

## Establishment of melanoma primary cultures from patient tumor samples

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### Organisation

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## SCOPE OF THE METHOD

<b>The Method relates to</b>	Human health: Cancer
<b>The Method is situated in</b>	Basic Research, Translational - Applied Research
<b>Type of method</b>	In vitro - Ex vivo
<b>Specify the type of cells/tissues/organs</b>	Cancer Cells

## DESCRIPTION

### Method keywords

primary cell culture

cancer cell line

Cell culture

Culture conditions

Culture Medium

### Scientific area keywords

melanoma

Cancer Plasticity

EMT

Cell Pigmentation

### Method description

The use of patient-derived primary cell cultures in cancer preclinical assays, including drug screens and genotoxic studies, has increased in recent years. However, their translational value is constrained by several limitations, including variability that can be caused by the culture conditions. Here, we show that the medium composition commonly used to propagate primary melanoma cultures has limited their representability of their tumor of origin and their cellular plasticity, and modified their sensitivity to therapy.

Indeed, we established and compared cultures from different melanoma patients propagated in parallel in low-tyrosine (Ham's F10) or in high-tyrosine (Ham's F10 supplemented with tyrosine or RPMI1640 or DMEM). Tyrosine is the precursor of melanin biosynthesis, a process particularly active in differentiated melanocytes and melanoma cells. We identified that growing primary melanoma cultures in low-tyrosine medium allows the maintenance of a clinically-relevant highly differentiated melanoma state. These cultures with highly differentiated features in high tyrosine media can be early drifted away to a less differentiated state or can be even lost through the entry into a senescence-like state. Our group establishes melanoma cultures (protocol design and optimization) including primary cultures. We have a culture unit with adequate infrastructure dedicated to cell culture and adheres to rigorous quality control programs that has established more than 150 primary lines and cultures of normal and tumour cells (mainly melanomas). We share our cell cultures with some 80 research teams around the world. Our current melanoma cultures (patient-derived cultures known as MM lines) were crucial and very relevant in several studies that identified regulatory networks underlying melanoma states, mechanisms and regulators of phenotype switching, translation and metabolic reprogramming mechanisms and signatures associated with resistance to therapy (Wouters et al., Nature Cell Biology 2020, Verfaillie et al., Nature Communications 2015, Corre et al., Nature Communications 2018, Rapino et al., Nature 2018, Janssen et al., Cell Death Discovery 2019, Rambow et al., Cell 2018). These melanoma cultures are available at Applied Biological Materials (abm) and CancerTools. <https://www.cancertools.org/cell-lines/161602>

## **Lab equipment**

Laminar Flow Cabinets (Cell Culture Hoods)

## **Method status**

Published in peer reviewed journal

## **PROS, CONS & FUTURE POTENTIAL**

### **Advantages**

Melanoma cultures are widely and still extensively used in cancer research and drug discovery. Here, we elucidate the causes contributing to their limitations demonstrating why these cell cultures have a phenotype that does not reflect melanoma behavior *in vivo* underlying the importance of culturing melanoma cells in a low-tyrosine-containing medium in order to maintain a clinically relevant highly differentiated melanoma state and preserving the phenotypic identity of origin. As the vast majority of the available melanoma lines are plated in high tyrosine media like RPMI1640, many primary cultures may have switched early (or even lost) and thereby not represent the original tumor anymore. This may also have an implication on preclinical and drug screening studies

### **Challenges**

- Tissue availability: Obtaining fresh tumor tissue from patients is very challenging.
- Culture Failure (efficiency in establishing primary cultures): The viability, proprieties, and quality of the tissue are crucial for successful culture establishment. Indeed, not all tumor cells are able to adapt to the *in vitro* microenvironment and grow successfully, leading to culture failure. Some cancer cells have a limited lifespan in culture.

### **Future & Other applications**

- Drug Screening

- Drug Resistance
- Epigenetic Mechanisms
- Metabolic Reprogramming Mechanisms
- Cytoskeleton Regulation
- Cell pigmentation
- Phenotypic studies
- Transcriptional networks

## REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

### References

1. Najem, A.; Wouters, J.; Krayem, M.; Rambow, F.; Sabbah, M.; Sales, F.; Awada, A.; Aerts, S.; Journe, F.; Marine, J.-C.; et al. Tyrosine-Dependent Phenotype Switching Occurs Early in Many Primary Melanoma Cultures Limiting Their Translational Value. *Front Oncol* 2021, 11, 780654, doi:10.3389/fonc.2021.780654.
2. Wouters, J.; Kalender-Atak, Z.; Minnoye, L.; Spanier, K.I.; De Waegeneer, M.; Bravo González-Blas, C.; Mauduit, D.; Davie, K.; Hulselmans, G.; Najem, A.; et al. Robust Gene Expression Programs Underlie Recurrent Cell States and Phenotype Switching in Melanoma. *Nat Cell Biol* 2020, 22, 986–998, doi:10.1038/s41556-020-0547-3.

### Associated documents

[Tyrosine-Dependent Phenotype Switching Occurs Early in Many Primary Melanoma Culture.pdf](#)

### Links

[Tyrosine-Dependent Phenotype Switching Occurs Early in Many Primary Melanoma Cu...](#)

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