

Single cell-derived clonal analysis of desmoid tumors

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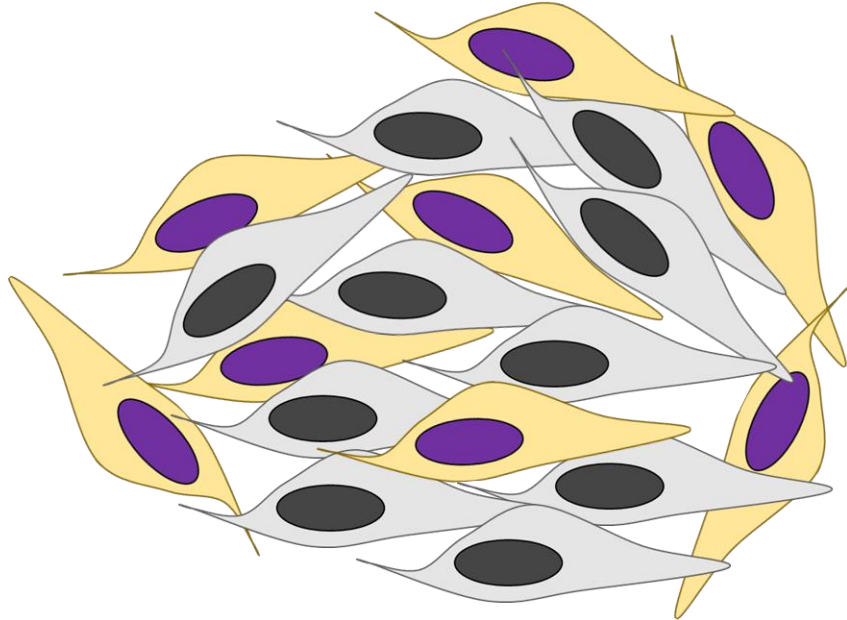
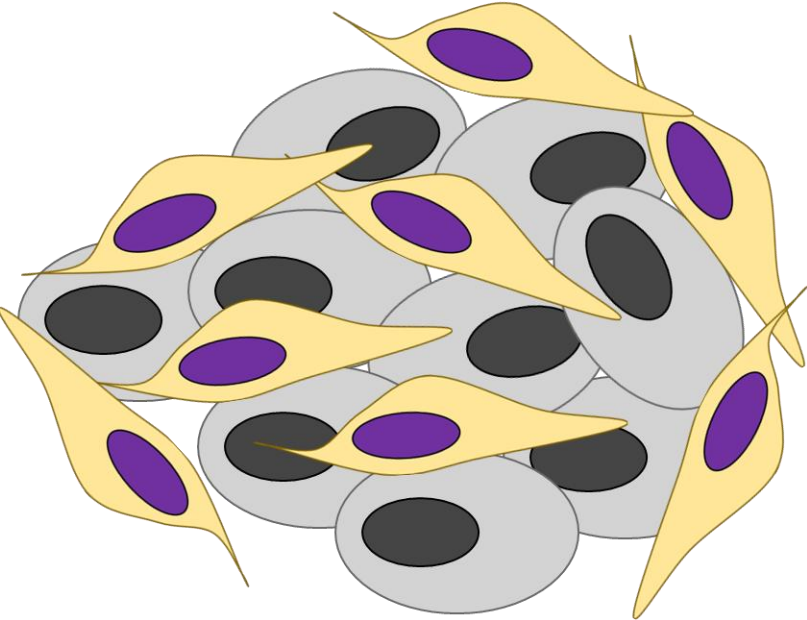
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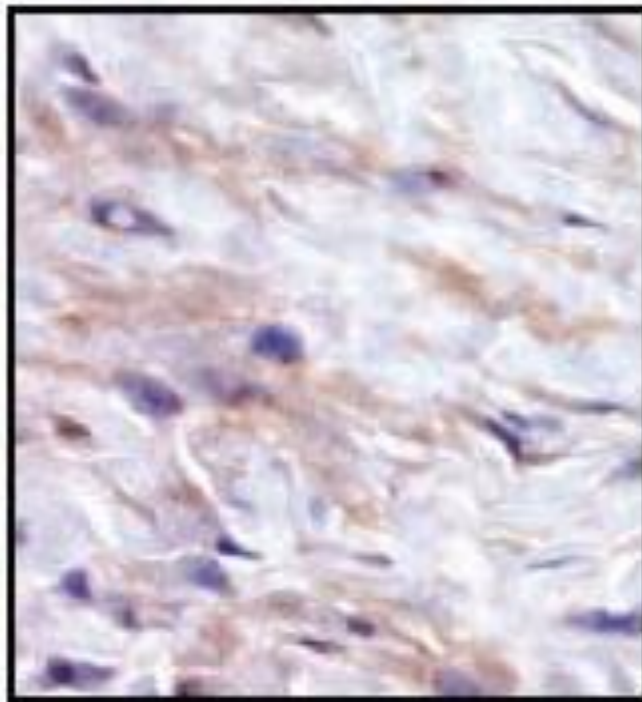
Laboratory Medicine and Pathobiology, University of Toronto

