic anticancer agents such as iriotecan, paclitaxel, ellipticine, camptothecin, acyclovir diphosphate, dimyristoylglycerol, doxorubicin, and chlorambucil can be included in this portfolio.

Additional solubility data

Not provided

Additional stability data

Not provided

API loading: Maximum drug quantity to be loaded

75-90 wt%

API co-administration

More than 4 different APIs : Not provided

LogP

Min: -1 Max: 7.1

Suitable for low and highly hydrophobic drugs

Scale-up and manufacturing prospects

Scale-up prospects

Not provided

Tentative equipment list for manufacturing

Not provided

Manufacturing

Manufacturing of the MSNP: 1. Synthesize mesoporous silica spheres using iron oxide nanocrystals or gold(III) chloride trihydrate and TEOS. 2. NPs are modified with a hydrophilic trihydroxylsilylpropyl methlphosphonate to prevent aggregation 3. Dissolve API in DMSO or an appropriate solvent. 4. Load the drug into mesoporous nanoparticles. 5. Redisperse drug-loaded nanoparticles in a hydrophobic solvent, or DMSO. 6. Sonicate, homogenize, and filter through a 0.44 µm syringe filter. 7. Mix with NaOH and H_2O; heat at 80 °C. For drugs with higher concentrations, reduce the heating temperature.

Specific analytical instrument required for characterization of formulation

1. Pore characterization is performed using X-ray Diffraction (XRD) 2. Nitrogen Adsorption desorption experiment - Brunauer-Emmett-Teller

Clinical trials

08103

Identifier

NCT00734682

Link

https://clinicaltrials.gov/study/NCT00734682

Phase

Phase I

Status

Completed

Sponsor

University of California, San Francisco

More details

This is a Phase I study of Nanoliposomal CPT-11 in patients with Recurrent high-grade gliomas. Patients must have a histologically proven intracranial malignant glioma, which includes glioblastoma multiforme (GBM), gliosarcoma (GS), anaplastic astrocytoma (AA), anaplastic oligodendroglioma (AO), anaplastic mixed oligoastrocytoma (AMO), or malignant astrocytoma NOS (not otherwise specified). Patients who are wild type or heterozygous for the UGT1A1*28 gene will received Nanoliposomal CPT-11. The total anticipated accrual will be approximately 36 patients (depending upon the actual MTD). The investigators hypothesis is that this new formulation of CPT-11 will increase survival over that seen in historical controls who

have recurrent gliomas because CPT-11 will be encapsulated in a liposome

Purpose

A Phase I Trial of Nanoliposomal CPT-11 (NL CPT-11) in Patients With Recurrent High-Grade Gliomas

Interventions

Intervention 1

Nanoliposomal CPT-11

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2008-08-01

Anticipated Date of Last Follow-up

2015-01-05

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2014-12-01

Actual Completion Date

2014-12-01

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: * Patients with histologically proven intracranial malignant glioma are eligible . -All patients must sign an informed consent * Patients must be \> 18 years old, and with a life expectancy \> 8 weeks. * Patients must have a Karnofsky performance status of \> 60. * Patients must have recovered from the toxic effects of prior therapy * Patients must have adequate bone marrow function (WBC \> 3,000/µl, ANC \> 1,500/mm3, platelet count of \> 100,000/mm3, and hemoglobin \> 10 gm/dl), adequate liver function (SGOT and bilirubin \< 2 times ULN), and adequate renal function (creatinine \< 1.5 mg/dL and/or creatinine clearance \> 60 cc/min) Patients must have shown radiographic evidence for tumor progression by MRI or CT scan.

