

# Gold nanoparticles against respiratory diseases: oncogenic and viral pathogens review

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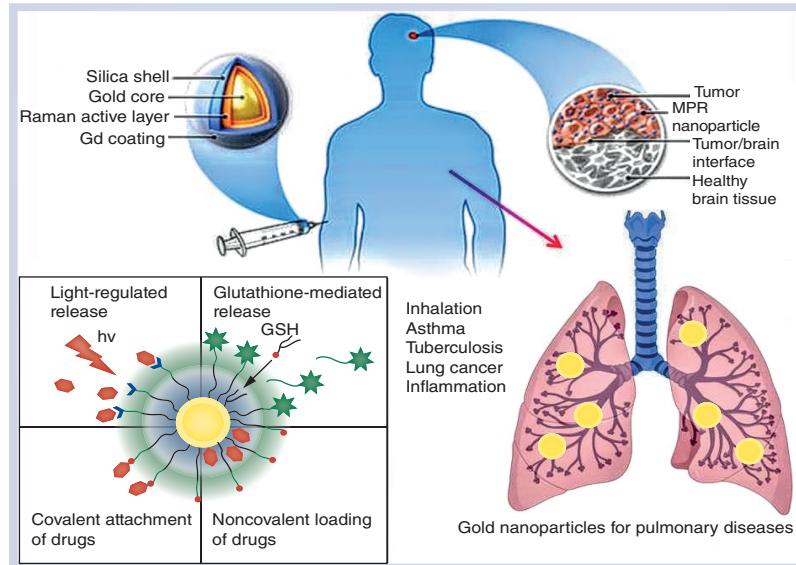
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Nanoscale size-dependent properties give nanomaterials unique specifications that are robust in many applications of human medicine. Gold nanoparticles (AuNPs) have recently gained attention because of their unique optical, physical and electrical properties. AuNPs increase the efficacy of biomedical applications in diagnostic treatments for infectious diseases, by targeting or labeling target cells/bioactive compounds. However, it is imperative to develop the regimens for more accurate diagnostic tools, preventive care and effective therapy. Our critical and comprehensive review presents emerging avenues of molecular diagnostics as well as therapeutics translated into clinical approaches. This manuscript critically reviews the rampant future of AuNPs in the diagnosis and treatment of the most important diseases, such as cancer and viruses of respiratory system.

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Respiratory infections in humans are attributed to cause some of the major global pandemics and hyper endemics faced by mankind. Classical and current examples of viral respiratory diseases include: influenza virus, severe acute respiratory syndrome (SARS-CoV-1), novel corona virus 2019 (nCoV-19) and respiratory syncytial virus. Recently, the coronavirus disease 2019 (COVID-19), generally known as SARS-CoV-2, is not the only global health issue but is the reason for universal fatality on a large scale [1]. There is a need to comprehensively review new challenges of one of most widely applied gold nanoparticles (AuNPs) against several pathogens. Hence, nanotechnology encompassing quantum dots, functionalized nanoparticles (NPs) and exclusive diagnostic mechanisms for designing vaccines and nanodrug delivery have opened up enormous avenues for inhibiting pathogenic viruses internalization and replication. However, expeditious diagnostics and therapeutic scopes against epidemics, along with vaccine augmentation for the prophylactic control of pathogens, are some of the major AuNPs applications.

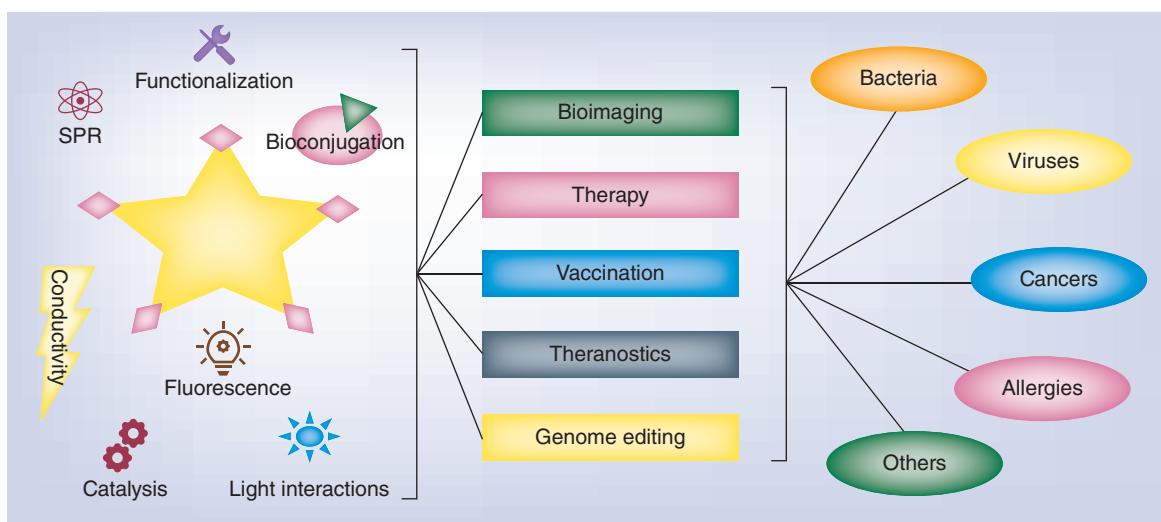
Major bacterial diseases of the respiratory system include tuberculosis, streptococcal infections and infections with MRSA, VRSA and MSSA, whooping cough (*Bordetella* infection) and diphtheria. These fungal infections are caused by aspergillus and histoplasma species. Most importantly, the carcinomas of the respiratory system (lungs in particular) are the second most prevalent and fatal type of cancers globally. Most importantly, the rapid spread and difficult control due to the air-borne transmission of COVID-19 virus indicates its highly pathogenic nature compared with other respiratory viruses [1]. Pneumonia and other organs affected by COVID-19 can present a great clinical challenge to patient's and the associated caregiver's health. The high prevalence and contagious nature indicates the need to develop workable and efficient solutions to the pathogens of the respiratory system.