Oct 18, 2015

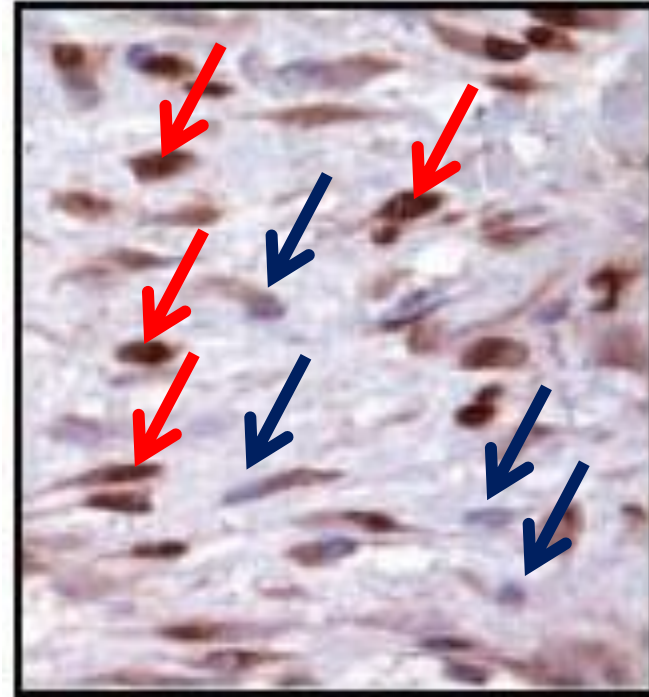
Tumor cells and the surrounding stroma



Not all cells in desmoid tumors show strong nuclear staining of β -catenin.



