Treatment Of Melanoma With Ferroptosis Inducing Agents

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SUMMARY

UCLA researchers in the Departments of Molecular and Medical Pharmacology and Medicine have developed a novel method to treat melanoma.

BACKGROUND

Immune checkpoint blockade immunotherapy with anti-PD1 antibody is the preferred treatment for patients with metastatic melanoma that has resisted other therapies. However, there remains a subset of patients that does not respond to or relapses following this therapeutic strategy, as de-differentiation of melanoma cells is known to increase resistance to conventional immunotherapies. So far there is no therapy specifically tailored to target these immunotherapy-resistant de-differentiated melanoma cells.

INNOVATION

Researchers at UCLA have developed a method to treat melanoma that resists conventional immune checkpoint blockade immunotherapy by using ferroptosis-inducing drugs. Ferroptosis is a type of cell death resulting from accumulation of reactive oxygen species that degrade lipids in the cell membrane. De-differentiating cells, such as the immunotherapy-resistant or kinase inhibitor-resistant melanoma, are highly susceptible to ferroptosis. Combination treatment with ferroptosis-inducing agents can be a valuable, new synergistic approach for overcoming resistance to melanoma therapy.

APPLICATIONS

- Combinatorial therapy for cancer treatment
- Stratification method for skin cancer treatment
- Screening method for immunotherapy-resistant or kinase inhibitor-resistant melanomas

ADVANTAGES

- Specifically targets a subset of cancer cells that resist other forms of therapy
- Combinatorial use with conventional immunotherapy or kinase inhibitors prevents tumor escape due to de-differentiation

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	12,213,977	02/04/2025	2017-879
European Patent Office	Published Application	3645739	05/06/2020	2017-879

RELATED MATERIALS

- Titz, Bjoern, et al. "JUN dependency in distinct early and late BRAF inhibition adaptation states of melanoma." Cell discovery 2 (2016): 16028.
- Zaretsky, Jesse M., et al. "Mutations associated with acquired resistance to PD-1 blockade in melanoma." New England Journal of Medicine 375.9 (2016): 819-829.
- Müller, Judith, et al. "Low MITF/AXL ratio predicts early resistance to multiple targeted drugs in melanoma." Nature communications 5 (2014): 5712.

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INVENTORS

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OTHER INFORMATION

KEYWORDS

melanoma resistant ferroptosis skin cancer drugs immunotherapy PD1 CTLA4 combination immune checkpoint blockade, MAP kinase pathway, MAPK, BRAF inhibitors, MEK inhibitors

CATEGORIZED AS

- Medical
- Disease: Cancer
- Disease: Dermatology
- Therapeutics

RELATED CASES

2017-879-0

▶ Tsoi, J, Robert, L, Paraiso, K, Galvan, C, Sheu, K, Lay, J, Wong, DJL, Atefi, M, Shirazi, R, Wang, X, Braas, D, Grasso, CS, Palaskas, N, Ribas, A, Graeber, TG. Multi-stage differentiation defines melanoma subtypes with differential vulnerability to drug-induced iron-dependent oxidative stress. Cancer Cell. 2018 May 14;33(5):890-904.e5.

▶ Kemeny LV, Fisher DE. Targeting the (Un)differentiated State of Cancer. Cancer Cell. 2018 May 14;33(5):793–795.

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

▶ Identification Of Pan-Cancer Small Cell Neuroendocrine Phenotypes And Vulnerabilities

▶ Statistical Comparison of Rank Lists and Molecular Profiles

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