G1 arrest and differentiation can occur independently of Rb family function.

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Public Summary:
The ability of progenitor cells to exit the cell cycle is essential for proper embryonic development and homeostasis, but the mechanisms governing cell cycle exit are still not fully understood. Here, we tested the requirement for the retinoblastoma (Rb) protein and its family members p107 and p130 in G0/G1 arrest and differentiation in mammalian cells. We found that Rb family triple knockout (TKO) mouse embryos survive until days 9-11 of gestation. Strikingly, some TKO cells, including in epithelial and neural lineages, are able to exit the cell cycle in G0/G1 and differentiate in teratomas and in culture. This ability of TKO cells to arrest in G0/G1 is associated with the repression of key E2F target genes. Thus, G1 arrest is not always dependent on Rb family members, which illustrates the robustness of cell cycle regulatory networks during differentiation and allows for the identification of candidate pathways to inhibit the expansion of cancer cells with mutations in the Rb pathway.

Scientific Abstract:
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