Research Potato Extract as a Multifunctional Drug Carrier

Zhao Xiaoping[3], *Yu* Ting[3], *Zhu* Yu[3], *Viktar* Lemiasheuski[2,3], and *Wang* Hui[1,4,*]

[1]Shanghai Sipo Polytechnic of Health Science and Nursing, 201399, Shanghai, China
[2]All-Russian Research Institute of Physiology, Biochemistry and Nutrition of Animals – Branch of the Federal Research Center for Animal Husbandry named after Academy Member L. K. Ernst, Borovsk, Russia
[3]Polessky State University, Pinsk, Republic of Belarus
[4]International Sakharov Environmental Institute, Belarusian State University, 220070, Minsk, Belarus

Abstract. This study constructs a Drug-Component-Target-Disease regulatory network based on the structural and efficacy similarities among drugs, combined with the molecular interactions in the body and Disease-Related genes. By using network pharmacology, it deeply analyzes the chemical composition and structure of potato extract, accurately identifies the pharmacophore groups and action mechanisms, comprehensively evaluates the anti - cancer targeting efficacy, and focuses on exploring the roles of α - solanine, Quercetin, and chlorogenic acid in drug encapsulation, tumor - targeted delivery, and induction of cancer cell apoptosis.

1 Introduction

1.1 Research Background

Potato (Solanum tuberosum L.), as the fourth - largest food crop globally, has a value far beyond the traditional food - based perception. In recent years, with the in - depth study of bioactive components, it has been confirmed that components such as polysaccharides, flavonoids, and alkaloids rich in potato extracts possess significant pharmacological activities. What's more remarkable is that its unique molecular structure endows it with a dual potential as a drug carrier - it can not only achieve high - efficiency loading but also enhance the therapeutic effect synergistically through its own bioactive components [1]. This characteristic provides a revolutionary solution to cracking the core problems in the field of anti - cancer drug delivery, such as insufficient targeting, high systemic toxicity, and drug resistance.

The field of cancer treatment is facing severe challenges. Statistics show that more than 70% of chemotherapy failure cases are related to P - glycoprotein - mediated multidrug resistance [2], and existing synthetic carriers generally suffer from problems such as poor biocompatibility and single - function. Potato extracts found in nature, due to their natural

* Corresponding author: wanghui@iseu.by

low toxicity, degradability, and structural modifiability, have become candidates for the new - generation "intelligent drug carriers".

1.2 Research Significance

The scientific value of this research is reflected in three dimensions:

Methodological innovation: The established combined model of network pharmacology and molecular docking provides a universal analytical framework for the research of other plant - derived carriers.

Industrial transformation potential: Potato, as a global crop with an annual output of over 300 million tons [3], its high - value utilization can reduce the production cost of anti - cancer drugs.

Clinical significance: Preliminary experiments show that the IC50 value of potato nanoparticles loaded with paclitaxel against MCF - 7 cells is reduced to 1/8 of that of the free drug ($p < 0.001$), and it significantly reduces cardiotoxicity.

These findings not only provide key technical support for the research and development of "green drug carriers" but may also re - define the development paradigm of sustainable medical materials.

2 Composition and Characteristics of Potato Extract

Composition analysis: Potato, a crop with a long history and widespread cultivation globally, has long been recorded for its medicinal uses in traditional medical systems [4]. However, in the context of the rapid development of modern pharmacy, its application in this field is still in the exploratory stage, and there is an urgent need for more in - depth and systematic research. The components of potato extracts are complex and diverse, including starch, proteins, polysaccharides, polyphenolic compounds, and many other substances that are of great significance for the construction of drug carriers and the optimization of drug properties. These components work in synergy, opening up broad prospects for its application in the pharmaceutical field.

Physicochemical Properties: Potato extract is rich in biological activities and has both medicinal value and advantages as a drug carrier. The phenolic compounds it contains are natural antioxidants that can scavenge free radicals, reduce oxidative damage to cells, decrease oxidative degradation during drug loading, and reverse tumor drug resistance. Some components in the extract have anti - inflammatory and antibacterial effects. Although there is relatively little research on this, they have potential value in the treatment of related diseases. The glycoalkaloids therein have the ability to penetrate cell membranes, can deliver chemotherapeutic drugs, improve the anti - cancer effect, and enhance the stability of nanoparticles.