Pneumonia claims 18% of child deaths (<5 years of age) worldwide [2]. The risk of contracting respiratory diseases may increase significantly with host factors such as hereditary make up, age, smoking, obesity, alcohol consumption, occupational exposure and environmental factors [3,4]. It has been shown that early detection of cancer may save patients from severe clinical disease. However, in resource-limited countries, the access to healthcare systems for diagnosis is lacking. Cancer is characterized by invasive, uncontrolled and rapid cell division in comparison with healthy cells. The occurrence and cancer progression is driven by DNA alterations (mutations) and may occur due to changes in gene expression regarding oncogenes, tumor suppressor and the gene's reformation ability to rectify resultant mutations in oncogenes [5–8]. Similarly, the influenza pandemics of high pathogenic values have claimed several lives that could be treated using functionalized, highly bio-compatible AuNPs [9]. It is expected that the number of cancer deaths may reach 12 million in 2030, if the incidence remains unchecked. Governments, all over the world are spending several billions of dollars each year for cancer treatment and cancer incidence reduction [10,11].

Regarding the economic burden, losses of human life in addition to suffering from disease symptoms and side effects of chemotherapeutics have led to a concerted effort to fight against these dangerous diseases [2]. Treatment regimens against cancer such as radiotherapy, chemotherapy and surgery are currently being sought, but the disease cure rate does not reach the target due to adverse physical and psychological side effects [12,13]. Surgical removal of tumors cannot eliminate the total volume of the tumor in some cases. Several cases may be treated using combination therapy, whether chemotherapy with radiotherapy or surgery. Chemotherapeutics, on the other hand, function by signaling or blocking cellular pathways of rapidly dividing cells. A similar approach to counter rapid cell divisions of cancerous cells is being followed by radiotherapy. These phenomena against cancerous cells may become detrimental for other nontarget, healthy and actively dividing cells of the body [14,15]. A clinical example of this phenomenon is doxorubicin (DOX), which is a popular chemotherapeutic option for cancer patients that induces apoptosis (programmed cell death of cancer cells), it induces not only apoptosis of the cancer cells but also healthy cells [16,17]. Although significant advances have been made in early detection, preventive actions and translational medical diagnostic research, an enormous effort is essential to progress and secure drugs [18].

Au is novel compared with other materials, due to its resistance to transmitting, while considerable ongoing research is being unveiled for potential anticancer, antimicrobial and biodiagnostic utilizations. In contrary to the majority of micro- and nano-particles, AuNPs possess tremendously remarkable properties earmarked for having a sufficient surface-to-volume ratio, physical and chemical properties which may be tuned depending upon structural shape and composition, qualitative and quantitative target-binding acres, and high robustness elaboration in this critical review analysis.

As of now, the significant role of AuNPs is increasing day-by-day due to its eminent cancer therapeutic capabilities as well as drug delivery. One particularly intriguing span of research comprises due to their provisional chemical



**Figure 1. Physiochemical properties and applications against respiratory diseases by gold nanoparticles.**  
SPR: Surface plasmon resonance.

stability that produces a less hazardous, smooth and genuine, cost-effective synthesis route and has a perfect biocompatibility and noninterference with other antibodies or biomarkers. Nowadays, the Au plays as an essential character for curing various diseases. Progress in gold nanoscience has enabled scientists to generate multifunctional nanostructures that may be conjugated to several kinds of biomolecules, antibodies and hormones that can reach targeted cells/receptors efficiently. This comprehensive review has opened gateways to smart technologies that mainly highlight the approaches and developments in treatment, diagnosis and prevention of respiratory diseases within the last 10 years, by utilizing AuNPs emerging techniques.

