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REVIEW

Molecular Convergence and Liposome-Enabled Therapeutics: Integrating Mechanistic Links Between Neurodegeneration and Cancer

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Abstract

Mounting mechanistic evidence increasingly supports the notion that cancer and neurodegenerative diseases, traditionally regarded as biologically disparate entities, are in fact governed by partially overlapping molecular and cellular determinants. Both conditions are characterized by disruption of proteostatic surveillance, mitochondrial insufficiency, sustained inflammatory activation, redox disequilibrium, and maladaptive stress-response signaling, particularly involving the unfolded protein response (UPR) and DNA damage response (DDR) networks. Recognition of these shared pathological infrastructures has catalyzed a paradigm shift toward therapeutic strategies capable of simultaneously interrogating and modulating convergent disease mechanisms rather than addressing each disorder in isolation. This review integrates molecular, pharmacological, and nanomedical perspectives to delineate the intersecting signaling axes linking tumor progression with neurodegenerative decline. Particular attention is devoted to preclinical and early clinical evidence supporting advanced liposomal platforms including stealth PEGylated vesicles, ligand-functionalized constructs, and stimuli-responsive formulations that are engineered to engage shared molecular liabilities. Collectively, these systems demonstrate the capacity to restore proteostasis, attenuate neuroinflammatory signaling, reduce oxidative and genotoxic stress, optimize intracellular trafficking, and enhance mitochondrial function across both malignant and neuronal microenvironments. Convergent findings indicate that liposomal therapeutics may exert dual-functional benefits through controlled release of anti-inflammatory or redox-modulating agents, targeted modulation of ER stress and chaperone activity, correction of disease-associated metabolic reprogramming, and improved penetration of the blood–brain barrier via receptor-mediated transport mechanisms. By acting directly at the molecular intersection points common to cancer and neurodegeneration, liposomal nanocarriers thus represent a rational platform for cross-disease intervention. Taken together, liposome-enabled nanomedicine provides a translatable cross-disease platform for targeting shared molecular pathways in cancer and neurodegeneration, enabling integrated anticancer and neuroprotective therapies with improved efficacy and safety.

Keywords: Molecular convergence- liposomal nanocarriers- targeted drug delivery- neurodegenerative disorders

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Introduction

Cancer and neurodegenerative diseases have long occupied opposite ends of the biological spectrum, representing, respectively, pathological states of uncontrolled cellular expansion and progressive neurocellular attrition, and thus have traditionally been interpreted as mechanistically and clinically unrelated processes [1, 2]. However, breakthroughs in molecular biology, systems pharmacology, and high-resolution omics sciences have fundamentally redefined this paradigm, revealing an unanticipated but increasingly substantiated convergence in which these ostensibly divergent disorders are governed by shared and highly interwoven pathogenic circuitry [3, 4]. Perturbations in proteostasis, sustained redox imbalance, mitochondrial dysfunction, aberrant UPR activation, defective DDR signaling, chronic inflammatory remodeling, and systemic metabolic instability are increasingly appreciated as shared molecular liabilities that converge to drive both malignant evolution and neuronal attrition [5, 6]. This emerging conceptual alignment effectively dissolves traditional therapeutic boundaries, thereby unveiling a translational landscape in which integrative, cross-disciplinary interventions can be rationally designed to engage common molecular hubs and convergent pathogenic networks [7]. Despite the recognition of these shared molecular underpinnings, therapeutic development in both cancer and neurodegenerative disorders remains fraught with formidable challenges [8]. Traditional chemotherapeutic agents are hindered by poor selectivity, toxicity-imposed dosing ceilings, and inefficient tissue distribution, while candidate neuroprotective compounds often fail to achieve clinical efficacy due to limited pharmacokinetic stability, rapid elimination, and inadequate traversal of the blood–brain barrier [9]. Taken together, these therapeutic shortcomings accentuate the urgent necessity for next-generation delivery architectures engineered to enhance drug stability, facilitate selective biodistribution to pathological niches, and precisely engage the convergent molecular networks driving both malignancy and neurodegeneration [10]. Accordingly, liposome-based nanocarriers have gained increasing recognition as a rational solution to these translational constraints [9]. As biocompatible, phospholipid bilayer vesicles, liposomes afford controlled spatiotemporal drug release, reduced off-target toxicity, and exceptional flexibility for the incorporation of structurally and chemically diverse therapeutic payloads [9]. Crucially, their surface architecture is amenable to molecular functionalization with ligands, peptides, antibodies, or synthetic polymers, conferring selective targeting capabilities that direct these carriers toward tumor populations, neuroinflammatory microglia, compromised neuronal compartments, or specific molecular signatures associated with UPR perturbation, redox imbalance, and mitochondrial insufficiency [11]. This intrinsic adaptability elevates liposomes beyond the role of inert carriers, redefining them as biointeractive nanoplatforms that can directly engage and recalibrate the convergent molecular circuitry governing both tumorigenesis and neurodegeneration [12]. Accumulating evidence further demonstrates that targeted liposomal constructs are capable of orchestrating multifaceted therapeutic effects, including attenuation of oxidative stress, restoration of proteostasis, dampening of pro-inflammatory signaling, reinforcement of mitochondrial integrity, and refinement of intracellular transport mechanisms pathophysiological axes fundamentally implicated in both oncogenic resilience and neurodegenerative vulnerability [13]. Furthermore, refinements in stealth PEGylation, stimuli-responsive (pH- or redox-activated) liposomal designs, and ligand-directed blood–brain barrier translocation mechanisms have markedly extended the functional versatility and translational applicability of liposomal systems, enabling their deployment beyond conventional therapeutic silos and across diverse pathological contexts [14]. Taken together, the growing appreciation of molecular convergence between oncogenesis and neurodegeneration, alongside the maturation of advanced liposomal nanotechnologies, underscores the urgency for an integrative conceptual framework. This review interrogates the shared pathogenic infrastructure that links these disorders and explores how rationally engineered liposomal systems can be deployed to therapeutically exploit these common vulnerabilities. Through the integration of molecular pathobiology with next-generation nanomedicine, we propose liposomal therapeutics as a translational bridge capable of enabling cross-disciplinary drug delivery solutions to confront two of the most consequential diseases of the modern era.

