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## TOXIC GRAPHENE OXIDE A BIG INDUSTRY SECRET, STU PETERS JUST SCRATCHING THE SURFACE. IS THIS WHY GATES REFUSED TO SHARE PATENTS?

by Silviu "Silview" Costinescu

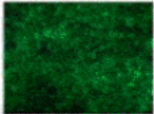
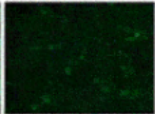

**Polyethylene Glycol-Engrafted Graphene Oxide as Biocompatible Materials for Peptide Nucleic Acid Delivery into Cells**  
Ahruem Baek, Yu Mi Baek, Hyung-Mo Kim, Bong-Hyun Jun , and Dong-Eun Kim\* 

**View Author Information**

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 PDF (8 MB)

**Target gene (eGFP) knockdown**

Con	anti-eGFP PNA	Scrambled PNA
		

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Silviu "Silview" Costinescu (<https://ko-fi.com/silview>)

 Buy me a coffee (<https://ko-fi.com/silview>)

Establishment fact-checkers are cognitively retarded and functionally illiterate copy-paste bots who still use Google, this is how you fact-check Stu Peters:

LATER UPDATES: A glimpse into the future or the present?

Status: pending



# BUT YOU'RE CRAZY TO BELIEVE THE INTERNET PPL..

Google Patents

## Nano coronavirus recombinant vaccine taking graphene oxide as carrier

**Abstract**

The invention belongs to the field of nano materials and biomedicine, and relates to a vaccine, in particular to development of 2019-nCoV coronavirus nuclear recombinant nano vaccine. The invention also comprises a preparation method of the vaccine and application of the vaccine in animal experiments. The new corona vaccine contains graphene oxide, carnosine, CpG and new corona virus RBD; binding carnosine, CpG and neocoronavirus RBD on the backbone of graphene oxide; the CpG coding sequence is shown as SEQ ID NO 1; the novel coronavirus RBD refers to a novel coronavirus protein receptor binding region which can generate a high-titer specific antibody aiming at the RBD in a mouse body, and provides a strong support for prevention and treatment of the novel coronavirus.

**Classifications**


**Other languages:** Chinese  
**Inventor:** 崔大祥, 高昂, 梁辉  
**Current Assignee:** Shanghai Research Center for Nanotechnology

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SOURCE (<https://patents.google.com/patent/CN112220919A/en>)

Status: Published March 2021, but submitted in April 2020, which means most of the research was done before the Plandemic.



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# Espacenet

Patent search

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☆ **KR20210028062A** Physiological Saline Containing Graphene

## BUT YOU'RE CRAZY TO THINK THEY'D PUT IT IN INJECTIONS...

**Description** ▾

**[0003]** The physiological saline solution containing dispersed graphene of the present invention is intended to be used as a therapeutic agent for all viruses such as MERS, SARS, and corona.

**[0004]** Graphene powder having a size of 0.2 nm or less is dispersed in a means used as an injection solution such as injection solution, Ringer solution, physiological saline solution, and glucose solution used in conventional hospitals to be used as a therapeutic agent.

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SOURCE

(<https://worldwide.espacenet.com/patent/search/family/075143365/publication/KR20210028062A?>

So the people who claim many vaccines are just saline and the people who claim they are just graphene oxide **can be** right at the same time.

If you are reading this, chances are you already know of La Quinta Columna researchers and Stu Peters shows that revealed large presence of very toxic graphene in Covid injections. If you don't, you need to research and catch up with the details, there's no cheating on the homework anymore.

Also read: [URGENT! IT'S IN MASKS TOO: SUPER-TOXIC GRAPHENE OXIDE CONFIRMED BY MANUFACTURERS](https://silview.media/2021/07/08/urgent-its-in-masks-too-super-toxic-graphene-oxide-confirmed-by-manufacturers/) (<https://silview.media/2021/07/08/urgent-its-in-masks-too-super-toxic-graphene-oxide-confirmed-by-manufacturers/>).

One of Stu's latest deliveries (<https://rumble.com/vkgdq7-deadly-shots-former-pfizer-employee-confirms-poison-in-covid-vaccine.html>) featured a very documented expert and Pharma analyst who formerly worked for Pfizer and revealed the graphene is hiding in the so called PEGs, I'll explain shortly what these are.

So I went to fact-check this, even though the whistle-blower sounded very compelling and having deep insights in the business.

My findings show that they only scratch the surface of a larger problem:

As I've shown before, graphene has a large spectrum of applications today, most endangering our health. But graphene oxide (GO) is especially toxic and they will pump it in us with other treatments too.

GO-based PEGs have been the new rising star of drug delivery for quite a few years before Covid and they are usually graphene based, as a several studies and invention patents prove beyond doubt. I don't think there's any mRNA vaccine that doesn't use them.

**Without these lipid shells, there would be no mRNA vaccines for COVID-19**

**c&en**  
CHEMICAL & ENGINEERING NEWS

The most effective nanoparticles were ones that the body mistook as low-density lipoprotein (LDL) cholesterol—commonly called bad cholesterol. Proteins that recognize LDL cholesterol in the blood bound to some of Alnylam's nanoparticles and carried them to LDL receptors on liver cells, which then caused the cells to engulf the nanoparticles in an endosome. It was the kind of complex interplay that studies in a petri dish missed.

"A lot of work has gone into studying what happens inside a cell, but trying to understand the transport that occurs before these nanoparticles reach their cells is another question entirely," says Kathryn Whitehead, a nanoparticle scientist at Carnegie Mellon University. As a consequence, "we don't even screen in vitro anymore," she says. "I find it more informative to test directly in an animal."

The work was grueling, and lipids that made great nanoparticles in a petri dish would often flop in animal studies. "You can have 50 different ionizable lipids that all deliver effectively to cells in culture, and 49 of them won't work a damn in vivo," recalls Thomas Madden, who worked at Inex and is now CEO of Acuitas Therapeutics.

**Carnegie Mellon University**  
Dr. Kathryn A. Whitehead  
Associate Professor, Chemical Engineering and Biomedical Engineering

**The PEGylated lipids contain graphene oxide. PEGylated LNPs are made by SINOPEG in China**

A lipid nanoparticle (LNP) contains hundreds of small interfering RNA (siRNA) molecules, each surrounded by ionizable lipids, phospholipids, and cholesterol. The outside of the particle is coated in pegylated lipids. LNPs for messenger RNA

... of a natural process called receptor-mediated endocytosis to get into cells. Upon binding to a cell, the nanoparticle becomes encapsulated in an even bigger organelle called an endosome. The endosome's acidic interior protonates the heads of the lipids, making them positively charged. That positive charge triggers a change in the shape of the nanoparticle, which scientists think helps it break free from the endosome and ultimately release its RNA cargo into the cell's cytoplasm. Once released, the RNA is free to do its job.

**4 lipids in LNPs**  
Pegylated lipid  
Ionizable lipid  
Phospholipid  
Cholesterol  
Nucleic acid (siRNA shown)

**MiFIGHT**  
Credit: Genevieve Sciences

<https://cen.acs.org/pharmaceuticals/drug-delivery/Without-lipid-shells-mRNA-vaccines/99/18>



They are not featured in injections inserts as separate ingredient, which they are, but as a process. Yup, they are the PEG in PEGylation. It's like saying Coca Cola was sweetened instead of listing several sweeteners!

PFE EUA #27034, Nov 20, 2020, pg. 11

Sec. 3. Pfizer/BioNtech COVID019 Vaccine (BNT162b)

3.1 Vaccine Composition, Dosign Regimen

The vaccine contains a nucleoside-modified messenger RNA (modRNA) encoding the viral spike glycoprotein (S) of SARS-CoV-2. The vaccine also includes the following ingredients: lipids ((4-hydroxybutyl)azanediyl) bis (hexane-6,1-diyl)bis(2-hexyldecanoate), 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 1,2-distearoyl-sn-glycero-3-phosphocholine, and cholesterol), potassium chloride, monobasic potassium phosphate, sodium chloride, dibasic sodium phosphate dihydrate, and sucrose.

Two (2) PEGylated Lipids in  
Pfizer BNT162b2  
ALC-0135 | **ALC-0159**

Here you can download ([https://file.medchemexpress.com/batch\\_PDF/HY-138170/ALC-0315-SDS-MedChemExpress.pdf](https://file.medchemexpress.com/batch_PDF/HY-138170/ALC-0315-SDS-MedChemExpress.pdf)) the safety Data Sheet for ALC-0135, it's bad stuff, really corrosive!