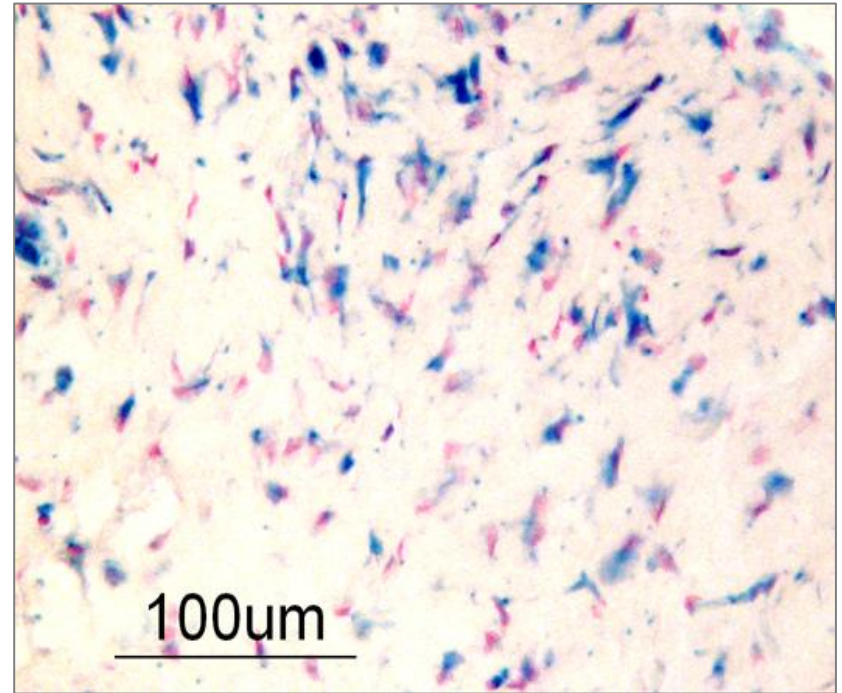
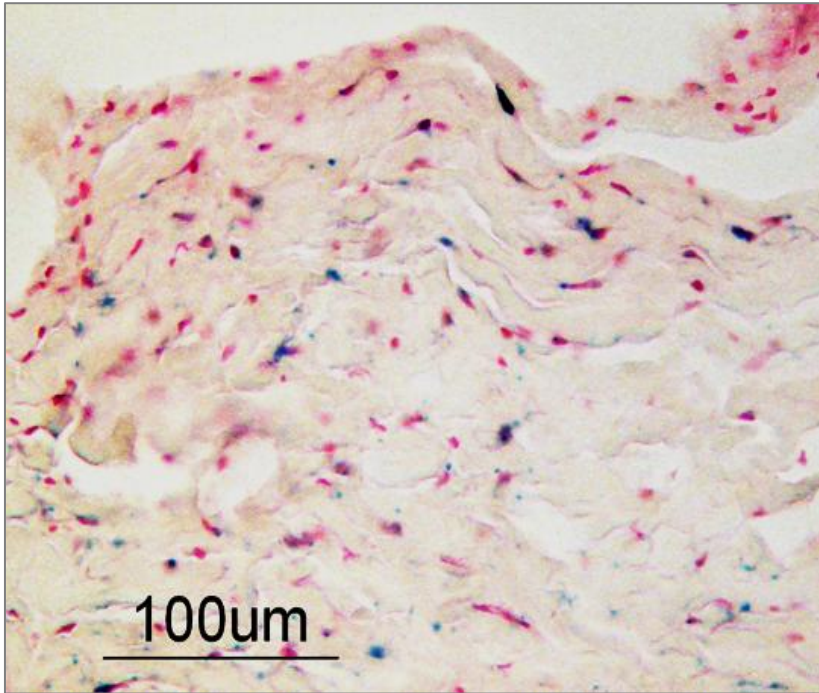
Normal Skin



