MedCrave
Step into the World of Research

Nursing & Care Open Access Journal

Research Article

Open Access

CrossMark

Anticancer drug development, challenge and dilemma

Abstract

Anticancer drug discovery and development is more difficult and requires high-quality than ever before. Biomedical, pharmaceutical, technology and economic factors must be overall reconsidered and reorganized. Despite great progress, many past obstacles and dilemma still remain. To solve these kinds of biomedical issues of therapeutic challenge and dilemma, this article provides multi-disciplinary perspectives of anticancer drug discovery and developments. Future trends are also discussed and highlighted.

Keywords: drug development, antineoplastic drug, neoplasm metastasis, modern technology, pharmaceutical innovation, drug combination; cancer stem cells, individualized cancer therapy

Volume 7 Issue 3 - 2020

Da-Yong Lu, Ting-Ren Lu
School of Life Sciences, Shanghai University, China

Correspondence: Da-Yong Lu, School of Life Sciences, Shanghai University, China, Email ludayong@shu.edu.cn

Received: September 18, 2020 | **Published:** October 20, 2020

Background

History

Cancer is different types of malignant disease that costs life of nine million annually worldwide. The great part of current therapeutic difficulty and challenge is lack of highly-effective and wide-spectra anticancer drugs.[1–4] As a result, drug discovery, development and production need to be reconsidered and shedding new light of both experimental and clinical.[5–10] Over the past two decades, the course of anticancer drug discoveries and developments changed a lot worldwide.[10–12] For this reason, new insights into updating anticancer developmental pipelines are updating for drug targets and mechanisms.[10–12] The patho-therapeutic relationship study is strengthened for creating more effective drug developmental pipeline.

Anticancer drug development, an adventurous task

Pathology

Anticancer drug development has a long history and high level of evaluative systems.[13] Single anticancer drug licensing expenditure could be about two billion USD in USA.[10–12] Huge number of new chemicals, biological materials and techniques are still waiting for being evaluated and promoted.[6] No country worldwide can persistently afford this size of huge pharmacologic/clinical evaluation and exploration. More importantly, many key biological or pathological pathways and network leading therapeutic failures in the clinic, such as neoplasm metastasis (unpredictable nature), enigma of cancer stem cells (cancer cell revival), cancer cell plasticity (EMT and MET) and drug resistance (long-term drug utility) are dilemma and still unclear to us from pharmacologic and therapeutic consideration.[14–24] These kinds of drug development slowdown and obstacles need new ideological inputs, modern medicine updating and pharmaceutical advances. Following topics provide our insights into these drug development difficulty, challenge, dilemma and possibly counteractive measures.

Economy concern

Owing to highly economic costs and drug development revenue shrinkage from leading drug developers, expanding global participation and cooperation for anticancer drug developers is quite necessary and useful for broader range of experts and specialists (medicinal chemists, pharmacologists, pathologist and clinical doctors), pharmaceutical markets (diagnostic instruments, different variety of medical options and supporting medical drugs) and huge financial invest powerhouse/social funds.[25] In order to smoothly implement these vast issues, global regulatory actions and pacts must be discussed first and play key roles.

Personalized/precision medicine (PM)

New genomic data explosion by the advent of next-generation sequencing (NGS)[26] and genomic testing and utility to greater number of normal people and cancer samples/patients, it needs time to consume and ethical safeguards.[26–31] In future, almost all patient's genomes or drug responses might be easier determined, which can be widely used for PM? No widely accepted solution has been established until now. This topic needs to be more frequently discussed and investigated in the future.

Main difficulty in drug development

Great diversity of cancer models

Overall, >1,000 in vivo and >10,000 in vitro tumor cell lines and models are scattered worldwide. How to effectively organize these rich pathological samples and resources is a key issue to decide the high quality of anticancer drug discovery and developments cost-effectively.

