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REVIEW: MELANOMA ONCOGENES: THE RECENT ADVANCEMENT IN SCIENCE AND TECHNOLOGY

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ABSTRACT

The review covers the management of highly aggressive metastatic melanoma and exploring several new ways for early diagnosis as well as investigating novel approaches of delivering drugs using nanotechnology with high efficacy, minimal harm, and success. In addition to current limitations and possibilities that could help to improve the effectiveness of nanodrugs in melanoma. Furthermore, several nano-therapies along with their different types of nanodrugs' interactions in the biological system. Metastatic melanoma is considered to be the most demanding in terms of its management during the time of the tumor resection or its recurrence soon after it gets resected. Moreover, exploring the main problem domain in terms of methods and analysis regarding melanoma therapy.

INTRODUCTION

Bassically, an ideal properties of nanoparticles drug delivery systems should be high efficacy, cost-effectiveness and should not make any type of risk for the patients, even if the methods fail to improvise the life quality of a patient[1, 2] Therefore, the materials and approach of preparation and techniques used for the development of effective nanoparticle drug delivery systems should be designed with an enhanced efficiency of low toxicity. To accomplishing the safety of a patient and better compliance. the efficiency could be improved by using the targeted moieties such as particular antibodies as well as selected delivery payload.[1] It is necessary to recognize the nanomaterials groups which have been improved for delivering the drug to identify particular markers, to avoid the drug from degrading, and for enhancing stability, and for application in melanoma therapy or diagnosis. An example of nanomaterials groups include structures of rods, nano- capsules, micelles, tubes, PNs, shells, liposomes.In nano therapies for skin melanoma, the nanotherapeutic approaches tend to handle various limitations consisting of cancer attributes, biological hindrance, as well as biocompatibility.[3] Furthermore, the management of nanostructures in a biological system, lead to create interaction between several host biomolecules as well as triggering harmful effects. Moreover, evaluate the physiological and chemical properties along with amount and action time of nanomaterials in absorption level, in vitro biological models, cellular distribution, and metabolism in in vivo models is a compulsory issue to overcome problems.[4]

Melanoma is the sixth highly diagnosed cancer in humans and causing agent for 80% deaths associated with skin.[5] Melanoma is variable in terms of indices of morbidity and mortality rates around the world, such as rare cancers found in Asia and Africa, while reported as an epidemic in nations of Caucasian predominance.[6] If cancer is diagnosed at an early stage, like locating a tumor in localized cutaneous, there is a possibility that it can be resected with a good prediction.[7] Also, if a melanoma gets converted to its metastatic state, it could turn out to be a highly aggressive malignancy that is usually hard to treat.[8] Additionally, once the melanoma enters the metastatic state, its management is a highly challenging task as there are chances that the tumor might enter the unresectable state or the same can recur after a short time period.[9] Such types of extreme cases. One study explained that different treatment options should be practiced in combination with surgeries and therapies (i.e., chemo, radio, targeted, immuno, etc), and photodynamic.[10]

Chemotherapeutic

The first chemotherapeutic approval by FDA (U.S.) was chemotherapeutic medication like Dacarbazine (DTIC), which is an alkylating agent, its the standard chemotherapy treatment for metastatic melanoma. for metastatic melanoma.[11] Studies founded that 2%–6% of patients was 5-year survival.[12] A similar derivative of

DTIC , Temozolomide (TMZ) was also found to be first-line therapy with the potential of crossing the barrier between blood and brain in cases of brain metastases[13],TMZ showed low progression in median improvement- survival (PFS), but no variation were founded in objective response rates (OS).[14] BRAF and MEK inhibitors are reported to be useful in treatment of melanoma which has a BRAF mutation accounting in 50 percent cases.[15] Similarly, immunotherapy and use of inhibitors such as ipilimumab, (anti-cytotoxic T-lymphocyte antigen 4 antibodies), nivolumab, and pembrolizumab are suggested to treat metastatic melanoma in some studies.[16]