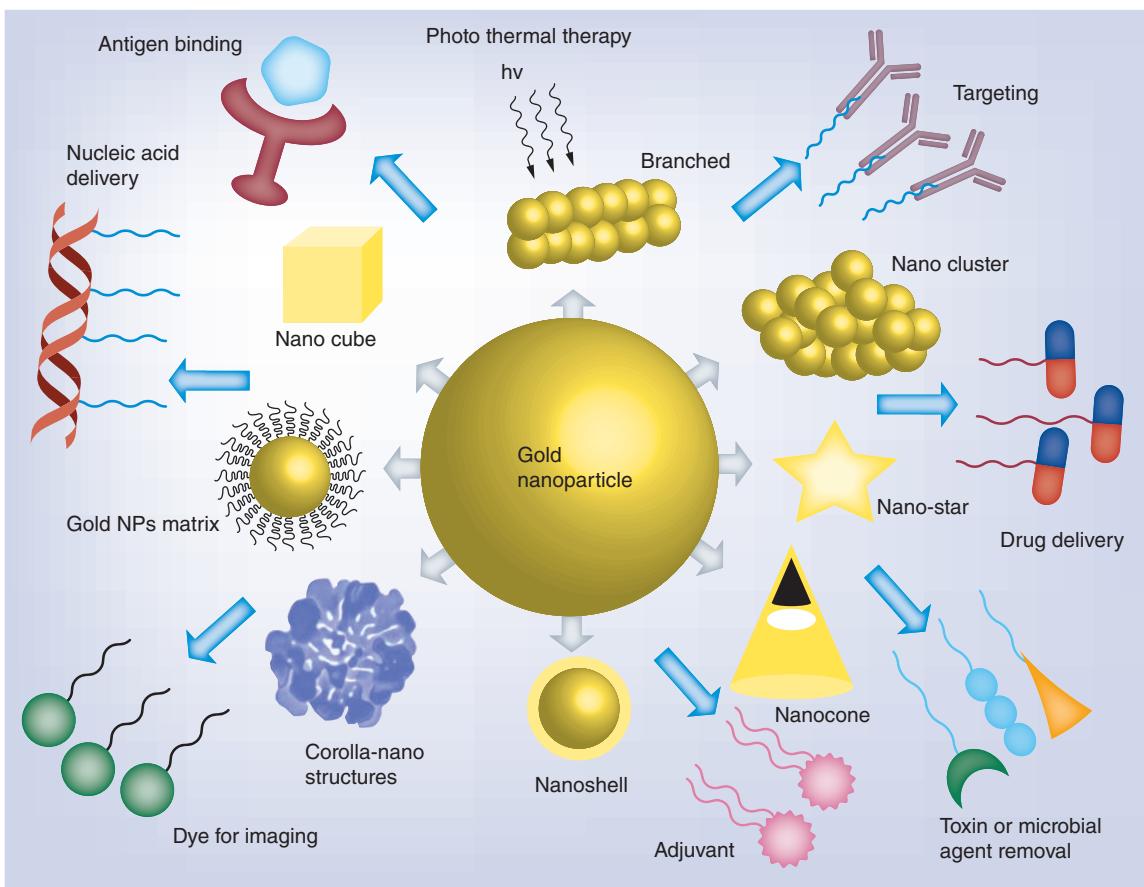
### What makes AuNPs stand out in diagnosing diseases?

Cancer nanotechnology has led to the development and strengthening of useful therapeutic regimens, modified drug delivery systems, in addition to novel methods for diagnosing, imaging and treating cancer [19–22], in order to minimize toxic effects on healthy tissues during treatment. Tumor targeting of NPs involves attaching molecules, such as ligands to the surface of NPs, which will recognize and attach with specific receptors onto the tumor cell surface [23,24]. Many organic and inorganic nanomaterials and nanocomposites have been engineered against cancer, with gold and silver NPs being the most widely applied. AuNPs are a robust nanomaterial with a broad application range [25,26]. The feasibility of tailoring explicit biophysical, biochemical and biomedical assets via structural morphology analysis as well as surface treatment distinguishes AuNPs among the most innovative and investigated techniques in nanotechnology, as depicted in Figure 1 [27,28].

Due to mass, size, surface and optical properties, AuNPs could be rapidly functionalized to many bio-medical applications. Because of the broad surface to volume ratio, AuNPs have a high adsorption ability and are relatively nontoxic and amenable to surface functionalization with specific organic moieties. Also, their surface plasmon resonance (SPR) makes AuNPs among the most widely used nanomaterials in many fields of NP research, as seen in Figure 1 [29,30].

Due to composite material processing approaches, scientists have developed a structural controlling composition, crystallinity and geometrical control over the structures of AuNPs so that they can tailor them for specific biomedical applications, which have a profound impact on their features, influencing stability, mobility and compatibility. The most commonly utilized shapes of AuNPs include those of a sphere, star, cuboidal, round, rod, cone, cluster, shell and matrix, which are arranged in a linear or branched manner as shown in Figure 2 [31–33].

Nanotechnologies have far-reaching potential applications with several usages to overcome cancer such as imaging, diagnosis and targeted therapy [34–36]. Nanotechnology progress will support genetic diagnosis and treatment, depending on each genetic profile and its genetic code sequences and functions [37]. AuNPs were investigated in different areas including *in vitro* and *in vivo* studies as a tissue culture, bio-imaging, cancer treatment and as a drug carrier [38–40]. Brief methodologies for the synthesis and characterization of AuNPs have been summarized in