Different types of animal or human tumor modality is suitable for different evaluations and assessments (wide-spectra and narrow-spectra). Approximately 1,200 human tumor cell lines are stored for the exploration of drug activity screening, target verification and anticancer mechanism in America Tissue Culture and Collection (ATCC), USA. Facing with this enormous tumor models, proper budget systems can be a way to improve the quality of anticancer drug evaluations such as global participations.[25]

In vivo drug evaluation

No good anticancer drug has been developed without animal tumor model utility. Different tumor inoculation routes can affect new compound responses/efficacy outcomes in experimental screen and evaluations. Common *in vivo* tumor models can be transplanted by various systems, such as subcutaneous locations (sc), intraperatoneal

(ip), intravenous (iv), hollow-fiber (hf), ectopic tumor origins or xenografts from human cancer tissues. Different transplantation routes may possibly obtain different types of anticancer agents and therapeutic efficacy data. Similarly, environmental factors, surroundings and neo blood vessels can aid primary tumor survival and seeding into distant tissues in animal or human bodies.[32–34] With these experimental animal model diversity and advancements, more effective anticancer drugs are expecting in terms of new generations of tumor modality selection/utility (tumor anatomic and historic origins) and different sites of tumor injections and transplantation pathways and routes.

Tumor metastasis models

Antimetastatic agents or drugs developments need to be greatly promoted because 90% cancer mortality comes from neoplasm metastasis.[35–38] As mentioned above, current antimetastatic drug development is deficit. The obvious example is that some agents highly effective to animal tumor metastasis models are useless in clinical trials. Even though widely notification, currently experimental tumor metastatic models are insufficient for harvesting enough highly effective antimetastatic drugs and therapeutic paradigms that can cure patients with metastatic spread and nodules at secondary sites by all means. Shortage of wide-spectra and highly active antimetastatic drugs is a serious challenge for clinical utilities and therapeutic significance for late-staged and aged cancer patient treatments.[14–23] Many scientific discoveries can gradually answer parts of these questions and therapeutic dilemma.[20,21]

Apart from diversity of metastatic models, optimal applications of different metastatic models for various antimetatatic drugs must be promoted due to mystery, multi-step and complicate nature of metastasis pathways and cascade.[35–38] Deeper knowledge and insights into neoplasm metastasis can support these studies and make a great difference.

Medicinal chemistry and herbal medicine

Chemical property

In anticancer drug development study, medicinal chemistry plays important role. After medicinal chemistry study, we can save a lot of pharmacology work and find effective agents as early as possible. After medicinal chemical and pharmacological study, it is obvious that natural chemotherapeutic drugs are many times more effective and less toxicity in cancer treatments.[39–45] Thus, developments of natural chemotherapeutic drugs will be a great pharmaceutical topic present and in future.

Computational assistance

Molecular-docking

Computational analysis of chemical structure of new compound (molecular-docking, in silico) is under investigation and popular now. We can also predict possible effective agents without any form of drug activity evaluations in biological ways. It can save times for anticancer drug developments.

Mathematics and artificial intelligence (AI)

Not only chemical/biomedical scientists, mathematical or physics-majored students or scholars are also very important for anticancer drug developments and basic biomedical studies.[46–49] The high quality communications and teamwork between biomedical scientists and mathematicians may sometimes make a great progress in scientific investigations and drug developments. It contains fast progress of AI in drug developments.[50,51]

New technology

Biomedical technology in drug evaluation

Parallel with human tumor model updating, avant-garde experimental equipments and lab facilities can also improve the quality of anticancer drug evaluation, shorten experimental evaluating terms, and make drug evaluations more precisely for gene-gene interaction and molecular-driven pathology. Nonetheless advancements of new anticancer drug discovery by this avenue at this moment have been very limited while the cost of anticancer drug developments is surging since this Millennium. Luckily, technological advancements (tumor models and screening automation) can help us to find out a number of withdrawal anticancer drugs.[52,53] The mechanisms behind the scenery are interesting topics of the quality enhancing for anticancer drug developments and clinical cancer trials. Overall, we welcome all positive advancements of biomedical technology into anticancer drug developments and clinical diagnosis.

Importance of human talents

Biomedical significance

Anticancer drug developments, a matter of money or a matter of ideas is an open question to be thought about.[8] From above-mentioned topics, greater parts of topics are addressing on an area of scientific investigations of money issue. However, high quality of researchers is more important than enlargements of funds and investment. Money is always easier to collect comparing with marvelous researcher's participation. But it is indispensable in initial stages of any milestones. Yet, these kinds of money issue can not sustain too long. High quality of drug researchers (medicinal chemists, experimental pharmacologists and clinical doctors) will decide how long we can go through.