## 1. PRODUCT AND COMPANY IDENTIFICATION

### 1.1 Product identifier

Product name : ALC-0315  
Catalog No. : HY-138170  
CAS No. : 2036272-55-4

### 1.2 Relevant identified uses of the substance or mixture and uses advised against

Identified uses : Laboratory chemicals, manufacture of substances.

### 1.3 Details of the supplier of the safety data sheet

Company: MedChemExpress USA  
Tel: 609-228-6898  
Fax: 609-228-5909  
E-mail: sales@medchemexpress.com

### 1.4 Emergency telephone number

Emergency Phone #: 609-228-6898

## 2. HAZARDS IDENTIFICATION

### 2.1 Classification of the substance or mixture

**GHS Classification in accordance with 29 CFR 1910 (OSHA HCS)**

Skin corrosion/irritation (Category 2),H315

Serious eye damage/eye irritation (Category 2A),H319

Moderna comes with the goods too, all their invention patents  
(<https://www.modernatx.com/patents>)for the mRNA tech contain these PEGs:



## MODERNA MRNA THERAPY INVENTION PATENT

(57)

### ABSTRACT

A pharmaceutical composition which has a plurality of lipid nanoparticles that has a mean particle size of between 80 nm and 160 nm and contains a modified mRNA encoding a polypeptide. The lipid nanoparticles include a cationic lipid, a neutral lipid, a cholesterol, and a PEG lipid. The mRNA contains a 5'-cap, 5'-UTR, N1-methyl-pseudouridine, a 3'-UTR, and a poly-A region with at least 100 nucleotides.

**14 Claims, 14 Drawing Sheets**

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Think of an oral drug capsule. The PEG is a high-nanotech version of the capsule fabric, which can do a series of cool tricks, but its mainly roles are to protect the content and help it penetrate tissue/cells and reach specific targets.

**Now think the drug insert only lists the content ingredients. not the capsule.**

“Poly(ethylene glycol) (PEG), also known as poly(ethylene oxide) (PEO), is an amphiphilic polyether that is soluble both in water and most organic solvents. PEG and its derivatives are among the few polymers approved for medical uses by the FDA.

Functionalized PEG, also named activated PEG, is a family of PEG derivatives decorated with functional groups. Functionalized PEGs are used broadly for drug PEGylation, polymer engineering, nanotechnology, biotechnology, and biomedical engineering.”

This is the description given by Sinopeg ([https://www.sinopeg.com/pegs\\_c1](https://www.sinopeg.com/pegs_c1)), Chinese company that delivers PEGs for most Covid injection manufacturers.

From their September 2020 blog post we extract more details confirming my earlier claims:

“The coupling of PEG ([https://www.sinopeg.com/pegs\\_c1](https://www.sinopeg.com/pegs_c1)) to protein is also called protein polyglycolization, which is **essentially a drug delivery technology**. The coupling of activated peg with protein molecules can improve the three-dimensional space state of proteins, resulting in changes in various biochemical properties of proteins. For example, chemical stability increased, half-life prolonged, immunogenicity and toxicity decreased or disappeared, protein solubility increased. SINOPEG is a dynamic science company dedicated to drug delivery systems (DDS). **SINOPEG** (<https://www.sinopeg.com/>) are specialized in the R&D of long acting biopharmaceuticals, developing and manufacturing of block copolymers, lipids for drug delivery, medical devices, bio-engineering, and other broad uses.

Up to now, the FDA has approved 20 polyglycolic drugs. In addition to monoclonal antibodies, polyglycolic drugs have become the most powerful drug development technology.

As a leading company in polyethylene glycol derivatives (PEGs), SINOPEG is capable of supplying





small to large quantities of rich selection of PEG derivative products with unique molecular designs (chemical structure, molecular weights (MW)) and exceptional product quality control to serve biotechnology and pharmaceutical companies and research organizations worldwide."

At this point, you're probably asking when is graphene coming in. I got you covered:



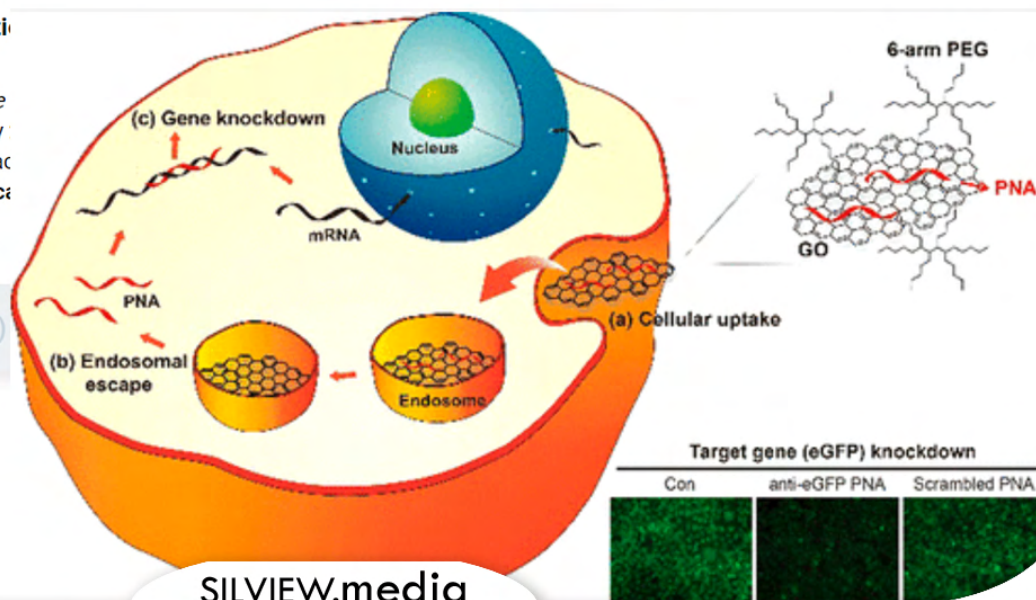
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View Author Information

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SOURCE (<https://pubs.acs.org/doi/pdf/10.1021/acs.bioconjchem.8b00025>).

## Polyethylene Glycol-Engrafted Graphene Oxide as Biocompatible Materials for Peptide Nucleic Acid Delivery into Cells

*Bioconjugate Chemistry* (<https://pubmed.ncbi.nlm.nih.gov/29376329/>). 2018 Feb 7.

Ahruem Baek ([https://pubmed.ncbi.nlm.nih.gov/?term=Baek+A&cauthor\\_id=29376329](https://pubmed.ncbi.nlm.nih.gov/?term=Baek+A&cauthor_id=29376329))<sup>1</sup>  
(<https://pubmed.ncbi.nlm.nih.gov/29376329/#affiliation-1>), Yu Mi Baek

([https://pubmed.ncbi.nlm.nih.gov/?term=Baek+YM&cauthor\\_id=29376329](https://pubmed.ncbi.nlm.nih.gov/?term=Baek+YM&cauthor_id=29376329))<sup>1</sup>  
(<https://pubmed.ncbi.nlm.nih.gov/29376329/#affiliation-1>), Hyung-Mo Kim

([https://pubmed.ncbi.nlm.nih.gov/?term=Kim+HM&cauthor\\_id=29376329](https://pubmed.ncbi.nlm.nih.gov/?term=Kim+HM&cauthor_id=29376329))<sup>1</sup>  
(<https://pubmed.ncbi.nlm.nih.gov/29376329/#affiliation-1>), Bong-Hyun Jun

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(<https://pubmed.ncbi.nlm.nih.gov/29376329/#affiliation-1>), Dong-Eun Kim



([https://pubmed.ncbi.nlm.nih.gov/?term=Kim+DE&cauthor\\_id=29376329](https://pubmed.ncbi.nlm.nih.gov/?term=Kim+DE&cauthor_id=29376329))<sup>1</sup>  
(<https://pubmed.ncbi.nlm.nih.gov/29376329/#affiliation-1>)

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- PMID: 29376329
- DOI: [10.1021/acs.bioconjchem.8b00025](https://doi.org/10.1021/acs.bioconjchem.8b00025) (<https://doi.org/10.1021/acs.bioconjchem.8b00025>)