Development of novel and efficient drugs to identify novel ways to diagnose the early stages the highly aggressive nature of cutaneous melanoma has been investigated[17] as well as investigating the new drug delivery approaches offered by nanotechnology to fulfill the Regarding nano-technology based approaches in the detection and diagnosis of melanoma, the key for increasing survival rates among patients with melanoma is an early diagnosis. Previous studies provided evidence on survival rates accounting for ten years for I A stage to be 93 percent, whereas for the IV stage it ranges from 10-15 percent.[18] It has been suggested that with each passing stage, the cost of treatment tends to increase[19] as several new techniques in nanomedicine are used for its early detection, such as clinical and histological (such as dermoscopy, photography of whole body, digital analysis based on multispectral imaging as well as microarray technique, particularly RNA).[20] However, there are limited investigations FISH, qRT-PCR, as well as genome hybridization needed for exosomes and molecular changes detection.[21] requirements of being highly efficient, less risky, and effective[22]'nano-therapies, nanodrugs action'.[23]

Nanotechnology

Currently, the tool to detect highly sensitive and specific melanoma and drug delivery i.e, nanotechnology using nanoparticles of size ranging from 1-100 nm as the size, has been promising and helps in protecting degradation, increases stability and provides targeted accumulation.[24] Nanoparticles such as use of quantum dots with fluorescence in conjugation with different cancer particular molecules (such as folic acid) or with HMB45, Tyrosinase (i.e., particular anti-melanoma antibodies) to help in distinguishing between normal and melanoma cells[25], and silica-based nanoparticle (NP) that is PEG-coated, is suggested as Cornell dots (C-dots) for guiding biopsy of sentinel lymph node.[26] Several applications of carbon-based nanotubes are also suggested such as loaded with DOX, Gold (for computed tomography in immunotherapy), magnetic (for MRI based SLNB detection), and Gadolinium loaded nanoparticles (i.e., Gd-FVT) and NPIO (RGD- targeted NP of iron oxide) for MRI lymphography. supported by evidence from several studies.[2] In another study that explain another application of nanotechnology to detect and quantify CTCs (circulating tumor cells) of melanoma using n-SiNPs and magnetite NP[2]

Radiotherapy

The first treatment uses in radiation oncologists with melanoma were marked with technologically inferior irradiation devices and the label of tumor expressed as radioresistant, which originally initiated from identity of tumor radiosensitivity by histological type.[14] In nano-therapy, the selective roles of radiotherapy to treat melanoma is limited, as they are resistant to radiations.[27] However, radioisotopes cause damage to DNA causing its cleavage due to the presence of free radicals. Hence, nanocarriers such as next-generation radiosensitizers (Glutathione coated with gold) are suggested as an effective alternative to increasing half the life of radioisotopes and preventing opsonization to be used in radiotherapy.[28]

The polymeric NP

The polymeric NP such as PLA (polylactic acid), PLGA (polylactic glycolic acid), and PCL (i.e., polycaprolactone) has a potential role to improve the biocompatibility and modify the amphiphilicity of polymeric nanoparticles, copolymers of PEG could be used for evading immune response.[29]

Nanocarriers

Other nanocarriers such as liposomes and niosomes have an impact in regular release of drug in blood circulation with an increasing precision to target tumor. The molecules are characterised as target-specific and controlled release of the drug through the incorporation of nucleic acids as well as other molecules inside the aqueous lumen. Several studies supported this statement in which phosphatidylethanolamine liposomal cisplatin was used to deliver drug efficiently for about 3.6 times in comparison to free drugs.[30] The niosomes are biodegradable and compatible carrying minimally toxic molecules with high solubility and are extremely flexible. Some evidence-based studies have been discussed which suggest that niosomes cause extended circulation with enhanced skin retention towards the drug. Niosomes, when combined with encapsulated artemisone, exhibit specific cytotoxicity for melanoma cells.[31]

The nanomedicine platform is nanohydrogels which are efficient nanoparticles that are used for multimodal treatment, specifically for hydrophilic molecules such as peptides, proteins or oligonucleotides. Nanohydrogels are considered to be highly efficient to uptake cell. The hydrogels are characterised by hydrophilic polymers which are in the form of cross-links (due to interactions caused between hydrophobic and hydrophilic ends, hydrogen and electrostatic bonds as well as covalent interactions) forming a tridimensional network consisting of large amounts of water.[32] A large amount of water in hydrogels promotes swelling, which is characterised by the degree cross-link. The PTX and DOX based drugs

can be easily loaded due to the difference in the charged surface proteins. Some studies were discussed that reported nanohydrogels have a functionalized si RNA system of delivery targeting EGF receptor. However, polymersome has been recognised to be a valuable particle to treat melanoma due to its benefits of increasing load of the drug, robust nature, persistence, prolonged circulation (*in vivo*).[33] It also provides the possibility of designing it to deliver various drugs such as they have been reported to take DOX in case of melanoma therapy to specific cells.[35,36]