Methods

To capture the evolving evidence base, a rigorous and methodologically structured literature survey was conducted to retrieve peer-reviewed studies addressing the shared molecular underpinnings of cancer and neurodegeneration, with particular emphasis on liposomal and nanocarrier-mediated therapeutic interventions. The search encompassed publications from January 2010 to December 2025 and systematically incorporated major indexing repositories, including PubMed, Scopus, Web of Science, and the Consensus academic database, using predefined keywords and Boolean combinations such as molecular convergence, liposomal drug delivery, nanocarriers, targeted nanomedicine, proteostasis dysregulation, mitochondrial dysfunction, oxidative stress, blood–brain barrier transport, neurodegeneration, and cancer therapeutics.

Convergent Molecular Pathways and Pathogenic Circuitry at the Cancer–Neurodegeneration Interface

Despite occupying seemingly opposite ends of the biological spectrum pathological hyperproliferation in cancer versus progressive neurocellular degeneration in neurological disease these conditions paradoxically converge upon a shared and deeply interconnected molecular architecture [3, 4], as schematically illustrated in Figure 1. At the core of this convergence lies a fundamental breakdown in proteostasis, characterized

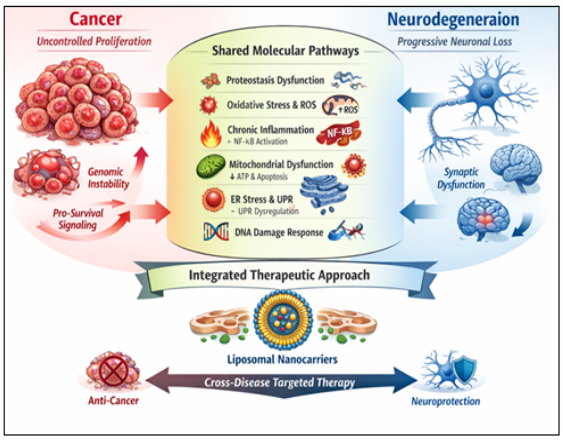

Figure 1. Schematic Representation of the Shared Molecular Landscape Linking Cancer and Neurodegenerative Disorders. Despite contrasting clinical phenotypes uncontrolled cellular proliferation in malignancy versus progressive neuronal loss in neurodegeneration both conditions converge upon common pathogenic mechanisms, including proteostasis collapse, oxidative stress and reactive oxygen species (ROS) imbalance, chronic NF-κB–mediated inflammation, mitochondrial dysfunction, endoplasmic reticulum stress with unfolded protein response (UPR) dysregulation, and altered DNA damage response (DDR) signaling. These interconnected pathways differentially drive oncogenic survival or neuronal vulnerability depending on cellular context. Liposomal nanocarriers are depicted as integrative therapeutic platforms capable of targeting these shared molecular nodes to enable cross-disease, mechanism-guided interventions that combine anticancer and neuroprotective strategies.

