Palbociclib Releases the Latent Differentiation Capacity of Neuroblastoma Cells

Neuroblastoma is the most common extracranial tumour in children. Despite the intensity of multimodal therapy, many children will relapse and only a small fraction of those children will survive past ten years. Neuroblastoma arise from neural crest-derived cells that have been stalled in their development, remaining in an undifferentiated aggressive state. Redirecting neuroblasts towards their original neuronal fate, i.e. driving tumour differentiation is a promising therapeutic approach for children with neuroblastoma.

In their recent study published in Developmental Cell, Ferguson and colleagues at the University of Cambdrige (UK) demonstrated how palbociclib, a small molecule inhibitor of CDK4/6 already in clinical trial, not only inhibits cellular proliferation but actually induce extensive cellular differentiation toward a more mature neuronal phenotype. Palbociclib also significantly inhibited the tumor growth in vivo, in genetically-engineered murine model of neuroblastoma, alone or in combination with retinoic acid, a known differentiation agent.

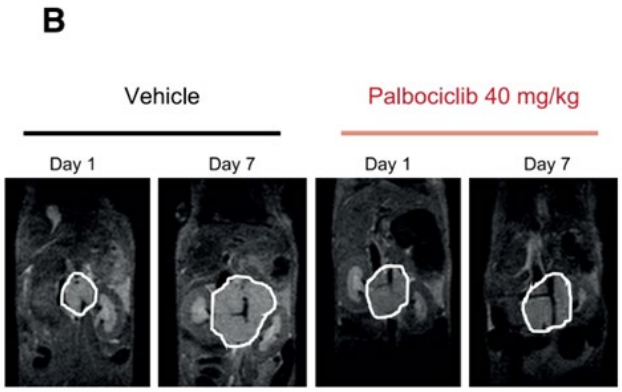
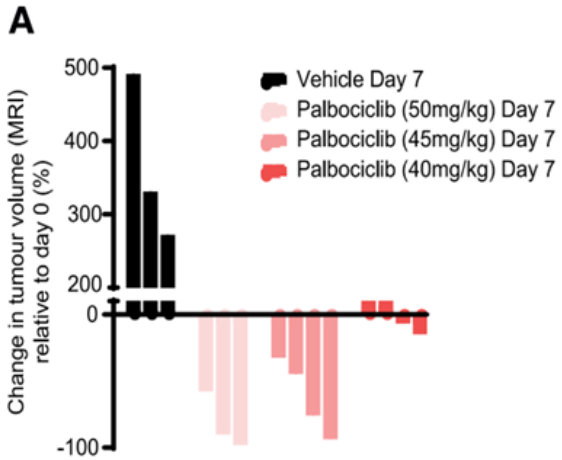


***Figure 1**. Palbociclib inhibits tumor growth in genetically engineered mouse (GEM) models of neuroblastoma (A) Waterfall plot documenting relative changes in tumor volume at day 7 in the Th-MYCN GEM model treated with vehicle control or palbociclib at the indicated doses. (B) Representative abdominal MRI fat-supressed T2-weighed images at days 1 and 7 of treatment with vehicle or palbociclib (40 mg/ kg). The white lines indicate the tumor boundaries.*



In this study, the use of our M-Series range of compact MRI was pivotal for quantifying tumor volume and evaluate tumor response to treatment with pabociclib in the transgenic Th-MYCN mouse model of neuroblastoma (Figure 1). The Aspect M-series range offers cost-effective, low maintenance and compact MRI solutions for mouse (M3), rat (M7) and non-human primate (M12), based on a unique permanent magnet design and effective workflow supported by integrated physiological monitoring and an user-friendly operating system. The field strength of the M-Series (1 Tesla) is optimal for lung imaging and the development of clinically translatable functional- and/or molecular- imaging approach.

In summary, this study warrants further clinical evaluation of Palbociclib in early-phase pediatric clinical trial in combination with retinoic acid to enhance neuroblastoma differentiation and potentially improve the outcomes of children with neuroblastoma.

References:

Ferguson et al., 2023, Developmental Cell 58, 1 16. DOI: https://doi.org/10.1016/j.devcel.2023.08.028