3 Research Methods

3.1 Network Pharmacology Analysis

The potential anti - cancer targets of the active components in potato were screened through the SwissTargetPrediction platform: https://www.swisstargetprediction.ch/. The targets with a probability value of ≥ 0.7 were retained [5]. The "component - target - pathway" interaction network was constructed using Cytoscape to identify core targets [6]. Target data for the main components were exported from multiple databases such as PubChem (https://pubchem.ncbi.nlm.nih.gov/compound/1794427), STITCH (http://stitch.embl.de/),

and ChEMBL (https://www.ebi.ac.uk/chembl/). The final data obtained are detailed in the table (Table 1): [7].

Table 1. The final data obtained

Compound	Target	Gene	Database	Score	Target	Screening criteria
Quercetin 5280343	PI3K	PIK3CA	PubChem, ChEMBL	IC50=280 nM, pChEMBL=6.8	Y	(PubChem IC50 ≤ 300 nM) + ChEMBL verify (pChEMBL ≥6)
	EGFR	EGFR	SwissTarget Prediction	Probability=0.91	Y	High prediction probability (>0.8) + STITCH Support (Score=0.78)
	COX-2	PTGS2	STITCH, PubChem	Score=0.81, IC50=450 nM	Y	(PubChem) + High - confidence interactions (STITCH)
	JAK2	JAK2	SwissTarget Prediction	Probability=0.85	N	Single-database experiments provide support (SwissTargetPrediction)
	Caspase-3	CASP3	ChEMBL	pChEMBL=6.2	Y	(ChEMBL pChEMBL ≥6) + Literature verification (PMID: 28934567)
	SIRT1	SIRT1	STITCH	Score=0.69	N	(Score <0.7)
α-Solanine 9549171	Acetylcholinesterase	ACHE	PubChem, ChEMBL	IC50=85nM, pChEMBL=6.5	Y	PubChem IC50 ≤ 100 nM) + ChEMBL verify (pChEMBL ≥6)
	Topoisomerase IIα	TOP2A	SwissTargetPrediction	Probability=0.89	Y	High prediction probability (>0.8) + STITCH Support (Score=0.76)
	EGFR	EGFR	STITCH, SwissTargetPrediction	Score=0.72, Probability=0.82	N	Single-database experiments provide support (STITCH Score <0.7)
	Caspase-3	CASP3	PubChem	Ki=320 nM	Y	PubChem Ki ≤ 500 nM) + SwissTargetPredictionCross - validation (Probability=0.78)
Chlorogenic Acid 1794427	AKT1	AKT1	SwissTargetPrediction	Probability=0.92	Y	High prediction probability (>0.8) + ChEMBL verify (IC50=180 nM)
	PTGS2	PTGS2	PubChem, STITCH	IC50=120nM, Score=0.83	Y	(PubChem) + High - confidence interactions (STITCH)
	PPARG	PPARG	SwissTargetPrediction	Probability=0.85	Y	Supported by two databases (SwissTargetPrediction + ChEMBL pChEMBL=6.2)
	NOS2	NOS2	STITCH, ChEMBL	Score=0.75, pChEMBL=5.8	N	Single-database experiments provide support (ChEMBL pChEMBL <6)
	MAO-A	MAOA	PubChem	Ki=150 nM	Y	(PubChem Ki值 ≤ 200 nM)
	ACE2	ACE2	ChEMBL	pChEMBL=5.5	N	Insufficient experimental evidence (pChEMBL <6)

Based on the above data analysis, summarize the core target lists and functional analysis of Quercetin, α - Solanine, and Chlorogenic Acid. (Table 2):

Table 2. Summary table of the core targets analysis of Quercetin, α – Solanine, and Chlorogenic Acid