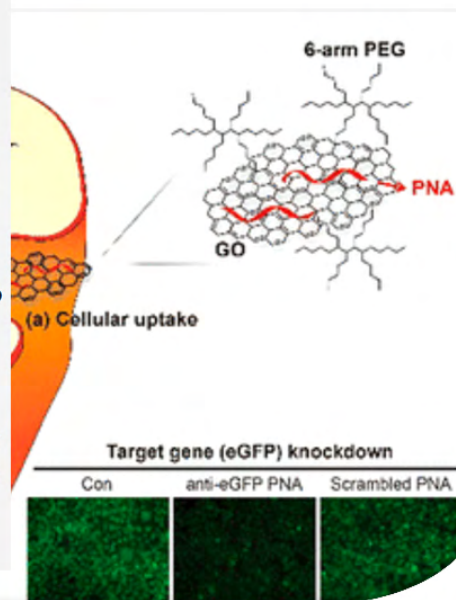


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### Abstract

Graphene oxide (GO) is known to strongly bind single-stranded nucleic acids with fluorescence quenching near the GO surface. However, GO exhibits weak biocompatibility characteristics, such as low dispersibility in cell culture media and significant cytotoxicity. To improve dispersibility in cell culture media and cell viability of GO, we prepared nanosized GO (nGO) constructs and modified the nGO surface using polyethylene glycol (PEG-nGO). Single-stranded peptide nucleic acid (PNA) was adsorbed onto the PEG-nGO and was readily desorbed by adding complementary RNA or under low pH conditions. PNA adsorbed on the PEG-nGO was efficiently delivered into lung cancer cells via endocytosis without affecting cell viability. Furthermore, antisense PNA delivered using PEG-nGO effectively downregulated the expression of the target gene in cancer cells. Our results suggest that PEG-nGO is a biocompatible carrier useful for PNA delivery into cells and serves as a promising gene delivery tool.



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Graphene Oxide

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CAS NO.: 7440-44-0

ID: XF244

Specifications: 20 ml,D:190-320 nm C:5mg/ml

Packaging: 20 ml

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- Covalent functionalization of graphene oxide with biocompatible poly(ethylene glycol) for delivery of paclitaxel. (<https://pubmed.ncbi.nlm.nih.gov/25216036/>) Xu Z, Wang S, Li Y, Wang M, Shi P, Huang X. ACS Appl Mater Interfaces. 2014 Oct 8;6(19):17268-76. doi: 10.1021/am505308f. Epub 2014 Sep 18. PMID: 25216036
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AND THEN WE FIND OUT THIS THING IS COMMONLY USED IN PCR TESTING!



ACS **APPLIED MATERIALS**  
& **INTERFACES**

## Facilitation of Polymerase Chain Reaction with Poly(ethylene glycol)-Engrafted Graphene Oxide Analogous to a Single-Stranded-DNA Binding Protein

Polymerase chain reaction (PCR), a versatile DNA amplification method, is a fundamental technology in modern life sciences and molecular diagnostics. After multiple rounds of PCR, however, nonspecific DNA fragments are often produced and the amplification efficiency and fidelity decrease. Here, we demonstrated that poly(ethylene glycol)-engrafted nanosized graphene oxide (PEG-nGO) can significantly improve the PCR specificity and efficiency. PEG-nGO allows the specificity to be maintained even after multiple rounds of PCR, allowing reliable

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SOURCE (<https://pubs.acs.org/doi/pdf/10.1021/acs.bioconjchem.8b00025>)

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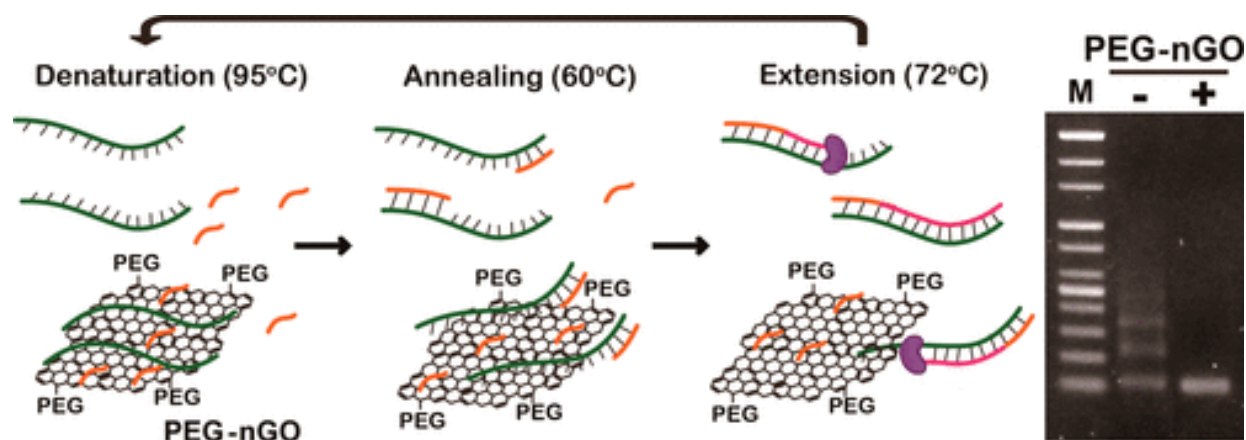
Applied Material Interfaces. 2016 Dec 14

Hyo Ryoung Kim ([https://pubmed.ncbi.nlm.nih.gov/?term=Kim+HR&cauthor\\_id=27960406](https://pubmed.ncbi.nlm.nih.gov/?term=Kim+HR&cauthor_id=27960406))<sup>1</sup>  
(<https://pubmed.ncbi.nlm.nih.gov/27960406/#affiliation-1>), Ahruem Baek  
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([https://pubmed.ncbi.nlm.nih.gov/?term=Lee+IJ&cauthor\\_id=27960406](https://pubmed.ncbi.nlm.nih.gov/?term=Lee+IJ&cauthor_id=27960406))<sup>1</sup>  
(<https://pubmed.ncbi.nlm.nih.gov/27960406/#affiliation-1>), Dong-Eun Kim  
([https://pubmed.ncbi.nlm.nih.gov/?term=Kim+DE&cauthor\\_id=27960406](https://pubmed.ncbi.nlm.nih.gov/?term=Kim+DE&cauthor_id=27960406))<sup>1</sup>  
(<https://pubmed.ncbi.nlm.nih.gov/27960406/#affiliation-1>)

- PMID: 27960406
- DOI: [10.1021/acsami.6b13223](https://doi.org/10.1021/acsami.6b13223) (<https://doi.org/10.1021/acsami.6b13223>)

## Abstract

Polymerase chain reaction (PCR), a versatile DNA amplification method, is a fundamental technology in modern life sciences and molecular diagnostics. After multiple rounds of PCR, however, nonspecific DNA fragments are often produced and the amplification efficiency and fidelity decrease. Here, we demonstrated that poly(ethylene glycol)-engrafted nanosized graphene oxide (PEG-nGO) can significantly improve the PCR specificity and efficiency. PEG-nGO allows the specificity to be maintained even after multiple rounds of PCR, allowing reliable amplification at low annealing temperatures. PEG-nGO decreases the nonspecific annealing of single-stranded DNA (ssDNA), such as primer dimerization and false priming, by adsorbing excess primers. Moreover, PEG-nGO interrupts the reannealing of denatured template DNA by preferentially binding to ssDNA. Thus, PEG-nGO enhances the PCR specificity by preferentially binding to ssDNA without inhibiting DNA polymerase, which is analogous to the role of ssDNA binding proteins.



## Similar articles

- Polyethylene Glycol-Engrafted Graphene Oxide as Biocompatible Materials for Peptide Nucleic Acid Delivery into Cells. (<https://pubmed.ncbi.nlm.nih.gov/29376329/>) Baek A, Baek YM, Kim HM, Jun BH, Kim DE. *Bioconjug Chem.* 2018 Feb 21;29(2):528-537. doi: 10.1021/acs.bioconjchem.8b00025. Epub 2018 Feb 7. PMID: 29376329
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- Redox-responsive biodegradable PEGylated nanographene oxide for efficiently chemo-photothermal therapy: a comparative study with non-biodegradable PEGylated nanographene oxide.



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My favorite today is this invention patent and its great background info:

**Method and process to make and use cotton-tipped electrochemical immunosensor for the detection of corona virus** United States Patent 11035817

SOURCE (<https://www.freepatentsonline.com/11035817.html>)



Patents/Apps  Other

### Method and process to make and use cotton-tipped electrochemical immunosensor for the detection of corona virus

: United States Patent 11035817

Several diagnostic methods are being developed for the detection of COVID 19. Biosensors have been widely used for many diagnostic applications showing fast, easy and reliable detection. Until now, only few biosensors have been developed for SARS-CoV-2 such as the graphene-based field-effect transistor (FET) biosensor reported by Seo. et al. The FET immunosensor was used for the detection of SARS-CoV-2 using spike 51 protein as biomarker. Plasmonic photothermal biosensors for SARS-CoV-2 through nucleic acid hybridization have been also developed. Half-strip lateral flow assays (LFA) for the detection of N protein was reported. However, LFA provide qualitative or semi-quantitative results and more work is still required to develop more accurate detection methods.