by defective chaperone-mediated quality control and the intracellular accrual of misfolded and aggregated proteins, processes that simultaneously facilitate oncogenic progression while exacerbating neurotoxicity and synaptic vulnerability in conditions including Alzheimer's and Parkinson's disease [5, 6]. Similarly, redox disequilibrium and dysregulation of reactive oxygen species (ROS) signaling constitute a central pathogenic axis shared by both disease states [12, 13]. In the oncogenic context, elevated ROS levels foster genomic instability and activate pro-survival and proliferative signaling cascades, thereby facilitating tumor progression, whereas in post-mitotic neuronal populations, excessive oxidative burden precipitates mitochondrial collapse and apoptotic cell death owing to inherently limited antioxidant defenses [6, 12]. A second major point of convergence lies in chronic inflammatory remodeling, predominantly orchestrated through NF-κB–dependent signaling networks. Neoplastic tissues co-opt inflammatory cytokines and NF-κB–mediated transcriptional programs to sustain proliferation, angiogenesis, and immune escape [3, 4]. Conversely, persistent neuroinflammation particularly that driven by sustained microglial activation propagates synaptic dysfunction and progressive neuronal attrition through activation of analogous molecular circuitry [6]. Mitochondrial dysfunction represents an additional unifying determinant. While cancer cells exploit metabolic reprogramming and adaptive shifts in oxidative phosphorylation (OXPHOS) to support bioenergetic demands and cellular fitness, neurodegenerative disorders are typified by mitochondrial insufficiency that compromises ATP generation and triggers intrinsic apoptotic cascades [12, 13]. Parallel disruptions in endoplasmic reticulum (ER) homeostasis further integrate these pathologies within a shared stress-adaptation framework, as dysregulation of the unfolded protein response (UPR) emerges as a common feature [5, 6]. Malignant cells frequently reconfigure UPR signaling branches such as PERK, IRE1/XBP1, and ATF4 to tolerate proteotoxic stress, whereas neurons, inherently susceptible to prolonged ER perturbation, preferentially engage pro-apoptotic mediators including CHOP and downstream death pathways [3, 5]. The DNA damage response (DDR) likewise demonstrates mechanistic overlap despite divergent outcomes: tumor cells often attenuate checkpoint control to favor continued proliferation, while neurons exhibit sustained DDR activation that contributes to senescence and programmed cell loss [3, 4]. Collectively, these intersecting processes underscore that cancer and neurodegeneration, notwithstanding their contrasting clinical manifestations, operate within a common molecular landscape dominated by stress-response failure, proteotoxic accumulation, inflammatory signaling, and metabolic disequilibrium [4]. Notably, the opposing phenotypic consequences oncogenic persistence versus neuronal demise reflect differential exploitation of the same foundational pathways rather than fundamentally distinct mechanisms [3]. This systems-level convergence thus furnishes a compelling rationale for the development of integrative therapeutic platforms, including liposomal nanocarriers, capable of precisely targeting and modulating these shared molecular nodes across both pathological contexts [9].

Shared Cellular Stress Pathways

An expanding body of evidence increasingly implicates the unfolded protein response (UPR), DNA damage response, and mitochondrial stress signaling as an integrated molecular framework that functionally connects oncogenesis with neurodegeneration, forming a common stress-response backbone that is nevertheless associated with diametrically opposed biological consequences across these disease contexts [15, 16]. Within malignant systems, the UPR is frequently appropriated as an adaptive survival program that enables tumor cells to withstand proteotoxic pressure [17, 18]. Coordinated activation of PERK, ATF4, and IRE1/XBP1 augments protein-folding capacity, promotes metabolic rewiring, and facilitates angiogenic and pro-survival transcriptional outputs, thereby conferring resilience under conditions of sustained cellular stress [19, 20]. In contrast, neurons intrinsically constrained by limited proteostatic buffering capacity exhibit a markedly reduced tolerance to chronic ER perturbation [15]. Prolonged engagement of the PERK–ATF4 axis progressively transitions from compensatory to pro-apoptotic signaling, culminating in CHOP induction, mitochondrial destabilization, and irreversible programmed cell death, thereby positioning

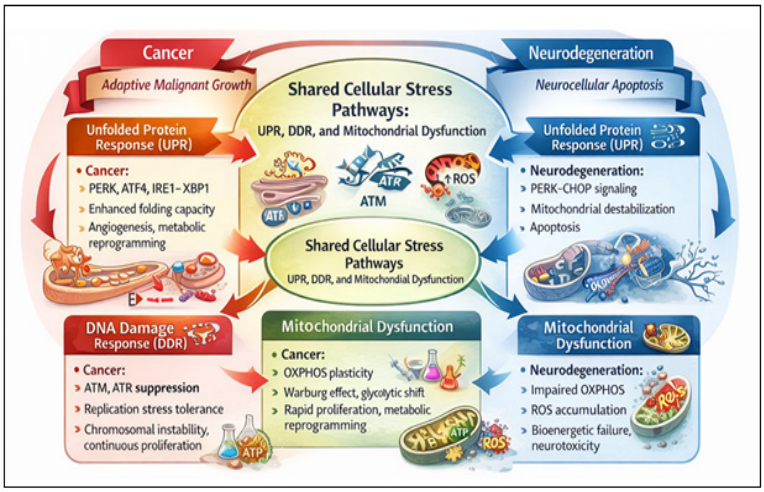

Figure 2. Schematic Overview of the Shared Cellular Stress-response Networks Linking Cancer and Neurodegenerative Disorders. The unfolded protein response (UPR), DNA damage response (DDR), and mitochondrial dysfunction constitute a common molecular backbone that is differentially exploited depending on cellular context. In cancer, these pathways are adaptively rewired to promote proteostasis tolerance, metabolic reprogramming, replication stress evasion, and sustained proliferation. In contrast, in neurons, persistent activation of the same stress circuits precipitates ER stress–mediated apoptosis, excessive DDR signaling, mitochondrial bioenergetic failure, and progressive neurodegeneration. This mechanistic overlap highlights how identical molecular pathways yield opposing outcomes tumor survival versus neuronal loss and underscores these stress-response nodes as rational targets for cross-disease therapeutic interventions.