Health status

Not provided
Other health status: intracranial malignant glioma

Study type

Interventional (clinical trial)

Enrollment

34

Allocation

Not provided

Intervention model

Single group assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Other : "once every 3 weeks "

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intramuscular

Use case

Treatment

Key resources

Not provided

3G-18-1

Identifier

NCT03739801

Link

https://clinicaltrials.gov/study/NCT03739801

Phase

Phase I/II

Status

Withdrawn

Sponsor

University of Southern California

More details

This phase I/II trial studies the side effects and best dose of MM-398 and ramucirumab in treating patients with gastric cancer or gastroesophageal junction adenocarcinoma. MM-398 contains a chemotherapy drug called irinotecan, which in its active form interrupts cell reproduction. MM-398 builds irinotecan into a container called a liposome which may be able to release the medicine slowly over time to reduce side effects and increase its ability to kill tumor cells. Immunotherapy with monoclonal antibodies, such as ramucirumab, may help the body's immune system attack the cancer, and may interfere with the ability of tumor cells to grow and spread. Giving MM-398 and ramucirumab together may work better in treating patients with gastric cancer or gastroesophageal junction adenocarcinoma.

Purpose

MM-398 and Ramucirumab in Treating Patients With Gastric Cancer or Gastroesophageal Junction Adenocarcinoma

Interventions

Intervention 1

Liposomal Irinotecan

Intervention 2

Quality-of-Life Assessment

Intervention 3

Questionnaire Administration

Intervention 4

Ramucirumab

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

2020-04-06

Actual Start Date

Not provided

Anticipated Date of Last Follow-up

2020-03-25

Estimated Primary Completion Date

2022-04-06

Estimated Completion Date

2023-04-06

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: * The patient has a histopathologically or cytologically confirmed diagnosis of gastric or gastroesophageal junction (GEJ) adenocarcinoma * The patient has metastatic disease or locally advanced and unresectable disease that is evaluable, by radiological imaging per Response Evaluation Criteria in Solid Tumors, Version 1.1 (RECIST 1.1). (MRI candidates must have measurable disease in liver. * The patient has documented disease progression or intolerance of chemotherapy during first-line platinum-based chemotherapy for metastatic disease, or during or within 6 months

after the last dose of neoadjuvant or adjuvant therapy * Additional lines of therapy are permitted as long as patient had received a platinum and/or a fluoropyrimidine component.

Health status

Not provided
Other health status: Gastric Cancer or Gastroesophageal Junction Adenocarcinoma

Study type

Interventional (clinical trial)

Enrollment

Not provided

Allocation

Not provided

Intervention model

Single group assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Other : "once every 2 weeks "

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intravenous

Use case

Treatment

Key resources

Not provided

PEP0208

Identifier

NCT00813163

Link

https://clinicaltrials.gov/study/NCT00813163

Phase

Phase II

Status

Completed

Sponsor

PharmaEngine

More details

The purpose of this study is to see the effect of PEP02 in the treatment of metastatic pancreatic cancer.

Purpose

Study of PEP02 as a Second Line Therapy for Metastatic Pancreatic Cancer

Interventions

Intervention 1

PEP02

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2009-01-01

Anticipated Date of Last Follow-up

2019-08-27

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2010-12-01

Actual Completion Date

2012-07-01

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

- All

Accepts pregnant individuals

Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

No

Comments about the studied populations

Inclusion Criteria: * Histologically or cytologically confirmed adenocarcinoma of exocrine pancreas * Metastatic disease * Documented disease progression after treatment with 1 line of prior gemcitabine-based regimen * Karnofsky performance status equal or more than 70 Exclusion Criteria: * With active CNS metastases * With clinically significant gastrointestinal disorder (e.g., bleeding, inflammation, occlusion, or diarrhea \> grade 1) * Major surgery or radiotherapy within 4 weeks * Prior participation in any investigational drug study within 4 weeks * With prior irinotecan treatment

Health status

Not provided

Other health status: Metastatic Pancreatic Cancer

Study type

Interventional (clinical trial)

Enrollment

41

Allocation

Not provided

Intervention model

Single group assignment

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Other : "Every 3 weeks "

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

Intravenous

Use case

Treatment

Key resources

Not provided

Excipients

Proprietary excipients used

No proprietary excipient used

Novel excipients or existing excipients at a concentration above Inactive Ingredients Database (IID) for the specified route of administration

No novel excipient or existing excipient used

Residual solvents used

No residual solvent used

Additional features

Other features of the technology

- Biodegradable
- Drug-eluting
- Non-removable
- Reservoir-type
- Requires stimuli from outside the body

Release properties

The release kinetics of MSNP are based on interactions between particles and cell membrane phospholipids during endocytosis, which can induce the release of encapsulated hydrophobic drugs. MSNP is designed to employ mechanical regulation of pore openings on the surface of NPs. Specifically, polymers, either adsorbed onto or covalently bonded to the MSNP surface, have been utilized as mechanized systems for controlled drug release.

