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Direct transdifferentiation of tumorigenic melanoma cells to non-tumorigenic neuron-like cells

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Melanoma is a type of aggressive skin cancer that is known to be highly lethal, particularly when it reaches advanced stages. Over the years, various approaches have been developed to alter the phenotype of somatic cells from one lineage to another, with evidence showing that changing the lineage of cancer cells can lead to a drastic reduction of their tumorigenic potential. Against this backdrop, my study sought to explore the possibility of transdifferentiating melanoma cells into neurons and assessing the characteristics of the transdifferentiated cells.
To achieve this, I employed an ectopic overexpression approach, where I introduced a neuron-specific set of transcription factors (Ascl1, Brn2, Myt1L, and NeuroD1) into melanoma cells. The results of my investigation showed that melanoma cells could indeed be transdifferentiated into cells with neuron-like characteristics. Specifically, these cells expressed neuronal markers and exhibited a neuron-like morphology. I went a step further and used RNA sequencing and DNA methylation assays to reveal the underlying mechanism behind this transdifferentiation process. Differentially expressed genes and differentially methylated CpGs enriched neuron-related pathways and predicted tumor feature loss.
Importantly, although achieving a 100% conversion rate was unattainable, the transdifferentiated cells demonstrated a loss of their melanoma features as well as a significant reduction in their tumorigenic and metastatic potential both *in vitro* and *in vivo*.
Lastly, I investigated how transdifferentiated cells reacted to radiotherapy and targeted therapy and found enhanced responsiveness to both forms of therapy compared to parental melanoma cells. I therefore conclude that transdifferentiation into terminally differentiated cells could represent a promising therapeutic option for the treatment of malignant melanoma.