ER stress as a central driver of neurodegenerative decline [16]. The DNA damage response exhibits a similarly paradoxical yet mechanistically overlapping pattern across cancer and neurodegeneration [21]. Cancer cells commonly attenuate checkpoint surveillance through functional suppression of ATM and ATR signaling, thereby permitting replication stress tolerance, chromosomal instability, and continued proliferative expansion [22]. Conversely, in neurodegenerative settings, persistent oxidative and mitochondrial insults provoke sustained DDR hyperactivation, resulting in cumulative repair exhaustion, synaptic dysfunction, and eventual neuronal apoptosis [23]. Thus, whereas tumor cells benefit from evasion of DDR-mediated constraints, neurons succumb to the deleterious consequences of chronic DDR engagement [21]. Mitochondrial dysfunction further exemplifies this shared yet divergent biology [24]. Perturbations in mitochondrial biogenesis, oxidative phosphorylation efficiency, and reactive oxygen species (ROS) homeostasis critically shape both tumor metabolism and neuronal viability [25]. Malignant cells frequently exploit mitochondrial plasticity and metabolic reprogramming often accompanied by Warburg effect–associated glycolytic shifts to sustain rapid proliferation even under hypoxic or nutrient-limited conditions [26]. In stark contrast, neurons remain heavily reliant on high-fidelity mitochondrial respiration; impairments in OXPHOS capacity, diminished biogenic renewal, and mitochondrial fragmentation directly compromise bioenergetic stability and precipitate neurodegeneration [27]. Collectively, these observations delineate a unified molecular architecture in which core stress-response systems UPR, DDR, and mitochondrial signaling constitute shared liabilities that are differentially exploited according to cellular context: adaptively leveraged to promote survival and expansion in cancer, yet maladaptively activated to drive vulnerability and cellular demise in neurodegenerative disease, as schematically illustrated in Figure 2.

Neuroinflammation and Cancer-Associated Inflammation

Despite emerging within distinct physiological milieus, tumor-associated inflammation and neuroinflammatory processes exhibit a strikingly conserved immunological architecture characterized by innate immune activation, cytokine imbalance, and sustained oxidative injury [28]. In the central nervous system, microglia function as the principal innate immune sentinels, responding to the accumulation of misfolded proteins, mitochondrial debris, and synaptic perturbations [29]. Persistent microglial activation fosters a chronic pro-inflammatory state marked by continuous secretion of cytokines including IL-6, IL-1β, and TNF-α, alongside sustained engagement of NF-κB signaling and the NLRP3 inflammasome, collectively amplifying neuronal toxicity and accelerating synaptic deterioration [30]. In parallel, the oncologic microenvironment harbors functional counterparts to microglia tumor-associated macrophages (TAMs) which adopt immunosuppressive, tumor-supportive phenotypes [31]. These cells secrete analogous cytokine repertoires and activate comparable inflammatory cascades to facilitate angiogenesis, immune evasion, and metastatic dissemination [28]. At the molecular scale, NF-κB signaling operates as a central regulatory hub across both pathologies: in malignancy, it sustains proliferative and survival programs, whereas in neurons, chronic NF-κB activation exacerbates oxidative burden, disrupts synaptic plasticity, and promotes apoptotic demise [31]. Similarly, activation of the NLRP3 inflammasome yields context-dependent yet mechanistically overlapping consequences potentiating tumor-promoting inflammation

Table 1. Therapeutic Barriers in Oncology and Neurodegeneration and the Corresponding Advantages of Liposomal Nanocarrier Systems

Disease Context	Major Therapeutic Barriers	Underlying Mechanisms	Clinical Consequences	Liposomal Nanotechnology Advantages	References
Cancer [Oncology]	Dose-limiting toxicity	Non-selective systemic distribution	Damage to healthy tissues, limited dosing	Targeted delivery, reduced off-target exposure	[36]
	Rapid drug clearance	Short circulation half-life	Subtherapeutic intratumoral levels	PEGylation prolongs systemic residence ["stealth" effect]	[36, 43]
	Tumor heterogeneity	Genetic/phenotypic variability	Variable response, resistance	Ligand-mediated targeting improves tumor specificity	[37]
	Drug resistance	Efflux pumps, metabolic rewiring, enhanced DNA repair	Treatment failure	Controlled release and higher intracellular accumulation	[38, 39]
	Poor tumor penetration	Dense stroma, abnormal vasculature	Limited drug diffusion	EPR-driven accumulation and stimuli-triggered release	[36, 45]
Neurodegeneration [CNS disorders]	Blood–brain barrier [BBB] exclusion	Tight endothelial junctions	<2% of drugs reach brain tissue	Surface-functionalized liposomes enable receptor-mediated BBB transport	[40, 41, 43]
	Low bioavailability	Instability and rapid metabolism	Insufficient therapeutic exposure	Encapsulation improves stability and protects payload	[35]
	Short half-life	Rapid systemic elimination	Frequent dosing required	Sustained/controlled release kinetics	[35, 43]
	Diffuse multifactorial pathology	Multiple pathways [oxidative stress, inflammation, proteotoxicity]	Poor efficacy of single-target drugs	Multi-drug co-encapsulation and combination therapy	[42]
	Neurotoxicity risk	Off-target effects in CNS	Safety limitations	Biocompatible lipid composition reduces systemic toxicity	[44]
Shared Challenges	Poor pharmacokinetics, limited tissue specificity, biological barriers	Tumor microenvironment & BBB	Low translational success	Liposomes enhance stability, targeting precision, and tissue penetration	[35, 36, 43, 44]