Injectability

MSNP preparations can be formulated for intravenous, subcutaneous, and intramuscular routes of administration.

Safety

A Phase I clinical trial of mesoporous silica nanoparticle-encapsulated irinotecan (MSNP-IRI) was conducted, starting at a dose of 120 mg/m² with incremental increases of 60 mg/m², up to a maximum dose of 150 mg/m². Dose-limiting toxicities (DLTs) observed included diarrhea, dehydration, and fatigue. Notably, MSNP-IRI did not exhibit any unexpected toxicities when administered intravenously.

Stability

In Situ Stability: The mesoporous silica nanoparticles (MSNPs) exhibit excellent colloidal and circulatory stability in physiological fluids at pH 7.4, maintaining a monodisperse state to facilitate systemic biodistribution. Product Stability: While chronic shelf-life studies are yet to be undertaken, preliminary analyses indicate that the formulation remains stable for up to six months under cold storage conditions.

Storage conditions and cold-chain related features

At least 6 months is possible when stored at 4 ° C

Potential application(s)

Therapeutic area(s)

Other(s) : "Bacterial Infections and Fungal Infections"

HIV

Oncology

Use case(s)

Treatment

Use of technology

Ease of administration

- Administered by a community health worker
- Administered by a nurse
- Administered by a specialty health worker

Frequency of administration

Every 3 weeks; Every 2 weeks

User acceptance

Not provided

Targeted user groups

Age Cohort

- Adults
- Older Adults

Genders

- All

Pregnant individuals

Unspecified

Lactating individuals

Unspecified

Healthy individuals

Unspecified

Comment

Not provided

Potential associated API(s)

irinotecan

Class(es)

Topoisomerase 1 inhibitors

Development stage

Phase II

Clinical trial number(s)

NCT00813163

Foreseen/approved indication(s)

Gliomas and solid tumors

Foreseen user group

Adults who are < 18 years old with recurrent glioma

Foreseen duration between application(s)

Every 3 weeks

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

camptothecin

Class(es)

Topoisomerase - 1 inhibitors

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Pancreatic ductal Adenocarcinoma (PDAC)

Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

paclitaxel, taxanes

Class(es)

Taxane

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Pancreatic Duct Adenocarcinoma (PDAC)

Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Patent info

Description

Cationic polymer coated mesoporous silica nanoparticles and uses thereof

Brief description

A submicron structure having a silica body defining a plurality of pores is described. The submicron body may be spherical or non-spherical, and may include a cationic polymer or co-polymer on the surface of said silica body. The submicron structure may further include an oligonucleotide and be used to deliver the oligonucleotide to a cell. The submicron structure may further include a therapeutic agent and be used to deliver the therapeutic agent to a cell. An oligonucleotide and therapeutic agent may be used together. For example, when the oligonucleotide is an siRNA, the composition may be used to decrease cellular resistance to the therapeutic agent by decreasing translation of a resistance gene.

Representative patent

US10343903B2

Category

Formulation

Patent holder

The Regents of the University of California

Exclusivity

Not provided

Expiration date

July 13, 2031

Status

Active

Description

MESOPOROUS SILICA NANOPARTICLES FOR BIOMEDICAL APPLICATIONS

Brief description

A submicron structure includes a silica body defining a plurality of pores that are suitable to receive molecules therein , the silica body further defining an outer surface between pore openings of said plurality of pores ; and a plurality of anionic molecules attached to the outer surface of the silica body . The anionic molecules provide hydrophilicity to the submicron structure and are suitable to provide repulsion between other similar submicron structures, and the submicron structure has a maximum dimension less than one micron .