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## Abstract:

A method and process to make and use cotton-tipped electrochemical immunosensor for the detection of corona viruses is described. The immunosensor were fabricated by immobilizing the virus antigens on carbon nanofiber-modified screen printed electrodes which were functionalized by diazonium electrografting and activated by EDC/NHS chemistry. The detection of virus antigens were achieved via swabbing followed by competitive assay using fixed amount of antibody in the solution. Ferro/ferricyanide redox probe was used for the detection using square wave voltammetric technique. The limits of detection for our electrochemical biosensors were 0.8 and 0.09 pg/ml for SARS-CoV-2 and MERS-CoV, respectively indicating very good sensitivity for the sensors. Both biosensors did not show significant cross reactivity with other virus antigens such as influenza A and HCoV, indicating the high selectivity of the method.

## BACKGROUND

The newly identified severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the last discovered member of the corona viruses that cause serious human respiratory infections. Other types of corona viruses were previously known such as the Middle East respiratory syndrome coronavirus (MERS-CoV), SARS-CoV1, HCoV-OC43, HCoV-229E, HCoV HKU1 and HCoV NL63. Since its first identification in China in 2019 until present, SARS-CoV-2 has spread globally causing significant morbidity and mortality. COVID-19; the disease caused by SARS-CoV-2; was declared as pandemic by the world health organization on March 2020. Until now, there are no available vaccines or drugs proven to treat COVID 19. Therefore, the timely detection of SARS-CoV-2, is urgently needed to effectively control the rapid spread of the infection.

The testing of the virus can be achieved by reverse transcription polymerase chain reaction (RT-PCR) test, detection of antigens, or by serological testing (the detection of the virus antibody). However, the serological tests are not reliable for the early diagnosis of SARS-CoV-2 infection due to the relatively long delay between infection and seroconversion. Molecular diagnosis using RT-PCR is the primary used method for the detection of corona viruses. **However, PCR takes relatively long time for analysis (minimum of 3 hours), and requires several steps including the collection of the specimens by swabbing, the transport of the sample into a solution and extraction of the viral RNA before amplification. Moreover, RT-PCR is relatively expensive which hindered its wide applicability for population scale diagnosis of SARS-CoV-2, particularly in low and middle income countries. Thus, sensitive, rapid and accurate diagnostic methods based on the direct detection of the viral antigens without pretreatment is highly demanded to control the COVID 19 outbreak. There are four main structural antigens for corona viruses: nucleocapsid (N), spike (S), matrix (M), and envelope (E). Among them, the S and N proteins have the potential to be used as biomarkers because they can distinguish different types of corona viruses.**

Several diagnostic methods are being developed for the detection of COVID 19. Biosensors have been widely used for many diagnostic applications showing fast, easy and reliable detection. **Until now, only few biosensors have been developed for SARS-CoV-2 such as the graphene-based field-effect transistor (FET) biosensor reported by Seo. et al.** The FET immunosensor was used for the detection of SARS-CoV-2 using spike 51 protein as biomarker. Plasmonic photothermal biosensors for SARS-CoV-2 through nucleic acid hybridization have been also developed. Half-strip lateral flow assays (LFA) for the detection of N protein was reported. However, LFA provide qualitative or semi-quantitative results and more work is still required to develop more accurate detection methods.

Electrochemical biosensors are one of the most popular types of biosensors which offer several advantages such as the low cost, capability of miniaturization, high sensitivity and selectivity. These advantages make them ideal for use as point-of-care devices for diagnostic applications. **Electrochemical biosensors have been widely integrated with carbon nanostructures to fabricate highly sensitive devices. Carbon nanofiber (CNF) is one of the materials that showed excellent applications in biosensors because of its large surface area, stability and ease of functionalization.**

**Cotton swabs have been recently used in the fabrication of immunoassays for the detection of different pathogens. In these assays, the colorimetric detection was achieved based on visual discrimination of the color change. These assays are simple, fast and easy to perform. However, they only give qualitative or semi-quantitative results. Thus, more accurate methods are still required.**

Want some graphene nano-flakes with your milk?

# COMPOSITION FOR PCR CONTAINING A POLYETHYLENE GLYCOL-ENGRAFTED NANO-SIZED GRAPHENE OXIDE United States Patent Application 20180155765



## COMPOSITION FOR PCR CONTAINING A POLYETHYLENE GLYCOL-ENGRAFTED NANO-SIZED GRAPHENE OXIDE

United States Patent Application 20180155765

Kind Code: A1

### Abstract:

Disclosed are a composition for PCR including polyethylene glycol-grafted nano-sized graphene oxide (PEG-nGO), the composition for PCR being capable of increasing the efficiency and specificity of PCR and shortening PCR time, and a PCR method using the same.

In addition, studies have been conducted to increase the efficiency and specificity of PCR using various nanomaterials such as gold nanoparticles, carbon nanotubes, carbon nanopowder, graphene nanoflakes, cadmium telluride quantum dots, graphene quantum dots, dendrimers, and titanium dioxide. For example, graphene nanoflakes serve to improve PCR efficiency by increasing thermal conductivity of a PCR mixture, and gold nanoparticles are capable of being adsorbed to DNA and proteins to reduce amplification of nonspecific DNA products. However, these methods have a disadvantage that the specificity and efficiency of PCR may not be fundamentally solved when each nanoparticle is present. It is also controversial as to whether gold nanoparticles play a role in increasing the specificity of PCR.

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## BACKGROUND

### 1. Field of the Invention

The present invention relates to a composition for PCR including polyethylene glycol-grafted nano-sized graphene oxide (PEG-nGO), the composition for PCR being capable of increasing the efficiency and specificity of PCR and shortening PCR time, and a PCR method using the same.

### 2. Discussion of Related Art



Polymerase chain reaction (PCR) is a method of artificially amplifying DNA and is an indispensable technology in modern biotechnology and molecular biology. PCR is widely used in diagnostics, gene manipulation, biosensors, and a variety of fields. However, the specificity and efficiency of PCR may be reduced due to unintended (re)annealing of single stranded DNA (e.g., primer dimerization, incorrect primer binding, and reannealing of PCR amplicons). Nonspecific primer binding in PCR steps may result in generation of a large number of nonspecific amplicons, which can be confirmed by agarose gel electrophoresis. That is, smearing of a PCR band, which is observed in an electrophoresed agarose gel, indicates the presence of a large number of DNAs having similar sizes (i.e., nonspecific amplicons). When a DNA template is excessively amplified in PCR and the same primers are used in the second or subsequent PCR, nonspecific amplicons may be generated. To solve these problems, various PCR techniques such as nested PCR have been developed. In the first step of nested PCR, a primer set for amplifying a broad range including a target sequence on a DNA template is used, and in the second step, primer sequences for amplifying only the target sequence are generally used as an inner primer (nested primer) set.

**In addition, studies have been conducted to increase the efficiency and specificity of PCR using various nanomaterials such as gold nanoparticles, carbon nanotubes, carbon nanopowder, graphene nanoflakes, cadmium telluride quantum dots, graphene quantum dots, dendrimers, and titanium dioxide. For example, graphene nanoflakes serve to improve PCR efficiency by increasing thermal conductivity of a PCR mixture, and gold nanoparticles are capable of being adsorbed to DNA and proteins to reduce amplification of nonspecific DNA products.** However, these methods have a disadvantage that the specificity and efficiency of PCR may not be fundamentally solved when each nanoparticle is present. It is also controversial as to whether gold nanoparticles play a role in increasing the specificity of PCR.