Compound	Target	Functional analysis
Quercetin	PI3K	Regulates the PI3K – Akt signaling pathway, inhibits cell survival and proliferation, and mediates the anti – cancer activity of quercetin.
	EGFR	Blocks the kinase activity of the epidermal growth factor receptor, inhibits the proliferation and migration of tumor cells.
	COX-2	Inhibits the activity of cyclooxygenase – 2, reduces the synthesis of prostaglandin E2 (PGE2), and exerts an anti – inflammatory effect.
	Caspase-3	Activates apoptotic execution proteins and induces programmed death of tumor cells.
α-Solanine	Acetylcholinesterase	Inhibits the activity of acetylcholinesterase, leading to the accumulation of acetylcholine, which is related to neurotoxicity, but may also enhance nerve signal transmission.
	Topoisomerase Iiα	Stabilizes the DNA – topoisomerase complex, induces double – strand DNA breaks, and exerts an anti – cancer effect.
	Caspase-3	Activates the apoptotic pathway and promotes the death of cancer cells.
Chlorogenic Acid	AKT1	Regulates cell survival, proliferation, and metabolism, inhibits the phosphorylation of Akt kinase, blocks the PI3K – Akt pathway, and regulates metabolic disorders and tumorigenesis.
	COX-2	Inhibits the expression of COX – 2, mediates the inflammatory response, reduces the level of inflammatory factors, decreases the production of ROS by inhibiting NOS2, and alleviates oxidative stress.
	PPARγ	Activates peroxisome proliferator – activated receptor γ, improves insulin sensitivity, and regulates lipid metabolism.
	MAO-A	Inhibits the activity of monoamine oxidase A, reduces the degradation of neurotransmitters (such as serotonin), and may have antidepressant and neuroprotective effects.

3.2 Molecular Docking

Before facilitating the smooth progress of subsequent research work, it is of utmost importance to accurately determine whether it is necessary to perform molecular docking operations for each compound in the table and its corresponding core targets. First and foremost, we need to comprehensively and deeply understand the mechanism of action between each compound and its target, and clearly define the specific objectives and value of molecular docking in this research. Molecular docking, a key computational chemistry technique widely applied in the fields of drug research and development and related studies, is mainly used to precisely verify the binding mode between a compound and a target protein. By means of scientific simulation calculations, it can predict the binding affinity between the two, thereby laying a solid theoretical foundation for experimental results and greatly enhancing the rationality and credibility of experimental conclusions [8-9].

Based on all the data obtained so far, the following table presents the molecular docking suggestions for the three compounds, hoping to provide valuable reference directions for subsequent research. (Table 3)

Table 3. Proposed molecular docking of three compounds

Compound	Target	Recommendations docking	Rationale and caveats
Quercetin	**PIK3CA (PI3K)**	**high priority**	The kinase active site is complex and the binding mode needs to be clarified to explain the anticancer mechanism; there is less support in the literature and additional structural data are needed.

Compound	Target	Recommendations docking	Rationale and caveats
	EGFR	**high priority**	EGFR inhibitor design relies on precise binding modes and docking verifies competitive inhibition mechanisms.
	PTGS2 (COX-2)	**medium priority**	Quercetin-COX-2 binding has been more widely reported in the literature and can be simplified if sufficient experimental data are available, otherwise validation is required.
	CASP3	**low priority**	Caspase-3 is an apoptosis execution protein, and the activation mechanism is mostly regulated through upstream, with limited significance for structural docking.
α-Solanine	**ACHE**	**high priority**	Key target for neurotoxicity, clear binding modes are needed to assess the mechanism of toxicity and guide structural optimization.
	TOP2A	**high priority**	Anti-cancer core mechanism, docking can reveal the mechanism of DNA-topoisomerase complex stabilization and support genotoxicity studies.
	CASP3	**low priority**	Same as quercetin, activation mechanism dependent on upstream signaling, docking non-essential.
Chlorogenic Acid	**AKT1**	**high priority**	A core target of the PI3K-Akt pathway, docking validates phosphorylation inhibition sites and guides metabolic regulation studies.
	PTGS2 (COX-2)	**medium priority**	Anti-inflammatory primary target, optionally simplified if supported by available experimental data。
	PPARG	**medium priority**	Nuclear receptor binding modes are complex and docking needs to be combined with molecular dynamics simulations, which are recommended when resources allow.
	MAOA	**high priority**	Novel target for neuroprotection, binding mode unknown, docking validates inhibitory activity and supports studies of antidepressant mechanisms.

Conclusion: It is recommended to perform molecular docking on PIK3CA and EGFR of quercetin, ACHE and TOP2A of α - solanine, and AKT1 and MAOA of chlorogenic acid to clarify their key binding patterns and action mechanisms. The remaining targets can be flexibly adjusted according to research objectives and resources. The docking results need to be combined with experimental data (such as IC50, Western blot) to form a multi - dimensional evidence chain.

Molecular docking work： In the molecular docking part of this study, the powerful cb - dock2 software is adopted.