Representative patent

US10668024B2

Category

Formulation

Patent holder

The Regents of the University of California

Exclusivity

Not provided

Expiration date

December 8, 2028

Status

Expired - Fee Expired

Supporting material

Publications

** Li Z, Barnes JC, Bosoy A, Stoddart JF, Zink JI. Mesoporous silica nanoparticles in biomedical applications. Chem Soc Rev. 2012;41(7):2590-2605. doi:10.1039/c1cs15246g **

This tutorial review provides an outlook on nanomaterials that are currently being used for theranostic purposes, with a special focus on mesoporous silica nanoparticle (MSNP) based materials. MSNPs with large surface area and pore volume can serve as efficient carriers for various therapeutic agents. The functionalization of MSNPs with molecular, supramolecular or polymer moieties, provides the material with great versatility while performing drug delivery tasks, which makes the delivery process highly controllable. This emerging area at the interface of chemistry and the life sciences offers a broad palette of opportunities for researchers with interests ranging from sol-gel science, the fabrication of nanomaterials, supramolecular chemistry, controllable drug delivery and targeted theranostics in biology and medicine.

** Lu J, Liong M, Sherman S, et al. Mesoporous Silica Nanoparticles for Cancer Therapy: Energy-Dependent Cellular Uptake and Delivery of Paclitaxel to Cancer Cells. Nanobiotechnology. 2007;3(2):89-95. doi:10.1007/s12030-008-9003-3 **

Biocompatible mesoporous silica nanoparticles, containing the fluorescence dye fluorescein isothiocyanate (FITC), provide a promising system to deliver hydrophobic anticancer drugs to cancer cells. In this study, we investigated the mechanism of uptake of fluorescent mesoporous silica nanoparticles (FMSN) by cancer cells. Incubation with FMSN at different temperatures showed that the uptake was higher at 37 degrees C than at 4 degrees C. Metabolic inhibitors impeded uptake of FMSN into

cells. The inhibition of FMSN uptake by nocodazole treatment suggests that microtubule functions are required. We also report utilization of mesoporous silica nanoparticles to deliver a hydrophobic anticancer drug paclitaxel to PANC-1 cancer cells and to induce inhibition of proliferation. Mesoporous silica nanoparticles may provide a valuable vehicle to deliver hydrophobic anticancer drugs to human cancer cells.

Additional documents

No documents were uploaded

Useful links

There are no additional links

Access principles

Collaborate for development

Consider on a case by case basis, collaborating on developing long acting products with potential significant public health impact, especially for low- and middle-income countries (LMICs), utilising the referred to long-acting technology

Not provided

Share technical information for match-making assessment

Provide necessary technical information to a potential partner, under confidentiality agreement, to enable preliminary assessment of whether specific medicines of public health importance in LMICs might be compatible with the referred to long-acting technology to achieve a public health benefit

Not provided

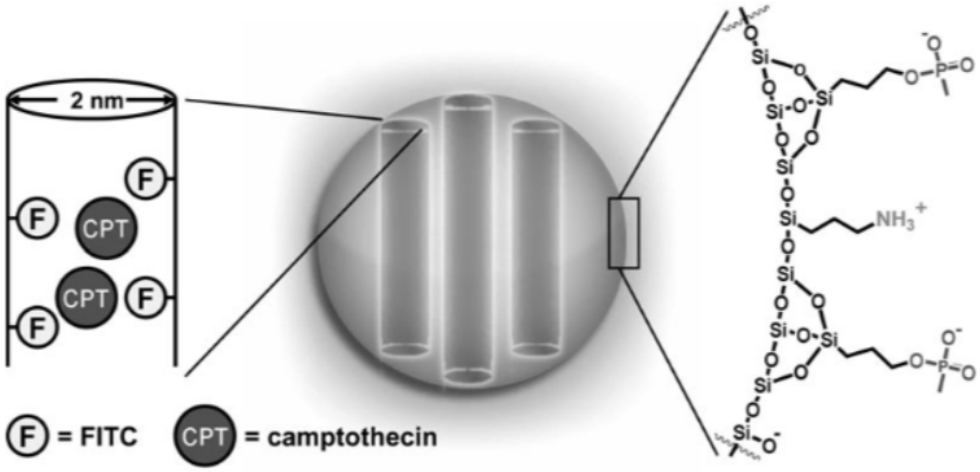
Work with MPP to expand access in LMICs

In the event that a product using the referred to long-acting technology is successfully developed, the technology IP holder(s) will work with the Medicines Patent Pool towards putting in place the most appropriate strategy for timely and affordable access in low and middle-income countries, including through licensing