Graphene oxide (GO) refers to a material having a honeycomb-like nanostructure in which carbons are arranged in a hexagonal lattice, and is prepared by oxidizing a single layer of graphite, i.e., graphene. The surface of GO may have various functional groups such as epoxy groups, hydroxyl groups, and carboxyl groups, which allow the GO to be dissolved in a water-soluble solvent. In addition, GO may bind to single-stranded nucleic acids via  $\pi$  stacking interaction and hydrogen bonding, but has low affinity to double-stranded nucleic acids. **Based on the functions of GO, GO has been widely applied in various areas such as DNA detection, biosensors based on energy transfer through fluorescence resonance, and real-time monitoring of fluorescently labeled nucleic acids.**

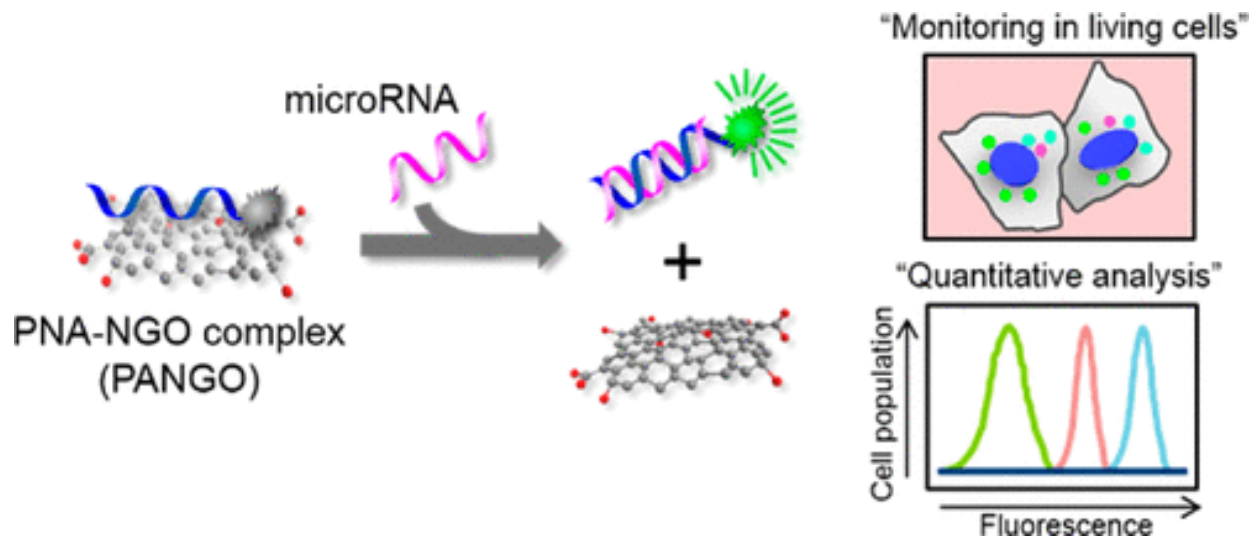
However, GO is not soluble in a buffer solution containing  $Mg^{2+}$  and a high salt concentration, such as a PCR buffer, and is adsorbed to proteins such as a DNA polymerase via non-covalent bonding. It is well known that divalent cations such as  $Mg^{2+}$  induce strong crosslinking between GO sheets, allowing the GO sheets to be aggregated. That is, when other salts are added to a PCR sample for buffering, GO sheets may be aggregated by divalent cations such as  $Mg^{2+}$ . In addition, it has been reported that GO is bound to proteins to induce protein aggregation, which may distort the structures of proteins and cause the loss of function of proteins. Polyethylene glycol (PEG) is known as a biocompatible polymer that reduces protein adsorption. Recently, to minimize nonspecific protein adsorption and increase the solubility of GO in a solution with a high salt concentration, nano-sized GO (nGO) was prepared, and the surface of the nGO was coated with PEG to prepare PEG-nGO (Non-Patent Document 1). In Non-Patent Document 1, it is disclosed that, when PEG-nGO interacts with a protein, a nano-bio interface may be formed due to PEGylation of the surface of GO, thereby significantly reducing adsorption of the PEG-nGO to the protein. Accordingly, PEG-nGO is attracting attention as a substance capable of interacting with proteins without impairing the structure and function of the proteins.

Therefore, the present inventors have tried to confirm the effect of PEG-nGO on the efficiency and specificity of PCR. During the denaturation step of PCR, polyethylene glycol-grafted nano-sized graphene oxide (PEG-nGO) was capable of being adsorbed to single-stranded primers and a DNA template. Accordingly, when PEG-nGO was added to a PCR sample and PCR amplification was

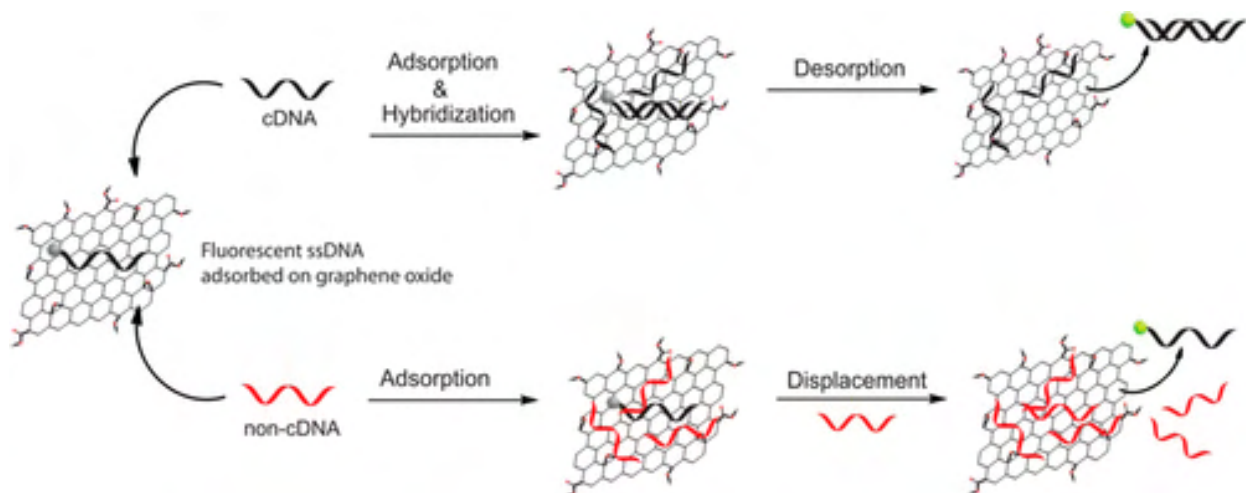
performed, in an initial PCR process in which an excessive amount of primers was included, primer dimerization was inhibited, and in a late PCR process in which amplified PCR products were accumulated, nonspecific reannealing between the amplified PCR products and other DNA strands was inhibited. Thus, it was confirmed that, when PCR was performed using a composition for PCR including the PEG-nGO of the present invention, the efficiency and specificity of PCR may be improved and PCR time may be shortened as compared with conventional PCR techniques. By confirming these results, the present invention was completed.

Or perhaps you want to find out about GO-based nano-biosensors:

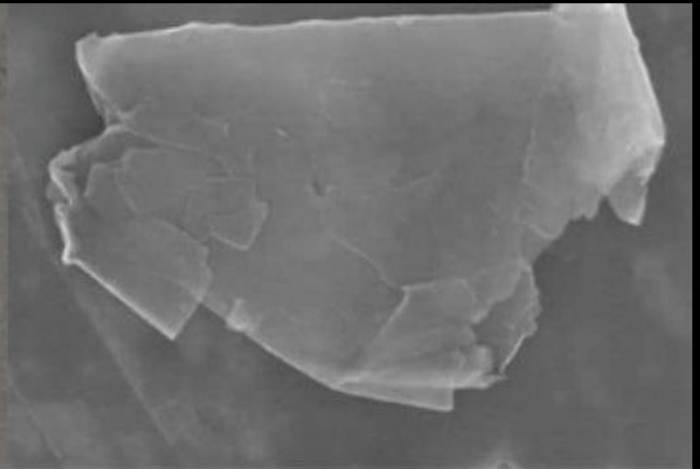
Quantitative and Multiplexed MicroRNA Sensing in Living Cells Based on Peptide Nucleic Acid and Nano Graphene Oxide (PANGO) (<https://pubs.acs.org/doi/full/10.1021/nn401183s>)



If you're curious about a Mechanism of DNA Adsorption and Desorption on Graphene Oxide (<https://pubs.acs.org/doi/full/10.1021/la503401d>), say no more!



So it shouldn't surprise us that La Quinta Columna eventually found similar stuff in older vaccines too.



**VAXIGRIP**

**ÓXIDO DE GRAFENO**

I bet there's going to be a long line of such revelations in the near future, until they put the shackles on us.