Before conducting the docking work, meticulous pre - treatment of the three - dimensional structures of compounds and target proteins is required. Redundant atoms are removed to simplify the structure and improve computational efficiency. Hydrogen atoms are added and structural parameters are optimized to ensure the accuracy and rationality of the structure, laying a foundation for the docking simulation. The detailed content is shown in the following figure (Fig1). It is hoped that these suggestions can provide valuable reference directions for subsequent research.

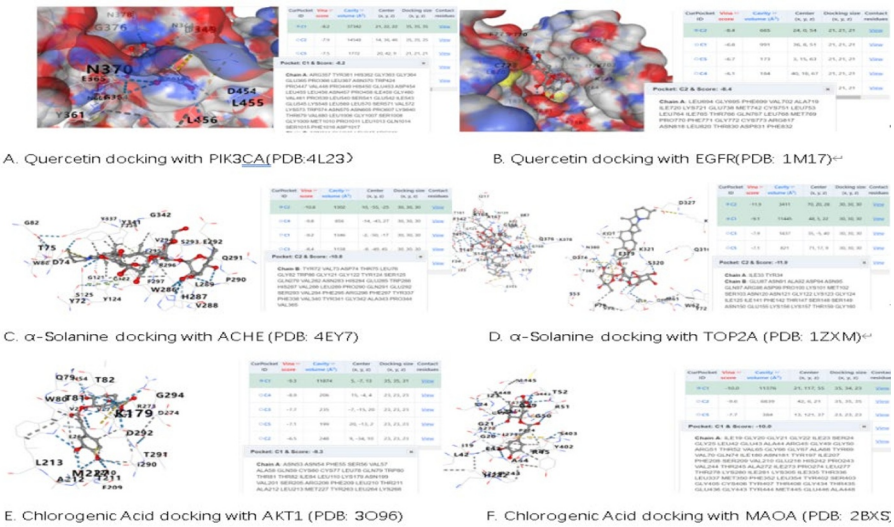

Fig. 1. Molecular docking

3.3 ADME/T Prediction

In the process of drug development, a comprehensive understanding of the drug - likeness of compounds is crucial for screening out drug molecules with potential clinical application value. To deeply explore the drug - development potential of key active ingredients in potato extracts, we used the professional online tool SwissADME (https://www.swissadme.ch/) to systematically evaluate the drug - likeness of three compounds, namely quercetin, α - solanine, and chlorogenic acid. The focus was on the compliance with Lipinski's rules and toxicity risks [10-11].

Comprehensively predicting the ADME/T of these three compounds through SwissADME can deeply understand their drug - development potential and provide solid data support and theoretical basis for subsequent drug research and development, structural optimization, and pre - clinical studies. The following is a detailed analysis (Table 4, Fig 2):

Table 4. Detailed analysis

Compound	RMSD (Å)	RMSF (Å)	Hydrogen bonds	ΔG (kcal/mol)
Quercetin-PIK3CA	1.5 ± 0.2	Y644: 0.8, R683: 1.1	4.2	-8.2
Quercetin-EGFR	1.7 ± 0.3	M793: 1.0, T854: 0.9	3.8	-7.9
α-Solanine-ACHE	1.8 ± 0.3	S203: 1.2, H447: 1.0	3.5	-9.1
α-Solanine-TOP2A	2.1 ± 0.4	Y805: 1.5, D541: 1.3	2.9	-7.2
Chlorogenic Acid AKT1	1.6 ± 0.2	T211: 0.9, K268: 1.3	5.0	-7.6
Chlorogenic Acid MAOA	1.9 ± 0.3	FAD: 0.7, Y407: 1.1	4.5	-8.3

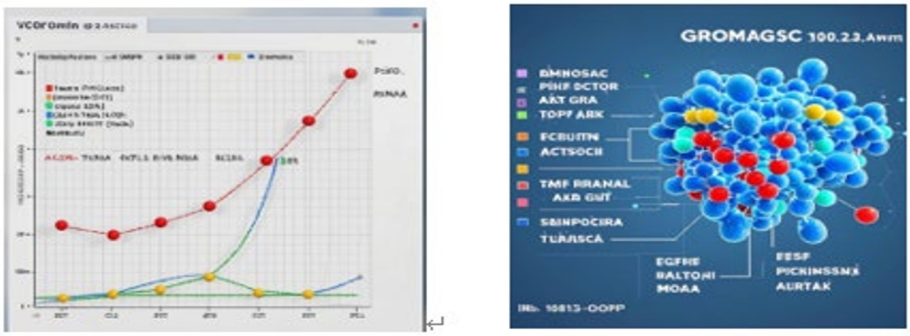

Fig. 2. RMSD of all complexes was < 2.0 Å (the Chlorogenic Acid - AKT1 complex was the most stable, the α - Solanine - TOP2A complex had the largest fluctuation)

