

## Review

## Functionalized 2D nanomaterials for gene delivery applications



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## ABSTRACT

During the last decade, two-dimensional (2D) nanomaterials have attracted tremendous interest in many different fields, including electrochemistry, energy storage/conversion, tissue engineering and biomedicine, owing to their unique chemical and optical properties. Recently, the promising potential of 2D nanomaterials, such as carbon based 2D nanomaterials and graphene analogues (such as transition metal dichalcogenides) as gene delivery systems has been explored and applied in various cancer theranostics. In this review, we focus on the applications of the functional 2D nanomaterials for gene delivery and optical imaging in cancer therapy. The properties and structure of different configurations of 2D nanomaterials are first summarized and compared. Then, the biomedical applications of functionalized 2D nanomaterials, particularly the potential of 2D nanomaterials as multifunctional delivery platforms and optical probes in gene delivery applications are briefly discussed and presented with a view to encourage clinical translations of this research.

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**Abbreviations:** 2D, two-dimensional; SCID, Severe Combined Immunodeficiency; CTL, cytotoxic T cell lymphocyte; MHC, major histocompatibility complex; TCR, T cell receptor; JAM1, junctional adhesion molecule 1; HIV-1, human immunodeficiency virus type 1; VSV-G, vesicular stomatitis virus G glycoprotein; LTR, long terminal repeat; CMV, cytomegalovirus; LDHs, layered double hydroxides; TMDs, transition metal dichalcogenides; TMOs, transition metal oxides; BP, black phosphorus; GO, graphene oxide; CVD, chemical vapor deposition; CMOS, complementary metal-oxide-semiconductor; GIC, graphite intercalation compounds; PEI, polyethylenimine; PAMAM, polyamidoamine; PS-NH<sub>2</sub>, amine terminated polystyrene; PS, polystyrene; PLL, poly-L-lysine; PAA, polyacrylic acid; PVA, poly(vinyl alcohol); PEG, polyethylene glycol; MSNs, mesoporous silica nanoparticles; QDs, quantum dots; USGO, ultra-small GO; CS, chitosan; CTAB, cetyltrimethylammonium bromide; FA, folic acid; IONPs, iron oxide nanoparticles; pSiNPs, mesoporous silicon nanoparticles; Mo, molybdenum; W, tungsten; Nb, niobium; Re, rhenium; Ti, titanium; S, sulfur; Se, selenium; Te, tellurium; PVP, polyvinylpyrrolidone; PTT, photothermal therapy; LDHs, layered double hydroxides; GRAS, Generally Recognized as Safe; HDTMA, hexadecyltrimethylammonium; RHEED, reflection high-energy electron diffraction; MBE, molecular beam epitaxy; PLD, pulsed laser deposition; ALD, atomic layer deposition; PDT, photodynamic therapy; NIR, near-infrared; BPQDs, BP quantum dots; PLGA, poly(lactic-co-glycolic acid); ROS, singlet oxygen species; UCNPs, upconversion nanoparticles; siRNA, small interfering RNA; GSH, glutathione.

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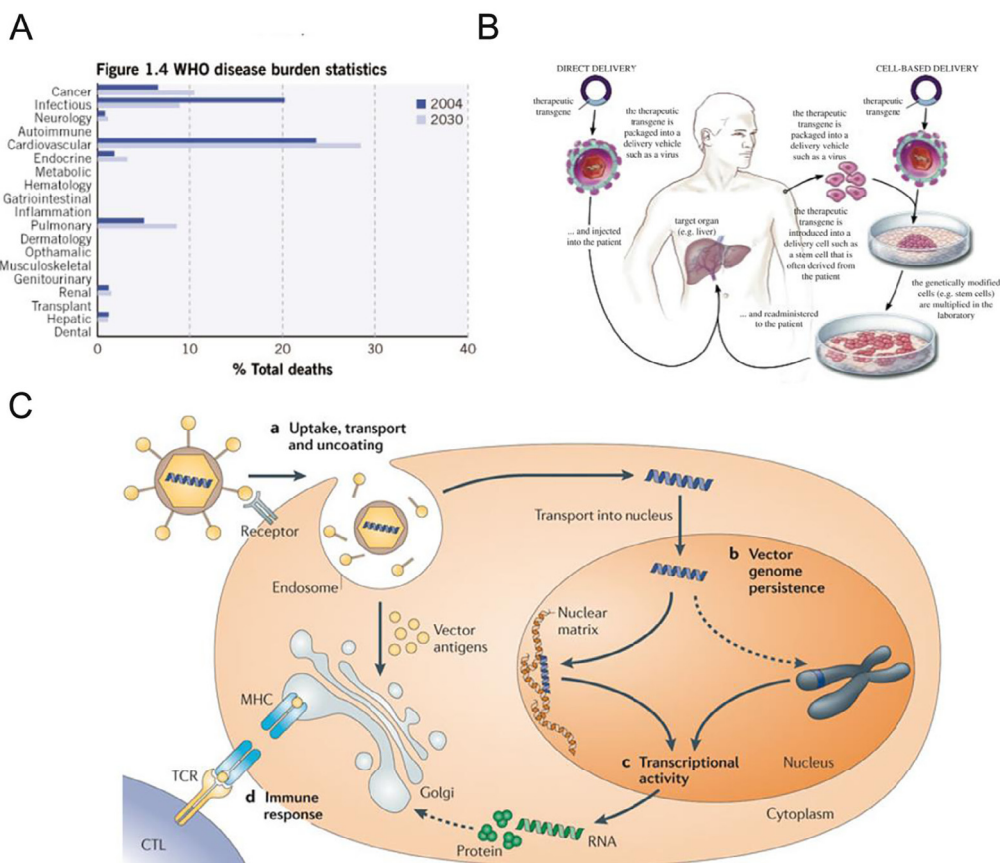
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## 1. Introduction

The fast pace development of present-day technology and high degree of industrialization offer better living conditions to people on one hand but serious environmental pollution and enormous daily pressure on the other. As a result of this stress, many diseases get induced and become the critical risk factors for death. Accord-

ing to the global diseases statistics in 2016, cardiovascular disease is the leading cause of death, which is estimated to account for more than 17.3 million deaths in a year [1]. Cancer, which has existed for over a thousand years has now become the second most devastating disease with limited effective treatments. Moreover, other diseases, such as diabetes, pulmonary tuberculosis, hepatic failure and neurology have also become threats to human health



**Fig. 1.** Disease statistics and gene therapy. (A) WHO disease burden statistics for the top causes of mortality and morbidity worldwide between 2004 and 2030. (Reproduced from Ref. [2] with permission of Nature Publishing Group.) (B) Strategies for delivering therapeutic transgenes into patients. (Reproduced from Ref. [3] with permission of Royal Society.) (C) The processes of successful gene therapy in cells. a. Gene vectors bind to the cell membrane and are internalized by various processes. b. It undergoes further processing upon reaching the nucleus. Depending on the vector, the DNA can exist as an episomal molecule (and associate with the nuclear matrix) or it can be integrated (by covalent attachment) into the host chromosome. c. Transcriptional activity. d. The immune response can limit the viability of the transduced cells and/or the expression of the transgene product. (Reproduced from Ref. [4] with permission of Nature Publishing Group.)

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