in cancer while precipitating pyroptotic or inflammatory cell death in neurodegenerative settings [32]. A shared biochemical driver underlying both environments is excessive production of reactive oxygen species and lipid peroxidation products, which destabilize membrane integrity and perpetuate self-reinforcing inflammatory circuits [25]. Within tumors, ROS-mediated lipid peroxidation contributes to mutagenesis and oncogenic transformation, whereas in the brain it compromises neuronal membranes and accelerates ferroptotic degeneration [33]. These observations underscore inflammation as a context-dependent yet universally amplifying pathological force [34]. By sustaining NF-κB–dependent transcriptional programs, intensifying cytokine cascades, and magnifying oxidative stress, inflammatory networks establish a feed-forward loop that drives tumor expansion on one end of the spectrum and progressive neuronal attrition on the other [31]. This convergent immunological landscape thus positions inflammation as a rational cross-disease therapeutic target and highlights the necessity for precision delivery platforms capable of selectively modulating shared inflammatory pathways.

Therapeutic Challenges in Oncology and Neurodegeneration: The Rationale for Liposomal Nanotechnology

Notwithstanding notable advances in molecularly targeted therapeutics, both oncology and neurodegenerative medicine remain encumbered by substantial translational bottlenecks that continue to compromise clinical efficacy and long-term therapeutic success [35]. In the oncologic setting, systemically administered cytotoxic and targeted agents are frequently constrained by dose-limiting toxicities, rapid systemic clearance, and widespread off-target distribution, collectively undermining the attainment of therapeutically meaningful intratumoral drug concentrations [36]. These pharmacokinetic shortcomings are further exacerbated by pronounced tumor heterogeneity manifesting both interpatient and intratumoral variability which fosters inconsistent drug responsiveness and facilitates the emergence of resistance phenotypes through mechanisms such as efflux transporter upregulation, metabolic reprogramming, and augmented DNA repair capacity [37-39]. Conversely, therapeutic development for neurodegenerative disorders must contend with a distinct constellation of anatomical and physiological barriers intrinsic to the central nervous system (CNS) [40]. Many candidate neuroprotective agents exhibit suboptimal bioavailability, poor metabolic stability, and abbreviated systemic half-lives; however, the most formidable impediment remains the blood–brain barrier, which effectively excludes the vast majority of small molecules and virtually all macromolecular therapeutics from entering the brain parenchyma [41].

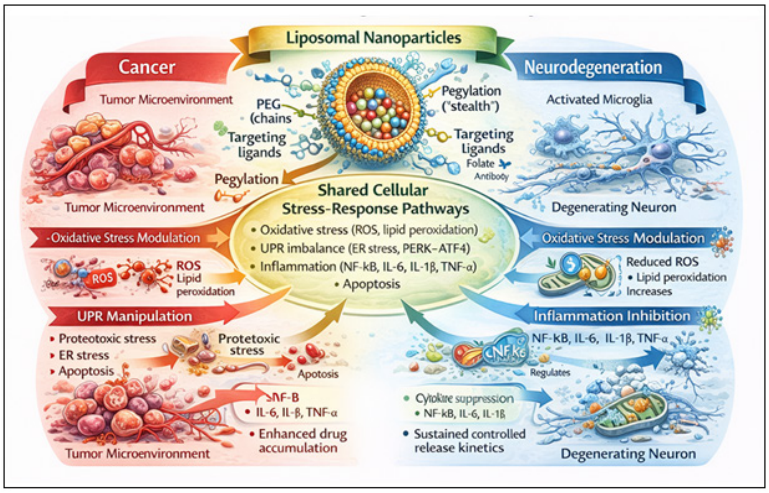

Figure 3. Schematic Illustration of Liposomal Nanocarriers as Active Modulators of Shared Stress-response Pathways in Cancer and Neurodegeneration. Engineered liposomes featuring PEGylation for prolonged circulation, ligand-mediated targeting, and stimuli-responsive release enable selective intracellular delivery of therapeutic cargos to pathological tissues. By encapsulating antioxidants, proteostasis regulators, anti-inflammatory agents, and mitochondria-targeted compounds, liposomes can differentially regulate oxidative stress, unfolded protein response (UPR) signaling, NF-κB–mediated inflammation, mitochondrial dysfunction, and apoptosis. These context-dependent effects promote tumor cell sensitization and programmed cell death in cancer while simultaneously enhancing neuroprotection and cellular homeostasis in degenerating neurons.