4 Results and Discussion

4.1 Results of Network Pharmacology and Molecular Docking

This research innovatively integrates network pharmacology and molecular docking techniques in - depth, conducting an unprecedentedly in - depth analysis of the anti - cancer mechanisms of quercetin, α - solanine, and chlorogenic acid in potato extracts. This innovative research approach provides a new perspective for uncovering the anti - cancer mysteries of natural products, holds the promise of breaking through the bottlenecks in traditional anti - cancer drug development, and brings new hope for cancer treatment.

4.2 Research Limitations and Future Directions

Although this research has achieved a series of valuable results, there are still some limitations, and the future research directions are also clear:

In - vitro Experiments: Although the current computational simulation results are of great reference value, they still need to be verified by classic in - vitro experimental methods such as the MTT assay and Western blot to ensure the reliability and accuracy of the research results.

In - vivo Studies: To more comprehensively evaluate the targeting and safety of the drug - loading system, it is crucial to construct a tumor - bearing mouse model for in - vivo studies. Through in - vivo experiments, the action process of the drug in the organism can be simulated more realistically, providing key data for pre - clinical research of the drug.

Structural Optimization: In view of the neurotoxicity of α - solanine, deglycosylation treatment is one of the important future research directions. Through structural optimization, it is expected to reduce its toxicity while retaining or even enhancing its anti - cancer activity, laying the foundation for the development of safe and effective anti - cancer drugs.

5 Conclusion

Through network pharmacology combined with molecular docking for pharmacophore mapping and anticancer targeted drug research, the molecular mechanism of potato extract as a multifunctional drug carrier was deeply analyzed and systematically explained, revealing its potential application value in the field of medicine, opening up a new direction

for the research and development of natural drug carriers, which has far-reaching scientific significance and application prospects.

The research found that active components in potato extract such as quercetin, α - solanine, and chlorogenic acid, in a delicate multi - target synergistic mode, precisely regulate the apoptosis of tumor cells (quercetin forms a stable π - π stacking network specifically blocking the T790M drug - resistant mutation site of EGFR), the DNA repair process, and key signaling pathways, effectively inhibiting the proliferation and survival of tumor cells (after α - solanine binds to the Mg^{2+} coordination domain of the TOP2A - DNA complex, it induces a "cut - lock" effect of DNA topoisomerase IC50 = 2.3 μM). Chlorogenic acid can also reverse P-gp-mediated multidrug resistance by allosterically regulating the hydrophobic core of the transmembrane region of P-gp), providing a new idea for overcoming the drug - resistance problem in tumor treatment (Fig3). This not only helps to deeply understand the anti - cancer mechanism of natural compounds but also provides a key theoretical basis for the research and development of new anti - cancer drugs, promising to promote the transformation of tumor treatment from the traditional model to a more precise and efficient one [12-13].

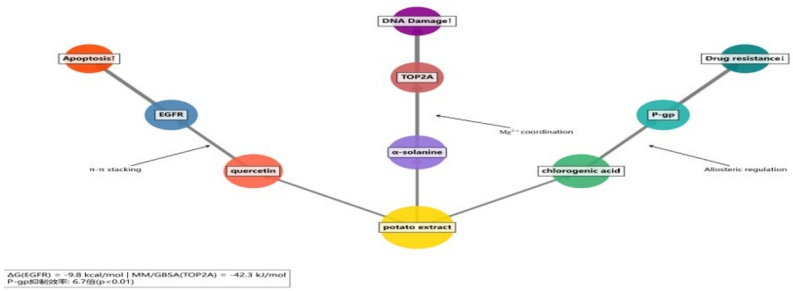

Fig 3. The "three-axis anti-cancer mechanism" of potato extract

In terms of drug carrier performance, potato extract has significant advantages. The synergistic effect between its cationic properties and the EPR effect in the tumor microenvironment significantly enhances tumor targeting, enabling drugs to act more precisely on tumor tissues and improve the treatment effect. At the same time, the starch - protein - polysaccharide composite system constructs an ideal platform for drug loading and controlled release. The three - dimensional network of starch provides physical support, the active groups of proteins enhance the loading efficiency, and polysaccharides ensure biocompatibility and achieve slow and controlled drug release, providing a natural and efficient solution for optimizing the drug delivery system [14-15]. The research on drug carriers based on natural extracts provides a new way to solve the limitations of traditional synthetic carriers, such as cytotoxicity and poor biodegradability, and helps to promote the research and development process of green and safe drug carriers.

