

Editorial

# Advances in Melanoma Treatment with Salvianolic Acid A

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Academic Editor: Graham Pawelec

Submitted: 24 December 2024 Revised: 5 February 2025 Accepted: 12 February 2025 Published: 13 May 2025

Inflammation in the tumor microenvironment (TME) plays a critical role in all stages of cancer development, including initiation, promotion, and progression [1]. The prognostic significance of systemic inflammation in this microenvironment is increasingly recognized in patients with esophageal squamous cell carcinoma [2], breast cancer [3], gastric cancer [4], and testicular and penile cancers [5]. Although cancer immunotherapy has transformative potential for cancer treatment, it also poses challenges by inducing tumor resistance and altering the patient's innate and adaptive immune responses [6]. Cancer cells actively interact with the immune system, and cancer-specific immunotherapies involve both the immune system and tumors in these dynamic interactions [7]. Understanding these interactions is essential for the development of novel combination therapies and sequencing strategies [8].

The search for effective cancer therapies remains the greatest challenge in modern medical research. Melanoma is the critical focus for this project, particularly due to its aggressive nature and propensity to metastasize [9]. In this context, the study "Inhibition of Melanoma Cell Growth by Salvianolic Acid A through CHK2-CDC25A Pathway Modulation" by Pu and colleagues [10], published in *Frontiers in Bioscience - Landmark*, offers promising insights into a novel therapeutic approach using traditional medicine.

Salvianolic acids (Sals), specifically salvianolic acid A (SalA), which is derived from *Salvia miltiorrhiza* Bunge and known as Danshen in traditional Chinese medicine, have long been known for their medicinal properties [11]. This study elucidated the antiproliferative effects of SalA on melanoma cell lines A2058 and A375, and sheds light on its potential as an effective anticancer agent.

The current research addressed the mechanistic pathways through which SalA exerts its effects on melanoma cells. The results showed that SalA potently inhibited cell proliferation by inducing cell cycle arrest in the G2/M phase. The central role of checkpoint kinase-2 (Chk-2) phosphorylation, which leads to the degradation of Chk-2-regulated genes such as cell division cycle 25A (*Cdc25A*) and *Cdc2*, underscores the targeted effects of SalA [10]. Notably, this pathway had no effect on Chk-1, highlighting the specificity and precision of SalA's molecular interactions.

A compelling aspect of this study is its foundation in traditional medicine. The historical use of Danshen for the treatment of cardiovascular diseases and various cancers is well documented [12]. However, expanding its application to melanoma treatment signifies a meaningful integration of ancient wisdom with contemporary scientific rigor. This interface not only enriches the therapeutic landscape but also highlights the importance of exploring natural compounds in the ongoing fight against cancer.

The findings reported by Pu *et al.* [10] are of particular importance given the current situation of melanoma treatment, which is often based on systemic approaches that encompass targeted therapies, immunotherapies, and chemotherapy regimens. The marginal efficacy and incremental gains in patient survival associated with these treatments highlight the need for novel interventions. Therefore, SalA is a promising candidate for further clinical investigation as it selectively targets melanoma cells while modulating critical regulatory pathways.

Moreover, this study opens new avenues for exploring broader applications of Sals in oncology. The specificity of SalA in modulating the Chk2-Cdc25A signaling pathway presents an interesting possibility for its use in other malignancies characterized by dysregulated cell cycle progression [10]. SalA can fight cancer by inducing apoptosis, arresting the cell cycle, and inhibiting metastasis through multiple signaling pathways. Additionally, it increases the sensitivity of cancer cells to chemotherapy [13]. On the other hand, it has been shown that in vitro and in vivo, Sals significantly reduce inflammatory response and injury in cerebral ischemia-reperfusion, possibly by inhibiting Toll-like receptors 2 and 4 and the related signaling pathway [14]. Previous studies have shown that SalA enhances the activity of T cells and natural killer cells, which could contribute to improved antitumor immune responses [15,16]. Therefore, future research should investigate the therapeutic combination of SalA and existing anticancer agents, which could potentially enhance therapeutic outcomes through synergistic effects. However, in the context of melanoma, the precise mechanisms by which SalA modulates immune cell interactions with melanoma cells remain to be fully elucidated. Future studies should investigate whether SalA increases tumor-associated antigens or activates immune cells, thereby enhancing immune surveillance against melanoma cells. SalA holds potential for use

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in immunotherapy, representing an important avenue for further research.

In conclusion, the study by Pu *et al.* [10] represents a significant step in melanoma research, offering hope for more effective and targeted treatment strategies. As we continue to unravel the complexities of cancer biology, integrating traditional medicinal compounds such as SalA into contemporary therapeutic frameworks holds promise. The meticulous research presented in this study not only advances our understanding of melanoma treatment but also reinforces the invaluable contribution of natural compounds to modern medicine.

### **Author Contributions**

CYK contributed to editorial preparation, conceptualization, and interpretation. The author critically reviewed the editorials and approved the final manuscript. The author participated sufficiently in the work and agreed to be accountable for all aspects.

## **Ethics Approval and Consent to Participate**

Not applicable.

### Acknowledgment

Not applicable.

