The Yin and Yang of BRAF, MEK and CDK4/6 targeted therapy.

The body's immune system can play an important role in clearing cancer cells and this is called anti-tumour immunity. Current treatment for BRAF mutant melanoma patients is a combination of BRAF and MEK targeted therapy, which not only kills cancer cells but can also boost anti-tumour immunity. Although BRAF and MEK targeted therapy have proven beneficial, resistance to this therapy often develops and the cancer starts to grow again. Using human melanoma cells in mice, previous studies from the McArthur & Sheppard lab showed that adding CDK4/6 targeted therapy to this dual therapy, overcame tumour drug resistance and led to long term survival (Martin et al. Int J Cancer. 2018;142(10):2139-2152 ; https://doi.org/10.1002/ijc.31220).

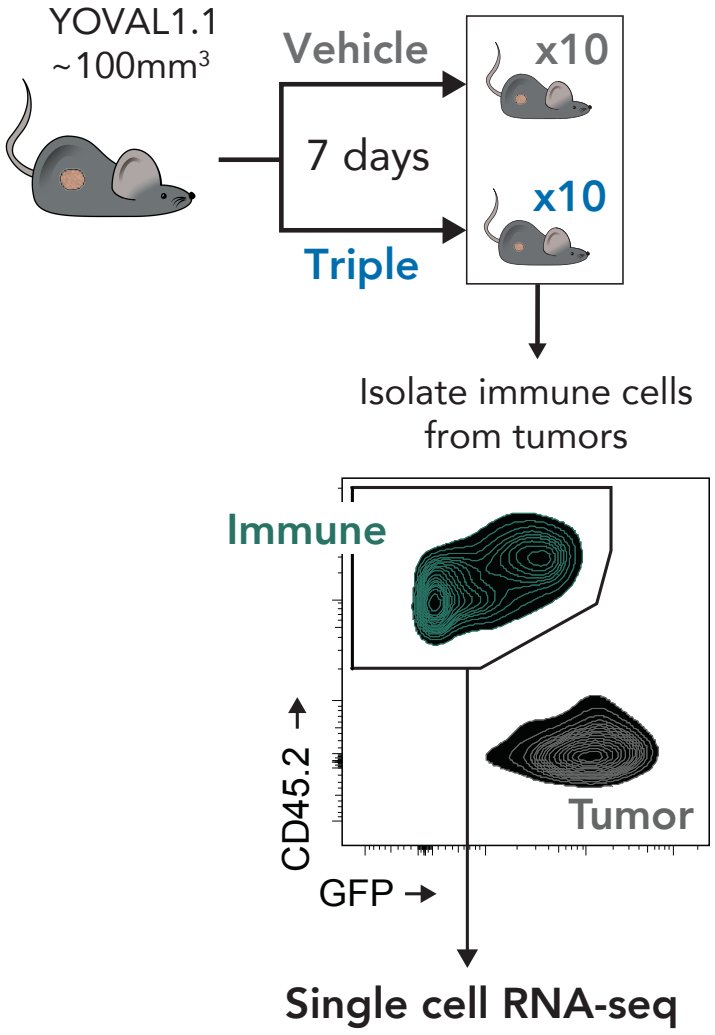
In a recent study from the lab, Lelliott et al looked at the changes in immune cell populations within the melanoma when mice were treated with this triple targeted therapy. Many of the beneficial changes in immune cells that are observed with the BRAF and MEK combinational therapy were also present with the triplet therapy. However, a set of immune cells that are important in helping other immune cells to recognize and attack tumour cells were decreased in number. The study has implications for clinical trial design as it highlights that, despite the potent tumour growth inhibiting effects (the Yin), this triple therapy modulates immune cells within the melanoma in a way that may adversely impact anti-tumour immunity (the Yang).

Full Article

https://cancerimmunolres.aacrjournals.org/content/early/2021/01/07/2326-6066.CIR-20-0401

The figure below shows different immune cell types found within the melanoma tumour when mice received either no treatment (Vehicle) or the triplet treatment. Each dot in the figure represents an individual immune cell that was detected within the tumour. There are many changes and in particular there is a clear loss of red and green dots associated with the triple treatment; these are the cells that are required to activate anti-tumour immunity.

Experimental Design



Single Cell RNA-Seq Analysis