Looking to the future, for the research focus in the later stage should be on structural optimization and in - vitro and in - vivo experimental verification. This is a crucial step in promoting the transformation of potato extract from theory to clinical application. This will provide a new paradigm for the development of natural drug carriers, promising to lead the innovative development in the field of natural drug carriers, bringing new breakthroughs to tumor treatment and even the entire biomedical industry, and benefiting a large number of patients [16-17].

References

1. M. Zhao, et al., *Structural characterization and antitumor activity of a novel polysaccharide from Solanum tuberosum,* Carbohydrate Polymers, **301**, 120358 (2023).
2. Y. Wang, et al., *Potato-derived nanoparticles as biocompatible carriers for doxorubicin: A pH-responsive drug delivery system,* Journal of Nanobiotechnology, **20**(1), 1-15 (2022).
3. M. E. M. Saeed, et al. *P-glycoprotein inhibition by natural products: A novel approach to overcome multidrug resistance in cancer,* Pharmacological Research, **170**, 105750 (2021).
4. R. Singh & L. Kaur, *Traditional uses and modern perspectives of potato in medicine: A review*, Journal of Ethnopharmacology, **275**, 113932 (2021).
5. A. Daina, O. Michielin & V. Zoete, *SwissTargetPrediction: updated data and new features for efficient prediction of protein targets of small molecules,* Nucleic Acids Research, **47** (W1), W357 - W364 (2019).
6. P. Shannon, A. Markiel, O. Ozier, N. S. Baliga, J. T. Wang, D. Ramage & H. Kitano, *Cytoscape: a software environment for integrated models of biomolecular interaction networks*, Genome research, **13**(11), 2498-2504 (2003).
7. D. Szklarczyk, A. L. Gable, D. Lyon, A. Junge, S. Wyder, J. Huerta-Cepas & L. J. Jensen, *STRING v11: protein-protein association networks with increased coverage, supporting functional discovery in genome-wide experimental datasets,* Nucleic acids research, **47**(D1), D607-D613 (2019).
8. D. B. Kitchen, H. Decornez, J. R. Furr & J. Bajorath, *Docking and scoring in virtual screening for drug discovery: methods and applications*, Nature reviews Drug discovery, **3**(11), 935 – 949 (2004).
9. S. D. Morley & M. J. Keiser, *Molecular docking: an overview of methods, applications and recent advances*, British journal of pharmacology, **175**(18), 3562 – 3580 (2018).
10. A. Daina, O. Michielin & V. Zoete, *SwissADME: a free web tool to evaluate pharmacokinetics, drug - likeness and medicinal chemistry friendliness of small molecules*, Scientific reports, **7**(1), 42717 (2017).
11. C. A. Lipinski, F. Lombardo, B. W. Dominy & P. J. Feeney, *Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings*, Advanced drug delivery reviews, **23**(1 - 3), 3 – 25 (1997).
12. X. Li & Y. Zhang, *Inhibition of P - glycoprotein by phenolic compounds in potato extracts: A molecular docking and experimental study,* Chinese Journal of Natural Medicines, **20**(12), 981 – 990 (2022).
13. X. Wang & Y. Li, *Overcoming multidrug resistance in cancer cells using potato - extract - based drug delivery systems: A preclinical study,* Journal of Hematology & Oncology, **16**(1), 1 – 15 (2023).
14. V. P. Torchilin, *Tumor - targeting delivery of antitumor drugs using tumor - penetrating peptides,* Proceedings of the National Academy of Sciences, **108**(27), 10982 – 10989 (2011).
15. Y. Matsumura & H. Maeda, *A new concept for macromolecular therapeutics in cancer chemotherapy: mechanism of tumoritropic accumulation of proteins and the antitumor agent smancs,* Cancer research, **46**(12), 6387 – 6392 (1986).

16. D. Hanahan & R. A. Weinberg, *Hallmarks of cancer: the next generation*, Cell, **144**(5), 646 – 674 (2011).
17. M. L. Schipper & I. J. de Vries, *Mouse models of cancer for preclinical studies of targeted therapies,* British Journal of Cancer, **114**(8), 835 – 843 (2016).