**Figure 2.** Most commonly utilized shapes of gold nanoparticles for functionalized applications.  
NP: Nanoparticle.

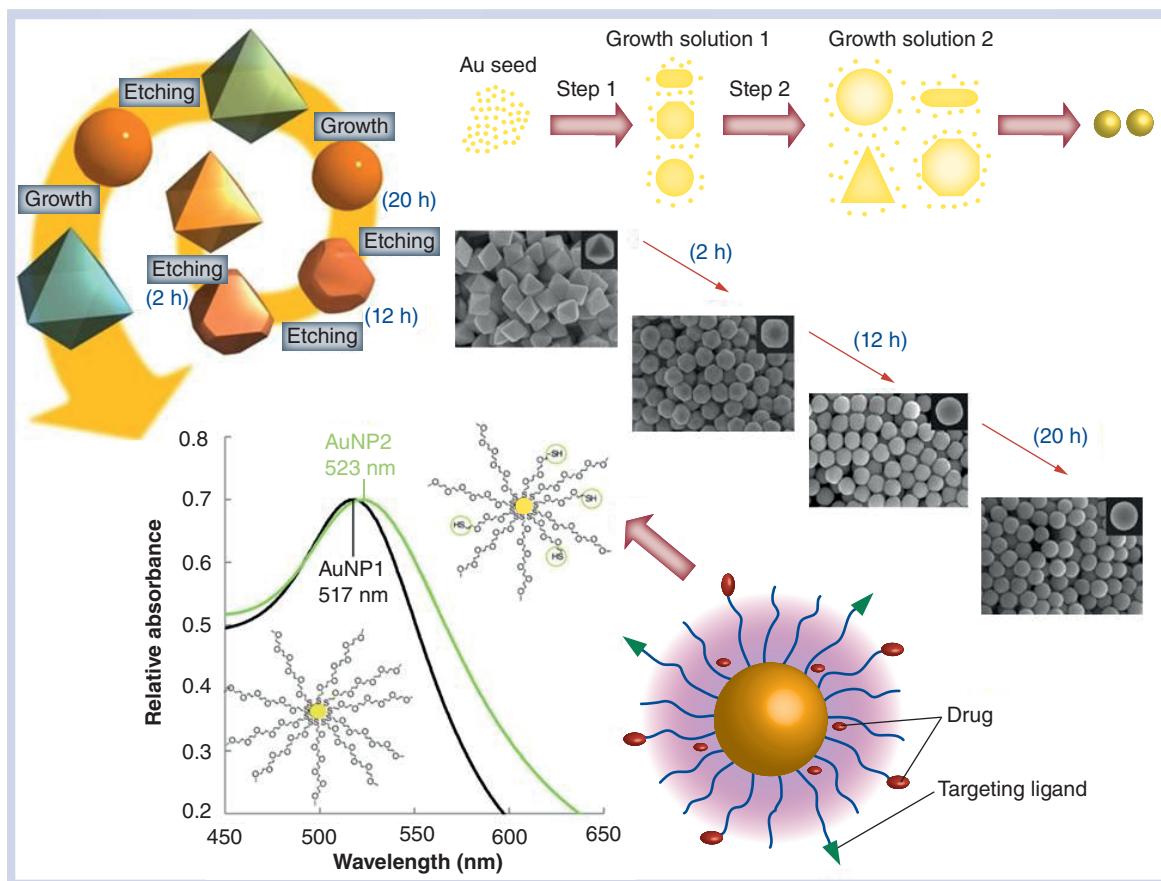
Figure 3. Principal steps in AuNPs include etching (in two to three steps) followed by primary growth, etching again for uniform surface properties and finally secondary growth leading to the production of desired AuNP shapes.

#### *In vivo* imaging for translational medical research

AuNPs are a perfect label due to their glutinous capability of visible light interaction [41,42]. Once exposed to light, free electron excitation occurs to a state of collective oscillation known as 'SPR' [41]. AuNPs are used as a label where they migrate to the needed site *in vivo* and help in ultrasound or x-ray visualization for targeting cancerous cells [41]. The versatile optical properties of AuNPs support the cell imaging of cells with a contrast mechanism [43,44]. Also, the higher extinction coefficient and excellent inherent photostability of AuNPs makes them an excellent candidate for biosensing applications [45]. Different kinds of NPs included nanoclusters, nanoshells, nanorods, dendrimers, biological polymers, nanoscaffolds and carbon nanomaterials [46,47].

Biomolecules (i.e., peptides, proteins, lipids and carbohydrates) can be brought together with AuNPs to form nanomaterials with specific characters that support its usage in imaging, photo-thermal therapy and as a drug carrier [48,49]. Hou *et al.* [50], reported in 2017 the gadolinium ion mediated self-assembly of Au-nanoclusters for multi-modality cancer diagnosis including MRI, CT and near-infrared fluorescence imaging. This kind of approach and design of nanomaterials is a gateway to simultaneous multimodal imaging for a clinical patient. Teymorian *et al.* [51], recorded that trypsin-stabilized Au-nanoclusters had near-infrared radiation properties for the bio-sensing of heparin transmitted on the surfacing of plasmon-enhanced transmission of energy as well as folic acid (FA)-modified gold nano construct (AuNCs) for *in vivo* cancer imaging and diagnosis.

The advantage of AuNPs in the detection of significant viruses that cause respiratory disease, for instance Middle-East Respiratory Syndrome CoronaVirus (MERS CoV) has been reported [52]. These colorimetric approaches toward the detection of viruses eliminate the chances of salt-aggregation and improve the overall specificity of diagnostic



**Figure 3. Basic methodology for synthesis and characterization of gold nanoparticles.**  
AuNP: Gold nanoparticle.

assays. Such assays have also been optimized to detect one of the most crucial genes linked with a highly pathogenic protein, termed the Spike (S) gene.

Only certain self-illuminating materials focused primarily on toxic quantum targets such as, CdSe and CdTe have been generated concerning new areas of molecular imaging applications. Herein, Hu *et al.* [53] reported a new novel design for nontoxic self-fluorescence Au nanoclusters ( $^{64}\text{Cu}$  doped Au NCs), which showed enhanced properties in comparison with the naked AuNPs based on Cerenkov's resonance energy transfer (CRET) for dual-modality positron emission tomography and near-infrared spectroscopy (NIRS).  $^{64}\text{Cu}$ -doped AuNCs exhibited efficient CRET-NIR and positron emission tomography imaging, both *in vitro* and *in vivo*. This imaging contrast agent can be used for biomedical applications, particularly molecular imaging, with it being relatively nontoxic and robustly biocompatible. AuNPs hold great potential as selective imaging tools in medicine, when compared with the traditional contrast agents.

Drug resistance is a significant problem that should be overcome to achieve excellent results in cancer treatment with chemotherapy. Au-DOX nanoconjugates were developed to reduce multiple drug resistance (MDR). The AuNPs were initially pegylated as Au PEG-NH<sub>2</sub>, and then a cleavable disulphide (Au-PEG-SS-DOX) was applied to the AuNPs. The Au-PEG-SS-DOX nanoconjugate design was very efficient in cytotoxicity experiments, where helped release the DOX intracellularly and increased its cytotoxicity in cancer cells, which had MDR. The study highlighted by Gu *et al.* [54], represented the potential of using AuNPs to reduce MDR in cancer treatment with approved chemotherapy. Wang used previous techniques of imaging to detect Au nanoshells in the brain blood vessels of a rat, through near-infrared absorption in the blood-brain barrier [55].