Not provided

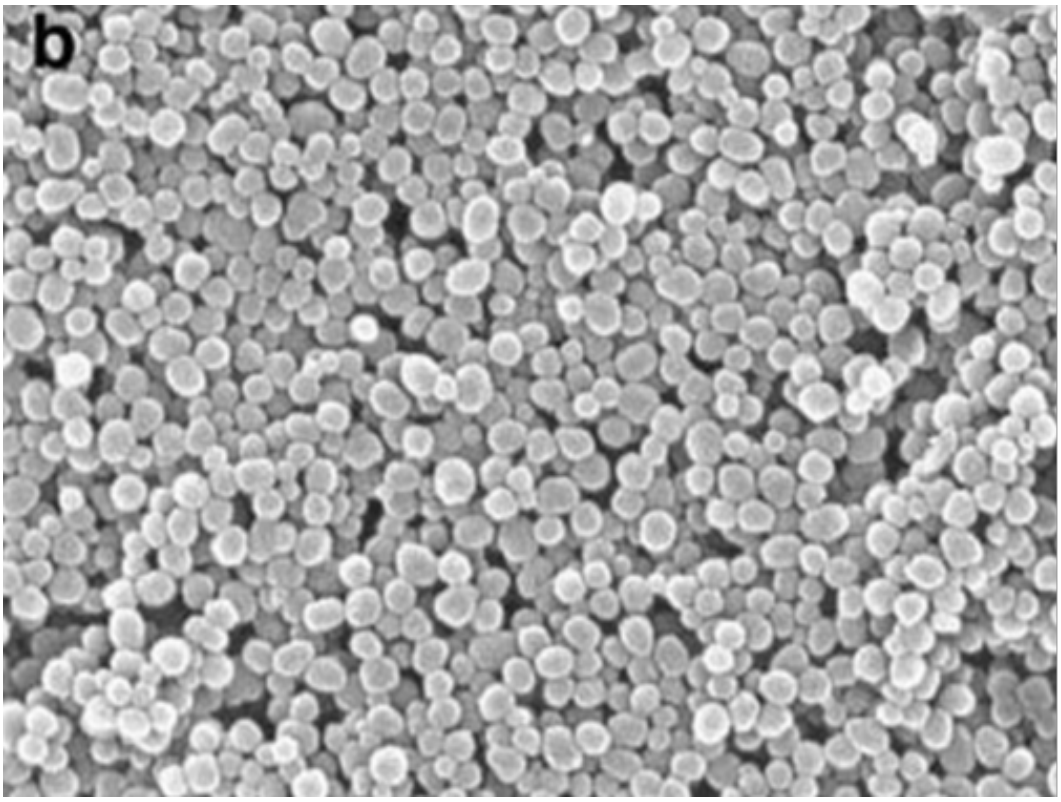
Comment & Information

Illustrations



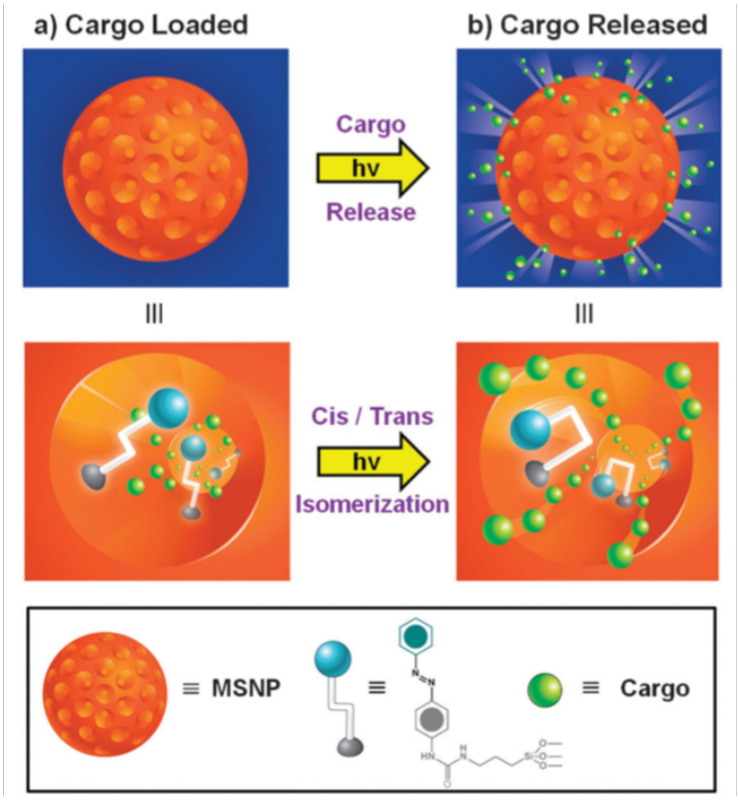
Schematic diagram of Camptothecin loaded nanoparticles