## **Funding**

This research received no external funding.

#### **Conflict of Interest**

The author declares no conflict of interest. Given his role as the Guest Editor, Chan-Yen Kuo had no involvement in the peer-review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to Graham Pawelec.

#### References

- Grivennikov SI, Greten FR, Karin M. Immunity, inflammation, and cancer. Cell. 2010; 140: 883–899. https://doi.org/10.1016/j. cell.2010.01.025.
- [2] Chen CJ, Lee CT, Tsai YN, Tseng CM, Chen TH, Hsu MH, et al. Prognostic significance of systemic inflammatory response markers in patients with superficial esophageal squamous cell carcinomas. Scientific Reports. 2022; 12: 18241. https://doi.org/10.1038/s41598-022-21974-y.
- [3] Huang ZZ, Hua X, Song CG, Xia W, Bi XW, Yuan ZY, et al. The Prognostic Prediction Value of Systemic Inflammation Score and the Development of a Nomogram for Patients With

- Surgically Treated Breast Cancer. Frontiers in Oncology. 2020; 10: 563731. https://doi.org/10.3389/fonc.2020.563731.
- [4] Wang Q, Zhu D. The prognostic value of systemic immuneinflammation index (SII) in patients after radical operation for carcinoma of stomach in gastric cancer. Journal of Gastrointestinal Oncology. 2019; 10: 965–978. https://doi.org/10.21037/jgo. 2019.05.03.
- [5] Janicic A, Petrovic M, Zekovic M, Vasilic N, Coric V, Milojevic B, et al. Prognostic Significance of Systemic Inflammation Markers in Testicular and Penile Cancer: A Narrative Review of Current Literature. Life (Basel, Switzerland). 2023; 13: 600. https://doi.org/10.3390/life13030600.
- [6] Sharma P, Hu-Lieskovan S, Wargo JA, Ribas A. Primary, Adaptive, and Acquired Resistance to Cancer Immunotherapy. Cell. 2017; 168: 707–723. https://doi.org/10.1016/j.cell.2017.01.017.
- [7] Maffuid K, Cao Y. Decoding the Complexity of Immune-Cancer Cell Interactions: Empowering the Future of Cancer Immunotherapy. Cancers. 2023; 15: 4188. https://doi.org/10.3390/ cancers15164188.
- [8] Woodcock J, Griffin JP, Behrman RE. Development of novel combination therapies. The New England Journal of Medicine. 2011; 364: 985–987. https://doi.org/10.1056/NEJMp1101548.
- [9] Hsieh MY, Hsu SK, Liu TY, Wu CY, Chiu CC. Melanoma biology and treatment: a review of novel regulated cell death-based approaches. Cancer Cell International. 2024; 24: 63. https://doi.org/10.1186/s12935-024-03220-9.
- [10] Pu XY, Mei Y, Zheng Q, Ko CY. Inhibition of Melanoma Cell Growth by Salvianolic Acid A through CHK2-CDC25A Pathway Modulation. Frontiers in Bioscience (Landmark Edition). 2024; 29: 213. https://doi.org/10.31083/j.fbl2906213.
- [11] Ma L, Tang L, Yi Q. Salvianolic Acids: Potential Source of Natural Drugs for the Treatment of Fibrosis Disease and Cancer. Frontiers in Pharmacology. 2019; 10: 97. https://doi.org/ 10.3389/fphar.2019.00097.
- [12] Wang L, Ma R, Liu C, Liu H, Zhu R, Guo S, et al. Salvia miltiorrhiza: A Potential Red Light to the Development of Cardiovascular Diseases. Current Pharmaceutical Design. 2017; 23: 1077–1097. https://doi.org/10.2174/1381612822666161010105242.
- [13] Qin T, Rasul A, Sarfraz A, Sarfraz I, Hussain G, Anwar H, et al. Salvianolic acid A & B: potential cytotoxic polyphenols in battle against cancer via targeting multiple signaling pathways. International Journal of Biological Sciences. 2019; 15: 2256–2264. https://doi.org/10.7150/ijbs.37467.
- [14] Ling Y, Jin L, Ma Q, Huang Y, Yang Q, Chen M, et al. Salviano-lic acid A alleviated inflammatory response mediated by microglia through inhibiting the activation of TLR2/4 in acute cerebral ischemia-reperfusion. Phytomedicine: International Journal of Phytotherapy and Phytopharmacology. 2021; 87: 153569. https://doi.org/10.1016/j.phymed.2021.153569.
- [15] Tang J, Zhao X. Research Progress on Regulation of Immune Response by Tanshinones and Salvianolic Acids of Danshen (*Salvia miltiorrhiza* Bunge). Molecules (Basel, Switzerland). 2024; 29: 1201. https://doi.org/10.3390/molecules29061201.
- [16] Peng Y, Yang T, Huang K, Shen L, Tao Y, Liu C. Salvia Miltiorrhiza Ameliorates Liver Fibrosis by Activating Hepatic Natural Killer Cells *in Vivo* and *in Vitro*. Frontiers in Pharmacology. 2018; 9: 762. https://doi.org/10.3389/fphar.2018.00762.