Au nanoshells increase the imaging contrast to 81% in an increased depth with precise details [56]. There are different types of applications for this technique of imaging, for example, in biomedical imaging either in diagnosis or in therapy follow-up, in addition to its usage in plasmonics and sensing and catalysis imaging [57]. On the other

hand, there are some limitations for *in vivo* imaging related to the external-light-mediated plasmonic properties of AuNPs, because it requires a high sensitivity for an external light wavelength to reduce a fully absorbed or scattered off visible light by skin layers and bone [58].

Deploying the exceptional properties of AuNPs, scientists have developed a rapid testing kit for COVID-19. The kit has been developed to detect the virus within 10 min for a naked-eye visual result [45]. This research is a significant breakthrough, which has a deep-rooted history of utilizing AuNPs for visual detection of target genes/antigens/proteins/sequences [59,60].

### Photothermal therapy applications

Localized AuNPs SPR property makes NPs an excellent candidate for photothermal therapy applications [61]. The significant side effect of traditional cancer therapies, such as radiation treatment, causes the destruction of healthy cells nearby to the tumor cells [41]. Nano photo-thermolysis using pulsed lasers and bio-conjugated AuNPs has demonstrated potential applications in selective destruction of cancer cells [62]. During exposure to pulsed lasers with low intensity, NPs become irradiated and their temperature rise leads to the damage of tumor cells alone, without causing any harmful effects to healthy cells [63].

In 2015, the ultra-small AuNCs were conjugated with the surface ligand glutathione (GSH) to synthesize and metabolizable biocompatible radio-sensitizers (GSH–AuNCs). The GSH–AuNCs was accumulated in the tumor area due to its good permeability and retention effect, increasing the efficiency of a radiotherapy session [64]. This productivity was recognized because of the disruption to DNA as the Au 25 nanoclusters had a photo-electric influence. Also, the compton dispersion had a significant reduction in the volume and weight of the U14 tumor [65]. GSH–AuNCs were excreted by the kidney, which is a critical point to reduce the accumulation of AuNPs in body tissues [64].

Increasing the affinity between AuNPs and receptors on pathogen/cancer cell membranes will help in efficient targeting, optimum retention and it will increase the synergistic advantages in cancer treatment as well as molecular imaging. In lung carcinomas, ligands on cell membranes are over expressed, increasing the affinity between gastrin-releasing peptide (GRP) receptors and bombesin (BBN) peptides. Chanda *et al.* synthesized a library of GRP receptors [66] and AuNPs nano platforms with a high bio-compatibility of BBN peptides. For example, by using AuNP–BBN and its radiolabeled surrogate ( $^{198}\text{Au}$ NP–BBN) *in vivo*, there was a high affinity with GRP-receptors in pancreatic acini of normal mice and tumor tissue of prostate tumor-bearing immune-deficient mice.

AuNP–BBN conjugates were administered intraperitoneally and it was uptaken at the tumor area as well as simultaneously decreasing in the reticuloendothelial system. The GRP-receptor-specific AuNP–BBN peptides increase the contrast of x-ray computed tomography imaging technique several folds, compared with a nontreated group [66]. The properties of NPs allow targeted drug delivery to the specific cells as well as the organelle. The molecule-specific binding and imaging by AuNPs were shown by targeting viral nucleotides [59]. This study reported the usage of unmodified AuNPs for easier and more practical, label-free detection.

Gene therapy is a technique used to insert a specific gene sequence into cells to regulate a specific defection in a specific gene. Reports suggest that it can be achieved by using nanomaterials such as Au and Ni nanorods [67]. Trials for the delivery of DNA and peptides using carbon nanotubes combined with polymeric chitosan molecules have shown promising outcomes in treating cancers. NP complexes with peptides were explored to achieve nuclear targeting in HepG2 *in vitro* models [68].

Advanced shapes of AuNPs have been synthesized by polymer nanocrystals, which were coated and loaded with specific active ingredients to give an excellent integration with various functionalities [60,69]. The colourimetric diagnosis of various viral and oncogenic pathogens mediated by exceptional physicochemical properties of AuNPs is worth mentioning. For example, regarding these functions, increasing the contrast of molecular imaging, helps to target the delivery of a specific drug or gene sequence and aids in the treatment through thermal therapy.

The hope and aim is to be able to synthesize a nanostructure complex which can help to follow-up a patient and their prognosis, through implanting this complex into the body without any side effect, while protecting healthy cells [70]. One of the very important, updated and new usages of AuNPs is utilizing it as a drug carrier to deliver molecules to target cells, described as ‘promising nanocarriers for therapeutics’ due to its function, biocompatibility, safety and blood clearance in addition to its easy synthesis [41].

A PEG-coated with a monolayer of AuNP and loaded with TNF- $\alpha$  (NPs delivery system) was synthesized and its efficacy has been proved through increasing tumor damage and decreasing the TNF- $\alpha$  toxicity in healthy cells.

There are many trials for using nanocomposites of TNF- $\alpha$  and Au nanoshells as a hydrogel and are being tested for their drug-delivery usage [71,72].

### Key challenges & opportunities of AuNPs

Recently, many subjects highlighted the enormous activity that nanotechnologies present in biomedicine for the examination and treatment of various human respiratory infections [73]. The summary of applications against respiratory disorders, using AuNPs has been given in Figure 4.