Consequently, numerous promising compounds including antioxidants, peptides, and anti-inflammatory agents fail to achieve therapeutically relevant concentrations within neural tissue [35]. Compounding these limitations, neurodegeneration is typically characterized by diffuse, multifactorial, and temporally evolving pathologies, rendering single-target interventions insufficient for sustained disease modification [42]. Collectively, these constraints underscore an urgent and unmet need for advanced drug-delivery architectures capable of optimizing pharmacokinetic performance, enhancing tissue selectivity, prolonging systemic circulation, and circumventing biological barriers such as the tumor microenvironment and the BBB [43], as summarized in Table 1. In this regard, nanocarrier-based strategies particularly liposomal systems have emerged as compelling translational solutions by enabling controlled drug release, targeted biodistribution, and mitigation of systemic toxicity, thereby directly addressing the shared therapeutic shortcomings observed across both disease domains [36]. Among available nanotechnological platforms, liposomal formulations represent one of the most versatile and clinically validated modalities for therapeutic delivery across diverse pathological contexts, including both malignancies and neurodegenerative disorders [44]. Structurally, liposomes consist of spherical phospholipid bilayer vesicles enclosing an aqueous core, thereby permitting the concurrent encapsulation of hydrophilic agents within the lumen and hydrophobic compounds within the lipid membrane [36]. Their intrinsic biocompatibility, architectural plasticity, and amenability to surface modification most notably through polyethylene glycol (PEG) conjugation confer extended circulation time, diminished immune recognition, and enhanced physicochemical stability, attributes that are particularly advantageous for complex systemic therapies [43]. To address the multifaceted challenges characteristic of oncology and neurodegeneration, diverse liposomal subtypes have been rationally engineered. PEGylated "stealth" liposomes attenuate opsonization and prolong systemic persistence, thereby stimuli-responsive formulations, designed to release their payloads in response to environmental triggers such as acidic pH, elevated reactive oxygen species (ROS), or disease-associated enzymatic activity, enable spatiotemporally controlled drug liberation within tumor microenvironments or inflamed neural niches [36, 45]. Ligand-functionalized liposomes, incorporating targeting moieties such as folate, peptides, or monoclonal antibodies, promote receptor-mediated uptake and increase cellular specificity, thereby improving delivery to tumor cells, activated microglia, or BBB-associated transport systems [43]. Furthermore, stealth-optimized systems minimize premature immune clearance, enhancing bioavailability and pharmacokinetic robustness. Taken together, these engineered liposomal platforms confer multiple therapeutic advantages, including improved stability, reduced systemic toxicity, heightened targeting precision, and enhanced penetration into otherwise inaccessible tissues such as solid tumors and the CNS [44]. Their capacity to modulate release kinetics and augment intracellular drug accumulation positions liposomes as uniquely suited to overcome the shared pharmacological and biological limitations that constrain conventional treatment strategies in both cancer and neurodegenerative diseases.

Nanoparticles as Modulators of Shared Molecular Pathways

Liposomal drug-delivery systems constitute a uniquely adaptable platform for therapeutically engaging the molecular circuitry shared between cancer and neurodegenerative disorders, enabling context-specific biological outcomes through precise intracellular targeting and controlled pharmacological release [36]. By virtue of

their capacity to encapsulate chemically diverse payloads and direct them toward defined cellular compartments, liposomes provide a means of selectively recalibrating stress-response networks that are otherwise dysregulated across both pathologies [44]. One of the most extensively exploited mechanisms involves attenuation of oxidative imbalance [25, 37]. This bidirectional functionality reflects the fundamentally distinct redox dependencies of proliferative malignancies versus post-mitotic neurons, underscoring how liposomal systems can differentially tune oxidative signaling according to cellular context [31]. Beyond redox modulation, liposomes exert critical influence over proteostatic control and unfolded protein response signaling [15]. In neurodegenerative settings, delivery of molecular chaperones or endoplasmic reticulum–protective agents can temper maladaptive PERK–ATF4–CHOP activation, thereby alleviating ER stress and limiting apoptotic neuronal loss [16]. Conversely, within tumor microenvironments, liposomal carriers may be employed to deliver agents that intensify proteotoxic pressure and exacerbate UPR stress, effectively overwhelming the adaptive capacity of malignant cells and precipitating programmed cell death [18]. Such pathway-selective manipulation highlights the strategic value of liposomal platforms in diseases where proteostasis imbalance represents a central pathogenic determinant [20]. Inflammatory signaling constitutes another shared vulnerability amenable to liposomal intervention [28]. Formulations incorporating anti-inflammatory therapeutics can suppress NF-κB–dependent transcriptional programs and reduce secretion of pro-inflammatory mediators such as IL-6, IL-1β, and TNF-α, thereby dampening chronic neuroinflammation and mitigating secondary neuronal injury [34]. In oncologic contexts, inhibition of NF-κB signaling not only curtails inflammation-driven proliferation but also sensitizes tumor cells to chemotherapeutic agents and apoptosis, enhancing overall treatment responsiveness [17]. Accordingly, modulation of inflammatory cascades via liposomal delivery confers clear cross-disease therapeutic relevance [15]. Targeted liposomal constructs further extend their impact to mitochondrial homeostasis, a central axis in both tumor metabolism and neuronal survival [24]. Mitochondria-directed formulations can stabilize bioenergetic output and reduce mitochondrial fragmentation in neurodegenerative conditions, whereas in cancer they may disrupt metabolic plasticity, amplify oxidative stress, or activate intrinsic apoptotic pathways to undermine tumor viability [25]. Finally, the capacity of liposomes to regulate apoptosis in a context-dependent manner represents a defining translational advantage [36]. By enhancing intracellular drug accumulation within tumors, liposomes promote pro-apoptotic signaling and malignant cell clearance, while simultaneously enabling delivery of neuroprotective agents that prevent excessive or unintended neuronal apoptosis [43, 44]. Collectively, these mechanistic insights position liposomal nanocarriers not merely as passive delivery vehicles but as active modulators of convergent stress-response networks, capable of directing cellular fate toward either neuroprotection or tumor suppression depending on therapeutic intent, as schematically illustrated in Figure 3.