The use of NPs to diagnose and treat theranostic nanomedicine in recent times such as lipo, exo, and polymersomes, nanocrystals, tubes, wires, etc. In several studies, there are pieces of evidence that suggest using metals like gold, gadolinium, act as an imaging tracer due to their antitumor properties.[35] In addition to this, Gadolinium-based nanoparticles have been put to use as a therapy for metastatic melanoma in animal models and as an agent of MRI contrast. Other nanostructure for melanoma to be a polymer of lactic acid characterzed by biodegradation and photoluminescent (i.e., BPLP-PLA) combined with a specific drug offering increased hope in the field of imaging and treating melanoma.[36]

The entrance of nanodrugs into the biological systems interacting with the immune system of the host, thus, causing premature cleaning and activating several toxic effects, need to be addressed. Other main limitations relate to the efficacy of nanodrugs which need to be addressed is immunologically contacted, biological hindrance creating barriers for nanodrugs accessibility to a particular target as well as heterogeneity.[37]

CONCLUSION

Undoubtedly understanding of melanoma pathogenesis was crucial for the improvement of new therapeutic modalities. It can be concluded that the change towards the regular application of nano molecules would be initially hindered by various biological barriers followed by the uncertainty to reach the target site of the disease. The nanomaterials tend to develop a 'bio-corona' form through their interaction with biological molecules on the surface and getting entrapped, hence, leading to hindrance in the properties of the relative nanodrug while controlling its efficacy. The nanoparticles are similar in size to biological aggressors interacting with the biological system, creating problems in the relevant evaluation of the nanodrugs effect when used as antitumor effectors.

REFERENCES

1. Bazak, R., et al., *Cancer active targeting by nanoparticles: a comprehensive review of literature.* Journal of cancer research and clinical oncology, 2015; 141(5): 769-784.
2. El-Kenawy, A.E.-M., et al., *Nanomedicine in Melanoma: Current Trends and Future Perspectives.* Exon Publications, 2017: 143-159.
3. Patra, J.K., et al., *Nano based drug delivery systems: recent developments and future prospects.* Journal of nanobiotechnology, 2018; 16(1): 71.
4. Soares, S., et al., *Nanomedicine: principles, properties, and regulatory issues.* Frontiers in chemistry, 2018; 6: 360.
5. Heo, J.R., et al., *Current treatments for advanced melanoma and introduction of a promising novel gene therapy for melanoma.* Oncology Reports, 2016; 36(4): 1779-1786.
6. Maverakis, E., et al., *Metastatic melanoma–a review of current and future treatment options.* Acta dermato-venereologica, 2015; 95(5): 516-527.
7. Younes, R., F.C. Abrao, and J. Gross, *Pulmonary metastasectomy for malignant melanoma: prognostic factors for long-term survival.* Melanoma research, 2013; 23(4): 307-311.
8. Brys, A.K., et al., *Nanotechnology-based strategies for combating toxicity and resistance in melanoma therapy.* Biotechnology advances, 2016; 34(5): 565-577.
9. Johnson, D.B., C. Peng, and J.A. Sosman, *Nivolumab in melanoma: latest evidence and clinical potential.* Therapeutic advances in medical oncology, 2015; 7(2): 97-106.
10. Mundra, V., W. Li, and R.I. Mahato, *Nanoparticle-mediated drug delivery for treating melanoma.* Nanomedicine, 2015; 10(16): 2613-2633.
11. Ancuceanu, R. and M. Neagu, *Immune based therapy for melanoma.* The Indian journal of medical research, 2016; 143(2): 135.
12. Kim, C., et al., *Long-term survival in patients with metastatic melanoma treated with DTIC or temozolomide.* The oncologist, 2010; 15(7): 765.
13. Chen, J., et al., *Applications of nanotechnology for melanoma treatment, diagnosis, and theranostics.* International Journal of Nanomedicine, 2013; 8: 2677.
14. Middleton, M.R., et al., *Randomized phase III study of temozolomide versus dacarbazine in the treatment of patients with advanced metastatic malignant melanoma.* Journal of Clinical Oncology, 2000; 18(1): 158-158.
15. Guy Jr, G.P., et al., *Melanoma treatment costs: a systematic review of the literature, 1990–2011.* American journal of preventive medicine, 2012; 43(5): 537-545.
16. Akhtar, M.J., M. Ahamed, and H.A. Alhadlaq, *Therapeutic targets in the selective killing of cancer cells by nanomaterials.* Clinica Chimica Acta, 2017; 469: 53-62.
17. Doane, T.L. and C. Burda, *The unique role of nanoparticles in nanomedicine: imaging, drug delivery and therapy.* Chemical Society Reviews, 2012; 41(7): 2885-2911.
18. Fernandez-Fernandez, A., R. Manchanda, and A.J. McGoron, *Theranostic applications of*