Drug combination

Basic study

Cancer is a malignant disease (multiple causality and steps—genetic and non-genetic levels) that is often difficult to be managed by single therapeutic drug and option. PM is very important in clinics.[54,55] To overcome these obstacles, anticancer drug combination is a useful way to improve therapeutic outcomes in clinical cancer trials. Obviously, it did not do very well in the past. These kinds of efforts need long-term hard work and sustainable governmental support. It needs shortcut and larger efforts to success in future.[56,57] We welcome these kinds of biomedical study and paradigm establishment in drug development by high-throughput technology.

Current difficulty and dilemma

Cancer pathology overcome

Due to the shortage of available anticancer drugs in clinical cancer trial, pinpointing tumor origins/categories for new tested compounds is suitable for making experimental, preclinical and clinical drug evaluation smarter. Some acquired tumor functionality, such as cancer stem cells (tumor cell revival and plasticity property) needs to be addressed from therapeutic perspective.[58–60] Previously, we like to find some agents that can inhibit cancer stem cells. However, this kind of efforts does not work because only less than 10% cancer stem cells are present in solid tumor tissue. If we can find some solutions

Citation: Da-Yong L, Ting-Ren L. Anticancer drug development, challenge and dilemma. *Nurse Care Open Acces J.* 2020;7(3):72–75.
DOI: 10.15406/ncoaj.2020.07.00222

for neoplasm metastasis and cancer stem cells (patho-therapeutic relationships and diversity) in real clinical circumstances? As a result, any small breakthroughs in this respect will be very useful for obtaining smarter cancer therapeutic drugs and paradigms.

Conclusion

Owing to the slow progresses of anticancer drug discovery and development, several pathways can be made in this regard. In the future, higher efficient tumor metastasis knowledge and models might be used for finding new anticancer drugs and building clinical paradigms worldwide. We welcome global participation and cooperation that can lead to new eras of anticancer drug discovery and developments finally.

Funding

None.

Acknowledgments

None.

Conflicts of interest

The authors declare that there is no conflict of interest to declare.