Translational Integration of Liposomal Nanotechnology Across Oncology and Neurodegeneration

Liposomal nanotechnology has progressively evolved from a conceptual drug-delivery strategy into a clinically validated therapeutic platform, with substantial translational impact first realized in oncology and increasingly extended toward neurodegenerative medicine [36]. Despite the historical separation of these disease domains, a growing body of mechanistic and pharmacological evidence indicates that both cancer and neurodegenerative disorders are constrained by remarkably similar therapeutic bottlenecks namely poor pharmacokinetics, inadequate tissue selectivity, systemic toxicity, and the presence of formidable biological barriers such as the tumor microenvironment and the blood–brain barrier [35]. Within this context, liposomal nanocarriers have emerged not merely as passive encapsulation vehicles, but as biointeractive systems capable of reshaping drug biodistribution, modulating intracellular signaling networks, and recalibrating stress-response pathways in a context-dependent manner [44]. The clinical maturation of liposomal therapeutics has been most clearly demonstrated in oncology, where multiple formulations have already achieved regulatory approval and routine clinical adoption [36]. Agents such as liposomal doxorubicin (Doxil®/Caelyx®), non-PEGylated liposomal doxorubicin (Myocet®), and liposomal irinotecan (Onivyde®) collectively provide compelling proof-of-concept that nanocarrier-based delivery can significantly enhance the therapeutic index of conventional chemotherapeutics [42]. Encapsulation within phospholipid bilayers alters systemic pharmacokinetics, prolongs circulation time, reduces rapid clearance, and attenuates dose-limiting toxicities most notably cardiotoxicity while simultaneously increasing intratumoral drug accumulation through enhanced permeability and retention (EPR) effects. These attributes have translated into improved tolerability and sustained efficacy, thereby validating liposomes as clinically meaningful drug-delivery systems rather than purely experimental constructs [36, 37]. Building upon these successes, a new generation of experimental liposomal systems has sought to further refine therapeutic precision by integrating pathway-directed modulation with improved delivery performance [43]. Liposomal encapsulation of poorly soluble or unstable agents including curcumin, paclitaxel, and platinum-based compounds has demonstrated superior intracellular uptake, enhanced induction of apoptosis, and more effective regulation of oxidative and inflammatory signaling relative to free drugs [37]. Notably, co-encapsulation strategies have enabled synergistic pharmacodynamics, in which multiple agents concurrently amplify reactive oxygen species generation, exacerbate DNA damage, and overcome chemoresistance by targeting complementary oncogenic vulnerabilities [20]. Concurrently, surface functionalization with targeting

ligands such as folate, transferrin, peptides, or monoclonal antibodies has enabled receptor-mediated endocytosis and selective drug accumulation within tumor tissues, further enhancing specificity while reducing collateral toxicity. Collectively, these advances illustrate how liposomal platforms can influence not only pharmacokinetics but also core molecular processes governing tumor survival, including proteostasis, redox balance, and microenvironmental inflammation [15, 43]. In parallel, liposomal nanocarriers are increasingly being recognized as promising therapeutic tools in neurodegenerative diseases, where treatment development is constrained by challenges distinct from yet conceptually analogous to those observed in oncology [44]. The BBB presents a formidable exclusionary interface, preventing the vast majority of free-form therapeutics from achieving effective concentrations within the central nervous system [41]. Liposomal systems, however, offer a versatile means of circumventing this barrier through rational surface engineering [35]. PEGylation prolongs systemic residence, while ligand-modified liposomes decorated with transferrin, lactoferrin, apolipoproteins, or cell-penetrating peptides facilitate receptor-mediated transcytosis into neural tissue. This capacity to enhance CNS penetration has enabled delivery of otherwise labile neuroprotective agents, including dopamine, antioxidants, and neuropeptides, thereby improving bioavailability and therapeutic persistence [44, 45]. Mechanistically, liposomal formulations in neurodegeneration are increasingly designed to modulate the same stress-response pathways implicated in cancer, albeit with opposite therapeutic intent [16]. Antioxidant-loaded liposomes attenuate ROS accumulation, lipid peroxidation, and mitochondrial dysfunction key drivers of neuronal degeneration [25]. Similarly, liposomal delivery of aggregation-inhibiting peptides mitigates misfolding of tau and α-synuclein, restoring proteostatic balance in Alzheimer's and Parkinson's disease models [30]. Anti-inflammatory formulations targeting microglial activation or NF-κB signaling suppress chronic cytokine release and interrupt self-propagating inflammatory cascades that accelerate neuronal loss [34]. Importantly, these strategies aim not to intensify stress, as in cancer therapy, but rather to buffer vulnerable neurons against proteotoxic, oxidative, and inflammatory insults [15]. This dichotomy in therapeutic philosophy stress amplification in tumors versus stress mitigation in neurons underscores one of the most compelling attributes of liposomal nanocarriers: their context-dependent adaptability [16]. Because both cancer and neurodegeneration converge upon shared molecular vulnerabilities, including oxidative imbalance, mitochondrial dysfunction, UPR dysregulation, and chronic inflammation, liposomes can be rationally engineered to engage these same pathways in divergent ways depending on disease context [15]. In malignancy, liposomes may enhance oxidative pressure, intensify proteotoxic stress, and promote apoptosis; in neurodegeneration, they may stabilize mitochondrial function, restore proteostasis, and suppress inflammatory signaling. Thus, identical nanotechnological architectures can be repurposed to produce fundamentally different biological outcomes through selective modulation of convergent molecular nodes [25, 44]. The translational implications of this shared-pathway paradigm are substantial [35]. Liposomal systems originally optimized for oncology may be re-engineered with BBB-penetrating ligands to deliver neuroprotective therapeutics to the brain, while CNS-targeted liposomes may be adapted for the treatment of brain tumors or metastatic lesions. Such bidirectional adaptability reframes liposomes not as disease-specific tools but as modular therapeutic platforms capable of spanning traditional disciplinary boundaries [36, 43]. Looking forward, advances in precision nanomedicine are poised to further expand the clinical potential of liposomal therapeutics [45]. Integration of multi-omics profiling, artificial intelligence–guided design, and patient-specific biomarker mapping will enable customization of liposomal size, charge, ligand density, and release kinetics to match individualized disease signatures. This level of engineering precision promises to enhance therapeutic selectivity while minimizing systemic toxicity, allowing liposomes to selectively engage shared stress-response networks with unprecedented accuracy [42, 43]. Taken together, liposomal nanocarriers represent a powerful translational bridge between oncology and neurodegeneration, offering a tunable, pathway-directed approach to therapy that transcends conventional pharmacological limitations. By simultaneously addressing pharmacokinetic constraints and molecular pathogenesis, liposomal systems provide a versatile framework for next-generation therapeutics capable of either eliminating malignant cells or preserving vulnerable neurons, thereby unifying two historically distinct fields within a common nanomedical strategy.

