Adult stem cell-derived organoids: innovative models to elucidate signalling mechanisms in Wnt-addicted cancers

*Dustin J Flanagan, Nick Barker, Renate HM Schwab, Bang M Tran, Hans Clevers, Toby J Phesse and Elizabeth Vincan**

University of Melbourne and the Victorian Infectious Diseases Reference Laboratory (VIDRL), Doherty Institute for Infection and Immunity, 792 Elizabeth St, Melbourne, VIC 3000, Australia

Presenting and Corresponding Author E-mail Address: evincan@unimelb.edu.au

Cancer initiation and progression are fuelled by cells with both stem cell and mesenchymal properties. The Wnt/β-catenin signal transduction pathway plays critical roles in these processes in colon cancer and in other Wnt-driven gastrointestinal cancers. Our aim is to understand how Wnt governs these properties.

Recently we demonstrated that Fzd7 functions as a Wnt receptor in intestinal[1] and gastric[2,3] stem cells and that this need for Fzd7 expression is carried through to cancers that arise in these tissues[4,5,6]. Blocking Fzd7-mediated Wnt signalling has potent anti-tumour effects (reviewed in Ref #7 & 8). Our more recent findings indicate that Fzd7 also plays a key role in liver cancer and we have identified oncogenic interplay between infection with the hepatitis B virus and Wnt/β-catenin signalling, two drivers of liver cancer (*unpublished).* Transgenic mouse models and mouse and human tissue derived organoids have been instrumental in these studies. These roles that we have identified for FZD7 in Wnt-driven gastrointestinal cancers (colon, stomach and liver), make FZD7 an attractive therapeutic target that has the potential to impact on cancer initiation, growth and progression and ultimately, patient survival.

References

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