Lu, J., Liong, M., Zink, J. I., & Tamanoi, F. (2007). Mesoporous silica nanoparticles as a delivery system for hydrophobic anticancer drugs. Small (Weinheim an der Bergstrasse, Germany), 3(8), 1341–13



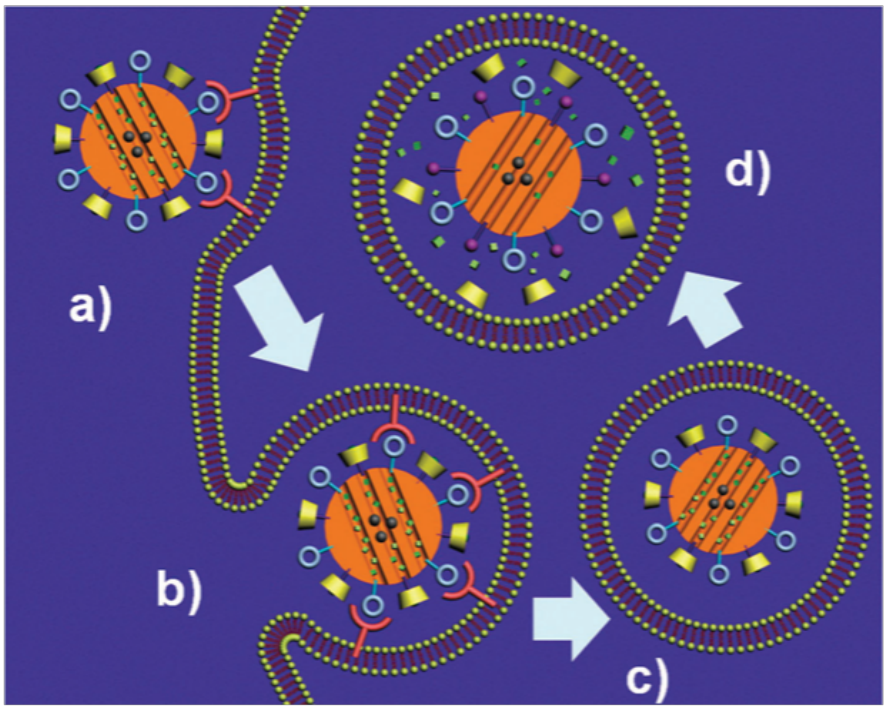
Scanning Electron Microscope of MSNP loaded with Paclitaxel

Lu J, Liong M, Sherman S, et al. Mesoporous Silica Nanoparticles for Cancer Therapy: Energy-Dependent Cellular Uptake and Delivery of Paclitaxel to Cancer Cells. Nanobiotechnology. 2007;3(2):89-95.



Mesoporous Nanoparticle Mechanism of Release of API

Li Z, Barnes JC, Bosoy A, Stoddart JF, Zink JI. Mesoporous silica nanoparticles in biomedical applications. Chem Soc Rev. 2012;41(7):2590-2605. doi:10.1039/c1cs15246g



Endocytosis of MSNP

Li Z, Barnes JC, Bosoy A, Stoddart JF, Zink JI. Mesoporous silica nanoparticles in biomedical applications. Chem Soc Rev. 2012;41(7):2590-2605. doi:10.1039/c1cs15246g