Meanwhile, top resear (<https://www.beilstein-journals.org/bjnano/articles/10/91>)chers from Pakistan and Saudi Arabia find that GO induces high oxidative stress to the cells, slowly killing us:





### The systemic effect of PEG-nGO-induced oxidative stress in vivo in a rodent model

**Qura Tul Ain<sup>1,2</sup>, Samina Hyder Haq<sup>3</sup>, Abeer Alshammari<sup>2</sup>, Moudhi Abdullah Al-Mutlaq<sup>3</sup> and Muhammad Naeem Anjum<sup>1</sup>**

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Receive

#### Conclusion

In the present study, our aim was to examine the oxidative stress in organ tissues after a single-dose administration (5 mg/kg) of biocompatible nano-graphene oxide. The oxidative stress caused by oxidants such as lipid peroxide, and the activity of antioxidants, including catalase, superoxide dismutase, glutathione, and glutathione S-transferase, was monitored. The increased concentration of MDA accompanied by reduced activity levels of antioxidant enzymes directly indicated that all organs were in oxidative stress after the intraperitoneal administration of PEG-nGO. These studies further reiterated the cytotoxicity of graphite oxide in vivo. Further safety evaluation and research must be undertaken in order to establish the use of these biocompatible polymer nanoparticles to be used in human tissues for clinical applications.

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Other studies compare graphene and carbon nanotubes to asbestos:



whereas in the report on environment, the authors have stated that "based on the scarce available evidence, it cannot be excluded that some forms of graphene will be as potent a toxicant as carbon nanotubes". This statement raises the spectre of asbestos-like properties of carbon nanotubes,<sup>(5)</sup> but according to a recent report published by the International Agency for Research on Cancer (IARC), only certain types of rigid, multiwalled carbon nanotubes can be classified as being possibly carcinogenic to humans.<sup>(344)</sup> Moreover, as we have discussed

**GRAPHENE  
THE NEW  
HI-TECH  
ASBESTOS  
?!**

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SOURCE (<https://pubs.acs.org/doi/10.1021/acsnano.8b04758>)

More from the study quoted above: "Furthermore, it is equally important that the material properties are reported in full in papers dealing with (eco)toxicity assessment of GBMs. Can the information that has been collected on safety of GBMs be applied to other 2D materials? We believe that some aspects might be common to all 2D materials, or even to all nanomaterials, while some "postcarbon" 2D materials will likely present with their own specific concerns. For instance, the propensity to dissolve in

a biological environment with the release of ionic species that are more biologically / chemically reactive than the parental 2D material is an issue that has not been described for GBMs.(346)(void(0);) Moreover, Guiney *et al.*(347)(void(0);) recently commented that “with a constantly expanding library of 2D materials, the ability to predict toxicological outcomes is of critical importance” and suggested that high-throughput screening approaches may prove useful in order to elucidate cellular interactions of 2D materials. However, the issue is not so much the low throughput of current approaches as much as the inconsistent design of commonly used toxicity assays and frequent lack of material characterization. Indeed, careful characterization of both the test material and the test system is required, and a proposal was recently put forward for minimum reporting requirements in publications dealing with nanobiointeractions. Though such reporting requirements have not yet been adopted, it is important to discuss these issues in the scientific community. To conclude, the hype that inevitably follows with technological advances should be tempered by sound, science-based assessment of the potential impact on human health and the environment to ensure safe and sustainable development of new products and applications.”

And we find out the cytotoxicity is widely known inside the industry, from a very interesting invention patent that I dug out and provides excellent background information, it's a lot, but it gives us great details as to the extent of GO usage and impact on health:



## PEGylation of Reduced Graphene Oxide Induces Toxicity in Cells of the Blood-Brain Barrier: An in Vitro and in Vivo Study

Monique Culturato Padilha Mendonça <sup>1 2</sup>, Edilene Siqueira Soares <sup>2</sup>, Marcelo Bispo de Jesus <sup>2</sup>, Helder José Ceragioli <sup>3</sup>, Ângela Giovana Batista <sup>4</sup>, Ádám Nyúl-Tóth <sup>5</sup>, Judit Molnár <sup>5</sup>, Imola Wilhelm <sup>5</sup>, Mário Roberto Maróstica Jr <sup>4</sup>, István Krizbai <sup>5 6</sup>, Maria Alice da Cruz-Höfling <sup>1 2</sup>

Affiliations + expand

PMID: 27712077 DOI: [10.1021/acs.molpharmaceut.6b00696](https://doi.org/10.1021/acs.molpharmaceut.6b00696)

### Abstract

Polyethylene glycol (PEG) coating has been frequently used to improve the pharmacokinetic behavior of nanoparticles. Studies that contribute to better unravel the effects of PEGylation on the toxicity of nanoparticle formulation are therefore highly relevant. In the present study, reduced graphene oxide (rGO) was functionalized with PEG, and its effects on key components of the blood-brain barrier, such as astrocytes and endothelial cells, were analyzed in culture and in an in vivo rat model. The in vitro studies demonstrated concentration-dependent toxicity. The highest concentration (100 µg/mL) of non-PEGylated rGO had a lower toxic influence on cell viability in primary cultures of astrocytes and rat brain endothelial cells, while PEGylated rGO induced deleterious effects and cell death. We assessed hippocampal BBB integrity in vivo by evaluating astrocyte activation and the expression of the endothelial tight and adherens junctions proteins. From 1 h to 7 days post-rGO-PEG systemic injection, a notable and progressive down-regulation of protein markers of astrocytes (GFAP, connexin-43), the endothelial tight (occludin), and adherens (β-catenin) junctions and basal lamina (laminin) were observed. The formation of intracellular reactive oxygen species demonstrated by increases in the enzymatic antioxidant system in the PEGylated rGO samples was indicative of oxidative

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Hey, kids, PEGylation is bad for you!

SOURCE (<https://pubmed.ncbi.nlm.nih.gov/27712077/>).

“The in vitro studies demonstrated concentration-dependent toxicity. The highest concentration (100 µg/mL) of non-PEGylated rGO had a lower toxic influence on cell viability in primary cultures of astrocytes and rat brain endothelial cells, while PEGylated rGO induced deleterious effects and cell death. We assessed hippocampal BBB integrity in vivo by evaluating astrocyte activation and the expression of the endothelial tight and adherens junctions proteins. From 1 h to 7 days post-rGO-PEG systemic injection, a notable and progressive down-regulation of protein markers of astrocytes (GFAP, connexin-43), the endothelial tight (occludin), and adherens (β-catenin) junctions and basal lamina (laminin) were observed. The formation of intracellular reactive oxygen species demonstrated by increases in the enzymatic antioxidant system in the PEGylated rGO samples was indicative of oxidative

stress-mediated damage. Under the experimental conditions and design of the present study the PEGylation of rGO did not improve interaction with components of the blood-brain barrier. In contrast, the attachment of PEG to rGO induced deleterious effects in comparison with the effects caused by non-PEGylated rGO.”

# **Biocompatible graphene quantum dots for drug delivery and bioimaging applications – United States Patent 9642815**

## **Abstract:**

In this work we have targeted two aspects of GQDs, Size and ROS to reduce their cytotoxicity. Small size can damage cell organelles and production of ROS (reactive oxygen species) can hamper cell machinery in multiple ways. We have shown that cytotoxicity can be significantly reduced by embedding GQDs inside the PEG matrix rather than creating a thin shell around each GQD. Thin PEG shell around GQD can control ROS production but cannot circumvent the toxicity due to small size. Thus it was essential to solve both the issues. We have used a simple electrochemical method (12 h at room temperature) for synthesizing GQDs and embedded them in PEG matrix via a simple one step hydrothermal reaction (24 h at 160° C.) involving only GQDs, PEG, and deionized water. The P-GQDs formed after hydrothermal reaction show nanoparticles of diameter of ~80-100 nm containing GQDs entrapped in PEG matrix. MTT assay showed significant 60% cells viability at a very high concentration of 5.5 mg/mL of P-GQDs compared to 10-15% viability for C-GQD and H-GQD. ROS production by P-GQDs was least compared to C-GQD and H-GQD in cell free and intracellular ROS assay suggesting involvement of ROS in cytotoxicity. In this work we have solved the issue of cytotoxicity due to ‘small size’ and ‘ROS generation’ without compromising with fluorescence properties of GQDs. P-GQDs was used for bioimaging and drug delivery in HeLa cells. In short we can obtain biocompatible P-GQDs in very short span of time with minimal use of hazardous chemicals and simple methodology.