There's no two opinions in the dynamic yet flexible properties of AuNPs. The ability of facile functionalization for downstream applications of therapeutics and diagnosis, vaccination and immunotherapy have been depicted. The binding to receptors and nucleic acids (DNA, RNA) ability to initiate immunogenetic, precise and tailor-made therapeutic machinery, makes AuNPs stand out from the crowd, compared with other potential therapeutics [45]. The steps for sensing and imaging applications of AuNPs have been illustrated. Step 1 comprises of the precise attachment (sandwiching) of antibodies with the target antigen. Step 2 shows the labeling with fluorescent (Raman) dyes leading to conjugate formation. Step 3 features the hybridization of the nanoconjugate with that of a DNA probe. Step 4 shows the formation of a electrode specific modified nanomaterial, followed by the addition of a hydrolytic enzyme, leading to the change in physicochemical properties of the target antigen for better imaging and diagnosis.

Moreover, the sensing applications of AuNPs in laboratory models have shown efficient labeling, illumination and diagnosis of diseases at preclinical stages. The prognostic value of AuNPs against human respiratory diseases has been established in lung cancers and viral pathogens (especially the corona virus family) of high importance [52]. Additionally, the precise targeting and toxicity in cancerous cells by specific ligand binding of AuNPs to cancerous cells is only of high value in biological models.

Notably, an excess of medically relevant results, including nanomaterials, is currently on being commercialized for human use. Regenerative and precision medicine, are approaches that have been applied for biomarker discovery such as nanobiosensors [74]. Models of nanopharmaceuticals for the precise distribution and assimilation of therapeutic materials however, need further optimization.

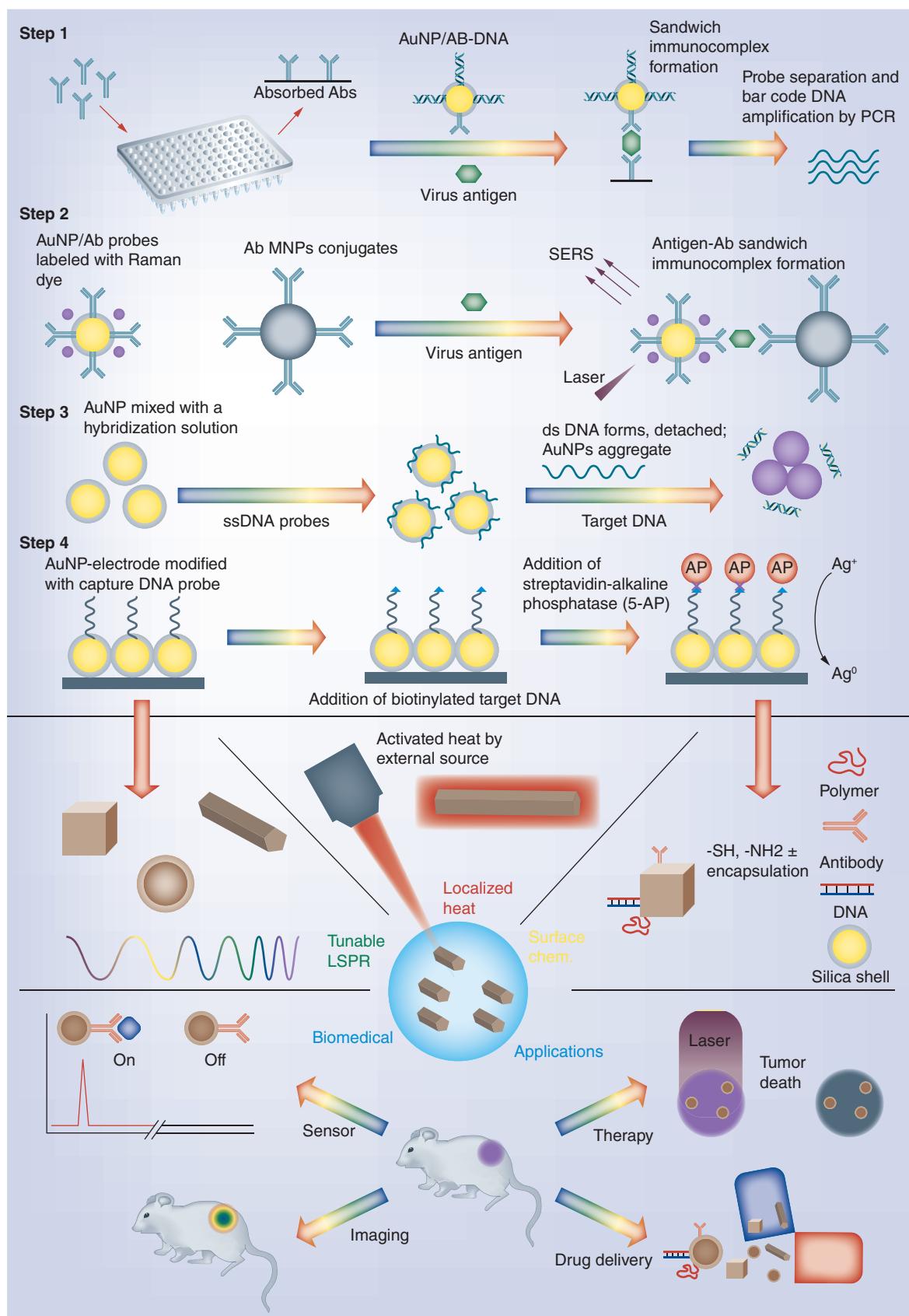
Unusual signs of progress have also been done in the area of Au nano-oncology by superseding the ability of conventional chemotherapy medicines [75]. These applications target the tumor position with various functional units, including AuNP captured peptides, enzymes, immunoglobulins and cytotoxic factors. In these circumstances, several investigations revealed that AuNPs could be used to achieve therapeutic units to modulate biological pathways such as oxidative stress, autophagy, metabolism and exercising anticancer action [76–79]. The capability of downregulation and upregulation of metabolic pathways in the host cell is of high value in the treatment of viral diseases of a respiratory origin.