Future Outlook and Research Directions

Advancing liposomal therapeutics at the interface of cancer and neurodegeneration will require coordinated progress in experimental modeling, molecular profiling, and translational technology development [46, 47]. One major priority is the establishment of shared animal models capable of capturing overlapping pathogenic processes such as ER stress, mitochondrial dysfunction, and chronic inflammation while also permitting evaluation of liposomal biodistribution in both the central nervous system and tumor-bearing tissues [48, 49]. Such dual-purpose models will be essential for assessing cross-disease efficacy and optimizing route of administration, targeting strategies, and long-term safety [46, 47]. Integration of multi-omics platforms, including genomics, proteomics, metabolomics, and lipidomics, offers another critical direction [50, 51]. These tools can identify molecular signatures that predict response to specific liposomal formulations, uncover pathway convergence points amenable to dual targeting, and support rational design of next-generation liposomes tailored to patient-specific molecular landscapes [50, 51]. In parallel, the development of liposome-based biomarkers, such as imaging-enabled nanocarriers or reporter-loaded liposomes, could enable real-time monitoring of therapeutic distribution, pathway

engagement, and treatment response in both oncology and neurodegenerative settings [49, 52]. Emerging computational approaches, particularly AI-driven liposome design, hold significant promise for accelerating optimization of particle size, surface charge, ligand density, and release kinetics [47, 51]. Machine learning models can also predict BBB penetration, tumor uptake, and off-target effects, thereby reducing experimental burden and improving formulation accuracy [47, 53]. Despite these opportunities, important clinical translation challenges remain. Scaling liposomal production while maintaining batch consistency, meeting GMP manufacturing standards, navigating divergent regulatory requirements for cancer versus CNS therapies, and demonstrating long-term biocompatibility are all essential steps toward broader adoption [47]. Other effective approaches include the treatment of diseases, particularly cancer, through in-depth exploration at the cellular and molecular levels, which enables a better understanding of pathogenic mechanisms and facilitates the development of targeted therapeutic strategies [54-56]. Addressing these hurdles will be critical for realizing the full translational potential of liposomal systems across disease boundaries.

In conclusion, the convergence of molecular pathways between cancer and neurodegenerative diseases reveals a unique therapeutic opportunity in which liposomal nanocarriers can operate as a shared platform for pathway-specific intervention. By targeting oxidative stress, proteostasis imbalance, mitochondrial dysfunction, and dysregulated inflammatory signaling, liposomes are capable of modulating central mechanisms that contribute to both uncontrolled tumor growth and progressive neuronal loss. As drug-delivery vehicles, liposomes effectively bridge the long-standing therapeutic gap between oncology and neurodegeneration by offering tunable pharmacokinetics, improved bioavailability, and context-dependent modulation of stress pathways promoting apoptosis in cancer cells while preserving neuronal survival. Their adaptability further supports translational crossover, enabling repurposing of oncology-derived formulations for CNS disorders and vice versa. Overall, liposomal nanotechnology represents a powerful and flexible therapeutic platform with the potential to reshape treatment strategies across traditionally distinct disease domains. With ongoing innovation and deeper mechanistic insights, liposome-based interventions are poised to transform the therapeutic landscape of both cancer and neurodegenerative disorders in the years ahead.

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Conflict of interest

The authors declare no conflict of interest.

Ethical considerations

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