## **BACKGROUND AND PRIOR ART OF THE INVENTION**

A quantum dot is a semiconductor nanostructure that confines the motion of conduction band electrons, valence band holes, or excitons in all three spatial directions. Quantum dots (QDs) are traditionally chalcogenides (selenides or sulfides) of metals like cadmium or zinc (CdSe or ZnS), which range from 2 to 10 nanometers in diameter.

QDs have unique optical and electronic properties such as size-tunable light emission, narrow and symmetric emission spectra, and broad absorption spectra that enable simultaneous excitation of multiple fluorescence. Moreover, QDs are resistant to photo bleaching than organic dyes and fluorescent proteins. These properties are well suited for dynamic imaging at the single-molecule level and for multiplexed biomedical diagnostics at ultrahigh sensitivity.

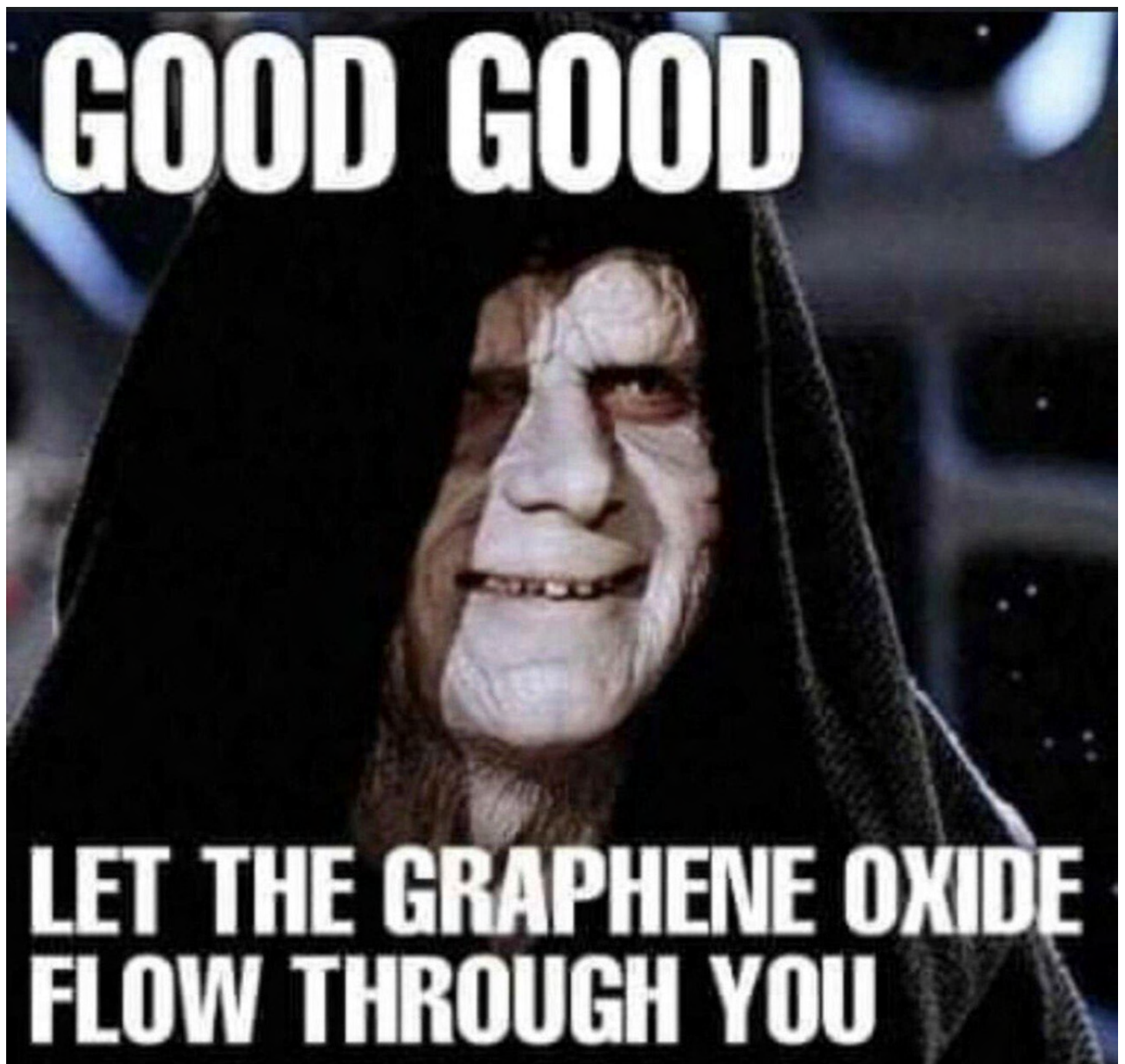
However, for in vivo and clinical imaging, the potential toxicity of QDs remains a major concern. The toxic nature of cadmium-containing QDs is no longer a factor for in vitro diagnostics, since emergent use of fluorescent QDs for molecular diagnostics and pathology is an important and clinically relevant



application for semiconductor QDs. (Kairdolf. B. et al., *Annual Rev. of Analytical Chem.* Vol. 6: 143-162.)

In prevalent practice, the use of carbon nanoparticles in synthesis of quantum dots, have emerged as a new class of quantum dot-like fluorescent nanomaterials. Carbon nanoparticles are used since their particle size can be controlled between 3-20 nm. Carbon atoms linked in hexagonal shapes, wherein each carbon atom is covalently bonded to three other carbon atoms to form graphene sheets. Graphene has the same structure of carbon atoms linked in hexagonal shapes to form carbon nanotubes, but graphene is flat rather than cylindrical.

Graphene quantum dots (GQDs) are used as fluorophores for bioimaging, owing to their physicochemical properties including tunable photoluminescence, excellent photostability, and biocompatibility. GQDs usually less than 50 nm in size have been reported to have excellent fluorescent properties. Due to luminescence stability, nanosecond lifetime, biocompatibility, low toxicity, and high water solubility, GQDs are demonstrated to be excellent probes for high contrast bioimaging and bio sensing applications.



It's  
really

good  
news  
that it's  
becom  
e a  
meme  
topic!

References may be made to prior art documents for methods of synthesizing GQDs using electrochemical processes, hydrothermal methods and the modified Hummers process for graphene oxide synthesis and cytotoxicity assays to determine the cellular uptake of the resultant GQDs formed by these processes.

US patent publication, US 2013/0175182 provides a process for the transformation of single walled, double walled or multi walled carbon nanotubes to nanoribbons composed of few layers of graphene by a two-step electrochemical process. The process involves oxidizing dispersed carbon nanotubes (CNT) to obtain CNT oxide and further reducing it to form graphene layers.

In research publication, *Chem. Commun.*, 2011, 6858-6860, Zhu et al, describe a method of GQD preparation wherein modified Hummers method is used for graphene oxide synthesis and hydrothermal method for GQD synthesis to obtain GQDs of particle size of 5.3 nm. At concentrations of 2.6 mg/ml, cell viability of 80% is observed.

Further Jianhua Shen et al. in *New J. Chem.*, 2012, 36, 97-101 reported one-pot hydrothermal reaction for preparation of graphene quantum dots surface-passivated by polyethylene glycol (GQDs-PEG) and their photoelectric conversion under near-infrared light, using small graphene oxide (GO) sheets and polyethylene glycol (PEG) as starting materials.

Juan Peng et al. (*Nano Lett.*, 2012, 12 (2), pp 844-49) describes the acid treatment and chemical exfoliation of carbon fibers, to provide GQDs in the size range of 1-4 nm. The publication provides that the GQDs derived have no toxicity at concentrations of 0.05 mg/ml. However, the cytotoxicity of GQDs at higher levels is unaccounted.

Chang Ming Li et al., (*J. Mater. Chem.*, 2012, 8764-66) provide a method to develop graphene quantum dots (GQDs) from XC-72 carbon black by chemical oxidation, however toxicity assays confirm maximum cell viability at concentrations of 0.1 mg/ml.

The toxicity of GQDs is attributed to their size, since small sized GQDs interact with various proteins and organelles inside the cell and disrupt cellular processes. Another reason for the toxicity is their ability to generate more reactive oxygen species (ROS). Polymers, especially PEG coating has been used in the literature to decrease the toxicity of GQDs. However, even after polymer coating the cell viability at higher concentrations (>1 mg/ml) is low. Probably because even though the ROS production is lowered by the polymer shell coating, the size of the GQDs after coating still remains small (sub 50 nm) and are still in the size range that can interact with intracellular proteins and organelles.

In the following research publications, references may be made to PEGylation of carbon nanoparticles and the cell viability determined at concentrations of 1 mg/ml or lesser than that.