References

1. Mina LA, Sledge GW. Rethinking the metastatic cascade as a therapeutic target. *Nat Rev Clin Oncol*. 2011;8(6):325–332.
2. Lu DY, Lu TR. Antimetastatic activities and mechanisms of bisdioxopiperazine compounds. *Anti-Cancer Agent Medicinal Chemistry*. 2010;10(7):564–570.
3. Lu DY, Lu TR, Cao S. Cancer metastases and clinical therapies. *Cell & Developmental Biology*. 2012;1(4):e110.
4. Lu DY, Lu TR, Wu HY, et al. Cancer Metastasis treatments. Current Drug Therapy. 2013;8(1):24–29.
5. Merris J. Productivity counts—but the definition is key. Science. 2005;309(5735):726–727.
6. Ruggeri BA, Camp F, Miknyoczki S. Animal models of disease: Preclinical animal models of cancer and their applications and utility in drug discovery. *Biochemical Pharmacology*. 2014;87(1):150–161.
7. Herter-Sprie GS, Kung AL, Wong KK. New cast for a new era: preclinical cancer drug development revisited. *J Clin Investigation*. 2013;123(9):3639–3645.
8. Lu DY, Chen EH, Lu TR. Anticancer drug development, a matter of money or a matter of idea? *Metabolomics*. 2015;5(2):e134.
9. Lu DY, Ding J, Chen RT, et al. Antimetastatic activities and mechanisms of action among Bisdioxopiperazine compounds. Pharmaceutical Formulation and Medicinal Chemistry: Mechanisms, Developments and Treatments. US: Nova Science Publishing; 2016.
10. Lu DY, Lu TR, Zhu H, et al. Anticancer drug development, getting out from bottleneck. Int J Mol Biol. 2017;2(1):10.
11. Lu DY, Lu TR, Yarla NS, et al. Anticancer drug development, breakthroughs are waiting. *Adv Pharmacology & Clinical Trials*. 2017;2(1):119.
12. Lu DY, Xu B, Lu TR. Anticancer drug development, pharmacology update. *EC Pharmacology & Toxicology*. 2020:1–6.
13. Lu DY, Lu TR, Xu B, et al. Anticancer drug developments, challenge from historic perspective. *EC Pharmacology & Toxicology*. 2018;6(11):922–936.
14. Behren A, Thompson EW, Anderson RL, Ferrao PT. Cancer plasticity and the microenvironment: Implications for immunity and therapy response. *Front in Oncology*. 2019:276.
15. Singla S, Sahai D, Mangal N. Clinical trials in oncology: a comprehensive review. EC Pharmacology & Toxicology. 2020;8(2):1–11.
16. Gupta GP, Massague J. Cancer metastasis: building a framework. *Cell.* 2006;127(4):679–695.
17. Talmadge JE, Fidler IJ. The biology of cancer metastasis: historical perspective. *Cancer Res.* 2010;70(14):5649–5669.
18. Valastyan S, Weinberg RA. Tumor metastasis: molecular insights and evolving paradigms. *Cell*. 2011;147(2):275–292.
19. Nieto MA, Huang RY, Jackson RA, et al. EMT: 2016. *Cell*. 2016;166(1):21–45.
20. Lu DY, Lu TR, Xu B, et al. Cancer metastasis, a clinical dilemma for therapeutics. *Current Drug Therapy*. 2016;11(2):163–169.
21. Lambert AW, Pattabiraman DR. Weinberg RA. Emerging biological principles of metastasis. *Cell*. 2017;168(4):670–691.
22. Watson J, Salisbury C, Banks J, et al. Predictive value of inflammatory markers for cancer diagnosis in primary care: a prospective cohort study using electronic health records. *Br J Cancer*. 2019;120:1045–1057.s
23. Zhu H, Liao SD, Shi JJ, et al. DJ-1 mediates the resistance of cancer cells to dihydroarteminisinin through cancer cells through reactive oxygen species removal. *Free Radical Biology and Medicine*. 2014;71:121–132.
24. Lu DY, Lu TR, Chen EH, et al. Anticancer drug development, system updating and global participation. *Current Drug Therapy*. 2017;12(1):37–45
25. Lu DY, Lu TR, Chen EH, et al. Keep up the pace of drug development evolution and expenditure. *Cancer Rep Rev.* 2018;2(5):165.
26. Lander ES. Initial impact of the sequencing of the human genome. *Nature*. 2011;470:187–197.
27. Rahimzadeh V, Bartlett G. Policies and practices of data-intensive primary care in the precision-medicine era. *Internal Medicine Rev*. 2017;3(9):1–14
28. Lu DY, Lu TR, Ding J, et al. Anticancer drug sensitivity testing, a historical review and future perspectives. *Current Drug Therapy*. 2015;10(1):44–55.
29. Volm M, Efferth T. Prediction of cancer drug resistance and implications for personalized medicine. *Front Oncol*. 2015:282.
30. Lu DY, Lu TR, Xu B, et al. Pharmacogenetics of cancer therapy: breakthroughs from beyond? *Future Sci OA*. 2015;1(4):FSO80.
31. Lu DY, Qi RX, Lu TR, et al. Cancer bioinformatics for updating anticancer drug developments and personalized therapeutics. Reviews on Recent Clinical Trials. 2017;12(2):101–110.
32. Dvorak HF. Tumor stroma, tumor blood vessels, and anti-angiogenesis therapy. Cancer J. 2015;21(4):237–243.
33. Lu DY, Chen XL, Ding J. Treatment of solid tumors and metastases by fibrinogen-targeted anticancer drug therapy. *Medical Hypotheses*. 2007;68(1):188–193.
34. Dvorak HF, Weanor VM, Tisty TD, et al. Tumor micro-environment and progression. *J Surg Oncol*. 2011;103(6):468–474.
35. Lu DY, Lu TR. Anticancer activities and mechanisms of bisdioxopiperazine compounds probimane and MST-16. *Anti-Cancer Agent Medicinal Chemistry*. 2010;10(1):78–91.
36. Lu DY, Wu FG, Shen ZM, et al. Different spontaneous pulmonary metastasis inhibitions against Lewis lung carcinoma in mice by bisdioxopiperazine compounds of different treatment schedules. *Sci Pharm*. 2010;78(1):13–20.

37. Lu DY, Lu TR, Xu B, et al. Anti-metastatic drug development, work out towards new direction. *Medicinal Chemistry*. 2018;8(7):512.

