# Nanomedicine: Tackling Undruggable Non-Small Cell Lung Cancer

Editorial

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## Editorial

Cancer is one of the leading causes of death worldwide, according to the Centers for Disease Control (CDC) with lung cancer the leading cause of death in the United States for both men and women [1]. There are two histologically different types of lung cancer, non-small cell lung cancer (NSCLC) which accounts for 85 percent of lung cancer cases [2], and small cell lung cancer (SCLC). An increasing concern is the limitation of treatment options, particularly in late-stage cancer, using chemotherapeutic agents due to multidrug resistance (MDR) [3]. Some cancers, such as NSCLC cells can have inherent resistance to certain drugs, or resistance may develop through drug treatment as in SCLC [3]. Lung cancer mortality rates are not only due to MDR, but also attributable to delayed diagnoses [4]. Nanotheranostics may be the solution to NSCLC due to its unique, targeted delivery system that simultaneously allows for diagnosis and treatment assessment as well as improving therapeutic efficacy.

Nanomedicine utilizes a multifaceted approach to cancer therapies that could result in treatment for both primary and metastatic adenocarcinomas. Nanometer size particles have proven successful in part due to higher retention time in the blood which allows for increased uptake and concentrations in tumor tissues [5] along with effective excretion through the liver and kidneys [6]. These effects are partially attributable to the emerging field of therapeutic nanoparticles (TNPs), using nanotechnology to deliver potent, but toxic, small molecule anti-cancer agents [5,7]. Nanoparticles encapsulate the molecules allowing for a targeted delivery system of the cytotoxic contents solely to malignant tissues. Studies continue to validate this important area of research, such as Santra et al. proposing a folate-doxorubicin conjugate as a prodrug, fluorescent and cytotoxic activated upon cell internalization [8].

Additionally, drug absorption is enhanced by occurring through different delivery routes in nanomedicine. These mechanisms include passive endocytosis and receptor-mediated delivery as well as nanocarriers taking advantage of tumor cell's leaky vasculature known as the enhanced permeability and retention (EPR) effect [9]. Currently, a number of delivery vehicles are being researched for NSCLC treatment including polymer-based and metal-based nanotheranostics, with successful application already being seen both *in vitro* and *in vivo*. Polymeric nanoparticles (PNPs) are of great interest in nanomedicine as they are stable and allow for easy surface modifications [10-12] and controlled drug delivery [13]. Multiple therapeutic agents targeting NSCLC using PNPs currently being researched include polymer-based micelles, dendrimers, liposomes, and more. One restriction facing treatment with polymer-based nanoparticles (NPs) has been limits imposed on amount and type of guest molecules held within the nanocavity [14]. A recent discovery of a novel PNP, aliphatic hyperbranched polyester (HBPE) NPs, removes this limitation due to their being globular in shape and highly functionalized [14]. This opens the already broad field of nanomedicine exploration even further. Various PNP-based nanoceria are being used to deliver target specific anti-cancer agents resulting in delayed tumor growth and increased survival rates in mice with NSCLC.

Metal-based nanotheranostics offer different but also effective approaches. Metal NPs show great nanotheranostic potential being used for gene silencing and specific targeting [15]. Different metals also contribute their own unique properties such as iron oxide, gold, silver, selenium, and cerium oxide. *In vivo* responses have now been imaged using a fluorescent platinum (IV) prodrug demonstrating DNA damage to tumor cells and surrounding malignant tissue, opening new insights into anti-cancer therapeutics and the potentially significant role of TNPs [16]. Impacts on tumor metastasis was also explored with encouraging results. Another study, focusing on a non-invasive method, proposed utilizing metal nanoparticles involves inhaling supermagnetic iron oxide (SPIO) NPs which resulted in increased inhibition of tumor growth in NSCLC *in vivo* [17]. Tumor suppression, cancer cell targeted cytotoxicity, and apoptotic cell death encompass only some of the many promising results for future treatment options for NSCLC.

Multifunctional nanocarriers allow for earlier detection, diagnostic capabilities, targeted drug delivery via several routes, and treatment assessment in one nano-sized package. These benefits are particularly important for adenocarcinomas with MDR, such as in the case of NSCLC. With NSCLC one of the leading cancers worldwide with one of the highest mortality rates, it is imperative to look to solutions other than conventional chemotherapeutic therapies. Nanomedicine promises to be a large contributor in the revolution of personalized medicine in the future, and a needed option today for tackling NSCLC.

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## Conflicts of Interest

The authors declare no conflict of interest.

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