Nano-informatics also promotes chemotherapy by developing the Au-nanostructures for the modelling of cancer cells and supports the discovery of drug-resistant growth regularly. Hyperthermia-based targeted drug control and gene treatment programs are the most advanced nano-informatics methods shown to treat cancer with the most invisible side effects [80,81]. Furthermore, exclusive investigations of AuNPs on antitumor therapy by drug delivery utilization is illustrated in Table 1.

### The performance improvement & biocompatibility of AuNPs *in vivo*

Still, the purpose of computational methods to nanomedicine is undeveloped and is an important area of study. The demand for computational uses at the nanoscale dimension has provided an increase in the area of nano-informatics. Powerful machine-learning algorithms and sinister analytics can considerably promote the idea of more effective nanocarriers. Such algorithms produce auspicious information on future data and have been primarily used for divining cellular uptake and movement. Data mining, network study, quantitative structure-property correlation, quantitative structure–activity relation, consumption, delivery, metabolism, elimination and toxicity are characteristic evaluations carried out in Au-nano informatics.

Nanotechnology owns the potential to afford a standard turn in demonstrative and therapeutic medications that are given to complete target specificity and improve recognition for significant development in the overall therapy of the prostate and different inoperable cancers [96,97]. Au-NPs occupy excellent abilities to identify, image or manage tumors at the molecular and cellular levels [98,99]. Between several metallic NPs, AuNPs possess exceptional tumor recognition abilities because of their inherent connection to broken tumor vasculature, which is displayed in the angiogenesis of cancer extension [100].



**Figure 4. Summary of gold nanoparticles engineering against respiratory diseases.**  
Ab: Antibody; AuNP: Gold nanoparticle; MNP: Magnetic nanoparticle.

**Table 1.** Brief utilization of gold nanoparticles in drug-delivery antitumor therapy.

Nanomaterials	Structural morphology (nm)	Results	Cells culturing	Ref.
Methotrexate (MTX)-gold nanoparticles (AuNPs)	8–80	Higher cytotoxicity toward numerous cells cutting as compared with free methotrexate (MTX). Suppression of tumor growth with MTX-AuNP but not with free MTX	Lewis lung carcinoma (LL2) cells	[82]
Doxorubicin (DOX)-Hyd@ AuNPs	30	Reinforced toxicity against multi drug-resistant cancer cells	MCF-7/ADR cancer cells	[83]
Cyclohexane-1,2-diamine:platinum [Pt(R,R-DACH)]-AuNPs	26.7	Platinum-tethering depicted higher cytotoxicity as compared with free oxaliplatin that could enter the nucleus	A549 lung epithelial cancer cell line, HCT116, HCT15, HT29 and RKO colon cancer cell lines	[84]
Transferrin peptide (Tfpep)-AuNPs consolidated with photodynamic pro-drug Pc 4	5.1	Cellular uptake of targeted particles was remarkably massive than that of the nontargeted ones	LN229 and U87 human glioma cancer lines	[85]
Cell puncturing peptides (CPP)-DOX-AuNPs	25	Higher cell death as compared with previously tested 41 nm AuNPs	HeLa cells and A549 cells	[86]
Folic acid (FA)-Au-succinimidyl (SMCC)-DOX	N/A	Enhanced drug accumulation and retention compared with free doxorubicin in multidrug-resistant cancer cells	HepG2-R, C0045C and HDF	[87]
FA-berberine hydrochloride (BHC)-AuNPs	20 to 60	Increased efficacy of BHC against cancer cells	Vero and HeLa	[88]
Au-poly L-aspartate (PLA-DOX)-b-polyethylene glycol (PEG)-OH/FA nanoparticle	34	Enhanced cellular uptake and cytotoxicity against cancer cells	4T1 mouse mammary carcinoma cell line	[89,90]
DOX @polyvinylpyrrolidone (PVP)-AuNPs	12	Induction of early and late apoptosis in lung cancer cells and upregulation of tumor-suppression genes	A549, H460 and H520 human lung cancer cells	[91]
DOX-bleomycin (BLM)-PEG-AuNPs	10	Enhanced half-maximal effective drug concentration, providing rationale for chemotherapy utilizing two drugs	HeLa cells	[92,93]
Epithelial cell adhesion molecule (EpCam)-RPAuN	48	Biomimetic nanoparticle loaded with paclitaxel was used in combination treatment (PTT and chemotherapy)	4T1 mouse mammary carcinoma cell line	[94,95]

Lately, Balogh and his colleagues also made groundbreaking innovations for the synthesis of radioactive polyethylene ( $^{198}\text{Au}$ ) radioactive dendrimer, composed of Au in sizes between 10 and 29 nm [101]. Their investigations have revealed that only an intratumoral dose of poly ( $^{198}\text{Au}^0$ ) d = 22 nm, allow nanocomposite devices in phosphate-buffered saline to provide a dose of 74  $\mu\text{Ci}$  over the next 8 days, which ended in a statistically executable 45% decrease ( $p = 0.0245$ ) in the growth volume, when associated with nontreated groups [101].

Biocompatible  $^{198}\text{Au}$ NPs will provide a distinct generation of therapeutic factors possessing the activity to reduce severe clinical difficulties connected with existing heterogeneous brachytherapy factors for the therapy of different kinds of human tumors. Specific studies *in vitro* and *in vivo* have been performed to support the usage of AuNP coated gum-arabic glyccoprotein (GA). The study conducted by Chanda *et al.* [97] confirmed that the combined polysaccharides and proteins within the GA backbone can irreversibly, yet efficiently bind AuNPs to give rise to nontoxic AuNPs that are permanent following *in vitro* and *in vivo* situations for possible uses in therapeutic applications [102].