38. Lu DY, Ding J, Chen RT, et al. Antimetastatic mechanisms of Bisdioxopiperazine compound study, a gateway to success. *J Cellular and Molecular Pharmacology*. 2017;1(1):e101.

39. Ali I, Saleem K, Uddin R, Haque A, et al. Natural products: human friendly anti-cancer medications. *Egypt Pharm J (NRC)*. 2010;9(2):133–179.

40. Lu DY, Lu TR, Lu Y, et al. Discover natural chemical drugs in modern medicines. *Metabolomics*. 2016;6(3):181.

41. Putta S, Yarla NS, Peluso I, et al. Anthocyanins: Possible role as multitarget therapeutic agents for prevention and therapy of chronic diseases. *Curr Pharm Des*. 2017;23(30):4475–4483.

42. Lu DY, Lu TR, Yarla NS, et al. Natural drug cancer treatment strategies from herbal medicine to chemical or biological drug. *Studies in Natural Products Chemistry*. 2020;66:91–115.

43. Lu DY, Lu TR. Herbal medicine in new era. *Hospice Palliative Medicine International J*. 2019;3(4):125–130.

44. Lu DY, Lu TR. Drug discoveries from natural resources. *J Primary Health Care & General Practice*. 2019;3(1):28.

45. Agarwal N, Majee C, Chakraborthy GS. Natural herbs as anticancer drugs. *Int J PharmTech Res*. 2012;4(3):1142–1153.

46. Lu DY, Lu TR. Mathematics or physics-majored students on the biomedical fields, insiders or outsiders? *Metabolomics*. 2015;5(4):e142.

47. Lu DY, Wu HY, Lu TR, et al. Updating biomedical studies by recruiting more mathematics or physics-majored talents. *Metabolomics*. 2016;6(2):e148.

48. Franssen L, Lorenzi T, Burgess AEF, et al. A mathematical framework for modeling the metastatic spread of cancer. *Bulletin of Mathematical Biology*. 2019;81:1965–2010.

49. Lu DY, Lu TR, Lu Y, et al. The acquisition of mathematical language in biomedical articles. *J Cell Developmental Biol*. 2017;1(1):8.

50. Muthuraman A, Thiagarajan URK, Paramakrishman N. Integration of artificial intelligence in pharmacological research with deep and machine learning process. *EC Pharmacology & Toxicology*. 2019;7(11):56–61

51. Freedman DH. Hunting for new drugs with AI. *Nature*. 2019;576:S49-S53.

52. Ali I, Wani WA, Saleem K, et al. Thalidomide: a banned drug resurged into future anticancer drug. *Current Drug Ther*. 2012;7(1):13–23.

53. Gupta SC, Sung B, Prasad S, et al. Cancer drug discovery by repurposing: teaching new tricks to old dogs. *Trends in Pharmacol Sci*. 2013;34(9):507–517.

54. Lu DY. Personalized cancer chemotherapy, an effective way for enhancing outcomes in clinics. UK: Woodhead Publishing, Elsevier; 2014.

55. Lu DY, Lu TR, Che JY, et al. Individualized cancer therapy, future approaches. *Current Pharmacogenomics & Personalized Medicine*. 2018;16(2):156–163.

56. Lu DY, Chen EH, Wu HY, et al. Anticancer drug combination, how far we can go through? *Anticancer Agents Med Chem*. 2017;17 (1):21–28

57. Lu DY, Lu TR, Yarla NS, et al. Drug combination in clinical cancer treatment. *Reviews on Recent Clinical Trials*. 2017;12(3): 202–211.

58. Yakisich JS. Challenges and limitations of targeting cancer stem cells and/or the tumour microenvironment. *Drug and Therapy Study*. 2012;2(1):e10.

59. Park TS, Donnenberg VS, Donnenberg AD, et al. Dynamic interactions between cancer stem cells and their stromal partners. *Current Pathology Reports*. 2014;2(1):41–52.

60. Magee JA, Piskounova E, Morrison SJ. Cancer stem cells: impact, heterogeneity, and uncertainty. *Cancer Cell*. 2012;21:283–296.

Citation: Da-Yong L, Ting-Ren L. Anticancer drug development, challenge and dilemma. *Nurse Care Open Acces J.* 2020;7(3):72–75.
DOI: 10.15406/ncoaj.2020.07.00222