Bhunia et al., (*Scientific Reports*, 2013, 3:1473) describe carbon nanoparticles (FCN) which are polymer coated with PEG and the dosage dependent cellular toxicity of these fluorescent nanoparticles. At 1 mg/ml concentration of the FCN-PEG composition, 55-60% cell viability is observed.

Zhuang Liu et al., (*J. Am. Chem. Soc.*, 2008, 130 (33), pp 10876-10877) describe pegylated nano-graphene oxide (NGO-PEG) of size 5-50 nm for delivery of water insoluble cancer drugs produced by Hummers method.

Omid Akhavan et al., (*J. Material. Chem.*, 2012, Vol. 22, 20626-33) describes nontoxic concentrations of pegylated graphene nanoribbons for selective cancer cell imaging and photothermal therapy. At concentrations of 1 mg/ml of the composition. 28% cell viability was obtained.

Further Lay C L et al. (*Nanotechnology*. 2010 Feb. 10; 21(6):065101) reports delivery of paclitaxel by physically loading onto poly (ethylene glycol) (PEG)-graft-carbon nanotubes for potent cancer therapeutics.

Toxicity assays of GQDs synthesized by methods of the above prior arts report minimum cell viability at GQDs concentrations of 1 mg/ml, and lesser than that, thus posing limitations in cellular imaging applications. However, to realize biomedical applications of GQDs, low toxicity of the GQDS at higher concentrations is desired for cellular imaging.

With a view to provide graphene quantum dots (GQDs) with decreased cytotoxicity levels at higher concentrations i.e. greater than 1 mg/ml, the present inventors have provided a biocompatible composition of one or more graphene quantum dots (GQDs) in a nanosized polymer matrix of polyethylene glycol which is larger compared to small sized GQDs as observed in the prior art. The PEG matrix aids in reducing the reactive oxygen radicals (ROS) generated by the GQD surface while keeping the small GQDs inside the matrix; thus, also reducing their undesirable interactions with cellular proteins and organelles.

Meanwhile, these nutjobs want to use it to treat bone cancer in kids!

### Graphene oxide toxicity in osteosarcoma



Or how about:

**Graphene quantum dots, their composites and preparation of the same**



## Abstract:

Procedures for the synthesis of zero dimension QDs based on exfoliation/reduction of surface passivated functionalized graphite oxide (f-GO PEG) are described. The synthesis procedures can include exfoliation/reduction f-GO PEG in presence of hydrogen gas, using focused solar radiation and under vacuum.

## BACKGROUND

...

Graphene nanoribbons address this drawback of single layer graphene, however, more recently, focus has been on another carbon nanostructure called graphene quantum dots (GQDs) or carbon quantum dots (CQD) (also known as graphene quantum discs). GQDs show very desirable photoluminescence properties, as the size and shape of the GQDs can be tuned to have desired band gap and emission properties. Moreover, GQDs have desirable characteristics, for example, high surface area, larger diameter, better surface grafting using the  $\pi$ - $\pi$  conjugated network or surface groups and other special physical properties due to the structure of graphene. Since most of the carbon nanomaterials including GQDs are biocompatible and nontoxic, GQDs can advantageously be used in biological applications for example, image scanning and sensing, drug delivery and cancer treatment. The photoluminescence properties of GQDs are useful for photovoltaic applications too as it has been theoretically proved that the energy gap in GQDs can be tuned by using electrostatic potentials.

The band gap of a QD depends on its size and shape. With existing technology it is possible to cut graphene in to desirable size and shape forms. As the number of atoms increases, the energy gap in almost all the energy spectra of GQDs decreases monotonously. In the case of GQDs, along with size and shape, the edge type plays an important role in electronic, magnetic and optical properties.



## THANKS FOR STAYING ON COURSE, THIS GOES DEEPER

This part of the article isn't fully substantiated with third part peer-reviewed evidence, but with some of my own logic and observations, feel free to arbiter for yourself:

The graphene nano-ribbons mentioned above, if you payed attention, are most likely what La Quinta Columna and others noticed on their microscopes. Either that or carbon nanotubes, which are about the same thing, but in 3D.



Check for updates

View PDF

# Liquid crystals of carbon nanotubes and graphene

Branched nanotubes and kinks of long nanotubes can be seen in weakly sonicated materials (figure 1a). By contrast, shorter nanotubes appear to be straighter (figure 1b).

Tools

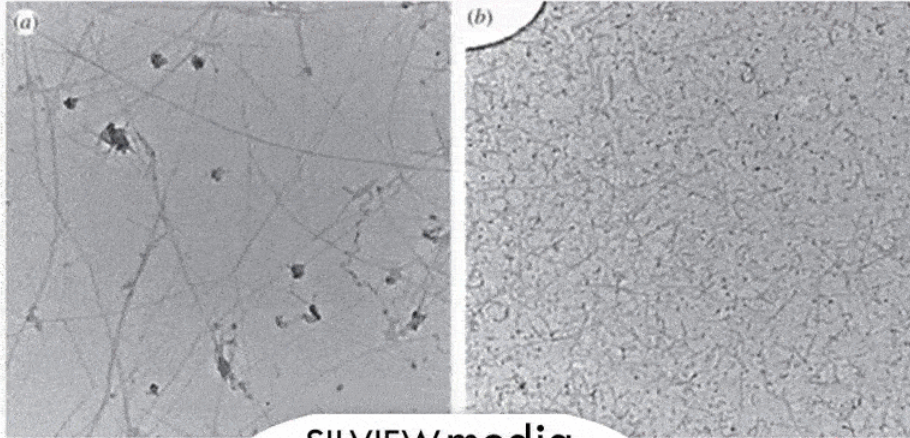
Cite this article

Section

Abstract

1. Introduction

2. Order parameter of  
conductivity  
carbon nanotubes  
crystals

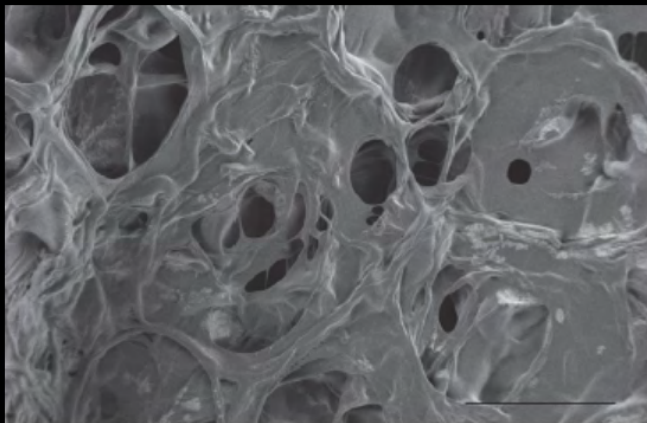


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Sinopeg claims (<https://m.made-in-china.com/company-sinopegmaggie/>) it works with US scientists and collaborates with Chinese Academy. Just like Bill Gates, who is one of the very few foreign members of the Academia there, as I revealed last year.

It's almost unconceivable that Gates didn't know of these PEGs and didn't want to protect the secret from the general public.

Sharing the manufacturing and the patents with the whole world would've almost certainly lead to information leaks, and that is what worried Gates more than money leaks, which are his last concern right now, I suspect.



Xiamen Sinopeg Biotech Co., Ltd.

J'aime cette Page · 10 juin · 🌐

PEG hydrogels are excellent candidates as biomaterials because of their potential for incorporating both biophysical and biochemical cues and their prevention of non-specific protein adsorption, biocompatibility and FDA approval for use in humans. Thermo-sensitive hydrogel based on PLGA-PEG-PLGA tri-block copolymers has been used for delivery of proteins and water-insoluble drugs. The proper LCST and good biocompatibility of PLGA-PEG-PLGA tri-block copolymers make it a good choice for in vitro cell culture matrix.

IN CONCLUSION:





## MODERNA MRNA THERAPY INVENTION PATENT

(57)

### ABSTRACT

A pharmaceutical composition which has a plurality of lipid nanoparticles that has a mean particle size of between 80 nm and 160 nm and contains a modified mRNA encoding a polypeptide. The lipid nanoparticles include a cationic lipid, a neutral lipid, a cholesterol, and a PEG lipid. The mRNA contains a 5'-cap, 5'-UTR, N1-methyl-pseudouridine, a 3'-UTR, and a poly-A region with at least 100 nucleotides.

**14 Claims, 14 Drawing Sheets**

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Ah, and in case you want to go even deeper into the science:

### Other References:

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