Chanda *et al.* [97] noted that for mice with a flank model of human prostate cancer a healing ability and pharmacokinetic considerations resulted from a five bis106 PC-3 cell subcutaneous implant. For therapeutic testing, single stable swelling was permitted to continue for 3 weeks.

The animal authority control agency should be authorized due to zenith weight decline observed on days 16 and 26. After, on day 28, five animals remaining under control were authorized as a result of extended weight refuse, declining overall fitness situation and the chance of lump maturation. In contrast, none of the seven animals in the therapeutics conjugation ended and ancient completion was established. They did show a temporary weight decline that topped at  $-17.5 \pm 2.5\%$  on day 17 but increased to  $-10.8 \pm 2.8\%$  by day 31 [97]. Casual or no radiotherapy in the liver, intestine and other nontarget organs were emphatically assured that the invigorating payload was alive in a period where the cancer lump location meanwhile had 30 days therapy control.

Nano-informatics has presented a significant additional program for AuNPs study and interpretation to defeat such *in vitro* barriers. The multidisciplinary approach toward existing major pandemics is therefore required [103]. Nano-informatics mainly bargain with the assembling, distribution, visualizing, modeling and evaluation of relevant nanoscale level data and knowledge. It is the perfect time to materialize the potential of AuNPs in developing and

optimizing rapid, ultra-sensitive and user-friendly approaches for imaging the emerging corona viruses. Most recently, a lipid NP-based vaccine has made its way to the fastest clinical trials for vaccine against COVID-19 [69]. As a matter of fact, this success is a huge milestone for nano-based vaccines, encouraging the use of highly biocompatible nanomaterials, including AuNPs against global health emergencies.

## Conclusion

It would be highly beneficial from new and promising AuNP-based diagnostics to be attributable to longer circulation times and localized accumulation at the disease site for efficient diagnostics within flexible detection limits. Indeed, it can be utilized to implement a wide diversity of therapeutics, such as: photothermal ablation, radiotherapy, drug delivery and nucleic acid delivery based on the AuNPs platform. The brief review discusses all the research done to aid diagnosis and treat respiratory diseases of humans by deploying AuNPs. Some recommendations that can drive the future outlook of research such as clinical trials may be vigorously conducted on susceptible populations to derive useful data including, the up-scaling of commercialization of AuNPs needs for laboratory-scale production, concerns associated with the use of NPs toward other organs of the human body need to be well-addressed and ecotoxic profiles of AuNPs may be established and well communicated to clinicians for mitigating the associated hazards.

Medical nanomaterials were developed rapidly in the current decade as one of the main essential applications in the nanotechnology field. Metal NPs are being used as biosensors and biolabels for cellular studies. Fluorescent NPs attached to biological ligands that bind with specific cellular receptors enable improved cellular imaging studies. AuNPs alone or in a combination have been used and applied in the therapy of high priority diseases of the respiratory system. The applications include early diagnosis, cellular imaging and photothermal therapy for different kinds of NPs such as nanoclusters, nanoshells and nanorods that gained considerable importance. Biomolecules such as amino acids, gene sequence, proteins and fats could be optimally functionalized on AuNPs to produce nanomaterials. These biologically conjugated nanomaterials possess more stable and improved properties for diversified applications as drug cargo and in bio-imaging, photothermal therapy and vaccination strategies. Localized SPR property of AuNPs enables an excellent applicant for photothermal therapy applications. The properties of NPs allow for targeted drug delivery to the specific cells as well as organelles. The potential of AuNPs during laboratory trials is a way forward to develop innovative solutions to combat various infectious diseases in humans. The tuning capabilities of their physical properties (size, shape and surface chemistry) along with a high biocompatibility and improved pathogen or concrogenic toxicity, borne out by AuNPs, based diagnostics and product formulations in clinical trials as therapeutics that could be exploited in current and future outbreaks of respiratory diseases.

## Future perspective

AuNPs have dynamic properties and a huge potential of diversified applications against cancer and other infectious diseases. Surface modification of AuNPs allows designing such materials with inherent properties to guide it toward its target. Current trends of future scopes are immuno-diagnostics, point of care therapy, translational medicine and nano imaging.

Furthermore, with the cytotoxicity of AuNPs being almost negligible, this makes them ideal as a template for drug delivery and molecular imaging in particular for computed tomography agents. AuNPs hold great potential in dual-modality imaging and thermal treatment with their ability to be directed toward targeted cells, and upon the exposure to a radiation source, they will absorb heat and cause cellular damage and disruption to the targeted cells. The approval of AuNP based diagnostic approaches for COVID-19 testing is a huge gateway for the bright future of these materials at clinical settings. Similarly, nano-assembly vaccines have the potential to reshape the future of adjuvants and provide new generation vaccines.

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**Executive summary**

- Gold nanoparticles (AuNPs) have a unique set of properties that are advantageous for applications at a clinical setting.
- Functional AuNPs are an excellent candidates for photothermal applications of translational research therapeutics.
- AuNP conjugate allows for targeted molecular nano-imaging investigations.
- Nanoparticles out-weigh the traditional therapeutic approaches by their multipronged functional properties.
- Metal nanoparticles are utilized for biosensors and biolabels for cellular studies.
- Molecular diagnostics have brought forward a broad range of AuNPs-based sensing platforms with remarkably improved sensitivity than those of conventional tests.

**References**

Papers of special note have been highlighted as: ● of interest; ●● of considerable interest

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