nanomaterials in cancer: drug delivery, image-guided therapy, and multifunctional platforms. Applied biochemistry and biotechnology, 2011; 165(7-8): 1628-1651.
19. Janib, S.M., A.S. Moses, and J.A. MacKay, *Imaging and drug delivery using theranostic nanoparticles.* Advanced drug delivery reviews, 2010; 62(11): 1052-1063.
20. Lammers, T., et al., *Nanotheranostics and image-guided drug delivery: current concepts and future directions.* Molecular pharmaceutics, 2010; 7(6): 1899-1912.
21. Lee, D.-E., et al., *Multifunctional nanoparticles for multimodal imaging and theragnosis.* Chemical Society Reviews, 2012; 41(7): 2656-2672.
22. Kim, B.Y., J.T. Rutka, and W.C. Chan, *Nanomedicine.* New England Journal of Medicine, 2010; 363(25): 2434-2443.
23. Scheinberg, D.A., et al., *Advances in the clinical translation of nanotechnology.* Current opinion in biotechnology, 2017; 46: 66-73.
24. Sanna, V., N. Pala, and M. Sechi, *Targeted therapy using nanotechnology: focus on cancer.* International journal of nanomedicine, 2014. 9: p. 467.The Pentose phosphate pathway dynamics in cancer and its dependency on intracellular pH
25. Zangabad, P.S., et al., *Nanocaged platforms: modification, drug delivery and nanotoxicity. Opening synthetic cages to release the tiger.* Nanoscale, 2017; 9(4): 1356-1392.
26. Ding, C., et al., *Recent advances in stimuli-responsive release function drug delivery systems for tumor treatment.* Molecules, 2016; 21(12): 1715.
27. Khan, N., et al., *The evolving role of radiation therapy in the management of malignant melanoma.* International Journal of Radiation Oncology* Biology* Physics, 2011; 80(3): 645-654.
28. Ajorlou, E. and A.Y. Khosroushahi, *Trends on polymer-and lipid-based nanostructures for parenteral drug delivery to tumors.* Cancer chemotherapy and pharmacology, 2017; 79(2): 251-265.
29. Kunz-Schughart, L.A., et al., *Nanoparticles for radiooncology: Mission, vision, challenges.* Biomaterials, 2017; 120: 155-184.
30. Poon, W., et al., *Targeting B16 tumors in vivo with peptide-conjugated gold nanoparticles.* Nanotechnology, 2015; 26(28): 285101.
31. Ag Seleci, D., et al., *Niosomes as nanoparticular drug carriers: fundamentals and recent applications.* Journal of nanomaterials, 2016. 2016.
32. Weissig, V., T.K. Pettinger, and N. Murdock, *Nanopharmaceuticals (part 1): products on the market.* International journal of nanomedicine, 2014; 9: 4357.
33. Bae, Y.H. and K. Park, *Targeted drug delivery to tumors: myths, reality and possibility.* Journal of controlled release, 2011; 153(3): 198.
34. Balch, C.M., et al., *Final version of 2009 AJCC melanoma staging and classification.* Journal of clinical oncology, 2009; 27(36): 6199.
35. Ahlgrimm-Siess, V., et al., *New diagnostics for melanoma detection: from artificial intelligence to RNA microarrays.* Future Oncology, 2012; 8(7): 819-827.
36. Ferris, L.K. and R.J. Harris, *New diagnostic aids for melanoma.* Dermatologic clinics, 2012; 30(3): 535-545.
37. Cooper, C., J. Sorrell, and P. Gerami, *Update in molecular diagnostics in melanocytic neoplasms.* Advances in anatomic pathology, 2012; 19(6): 410-416.