Tumour Tissue

Figures modified from Signoroni et al, 2007

Lineage tracing of desmoid tumor cells

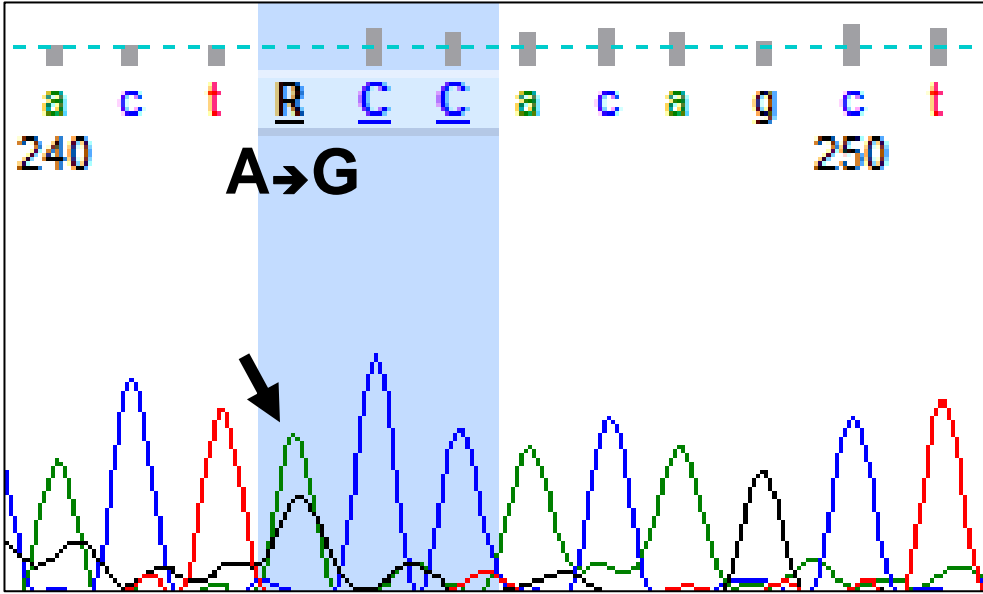


NG2-Cre; Rosa26R^{lacZ}; Apc^{+ / 1638N}

Courtesy of Dr Shingo Sato

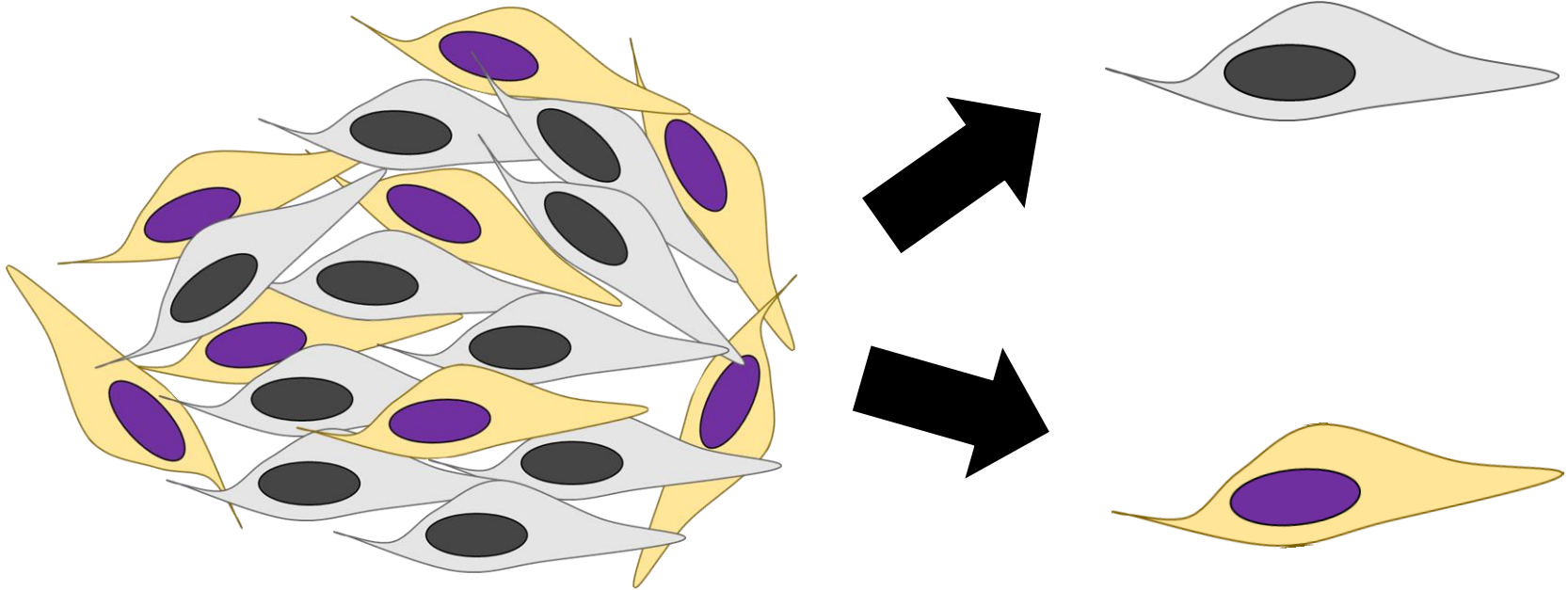
Desmoid tumor β -catenin sequencing suggests mutational heterogeneity.

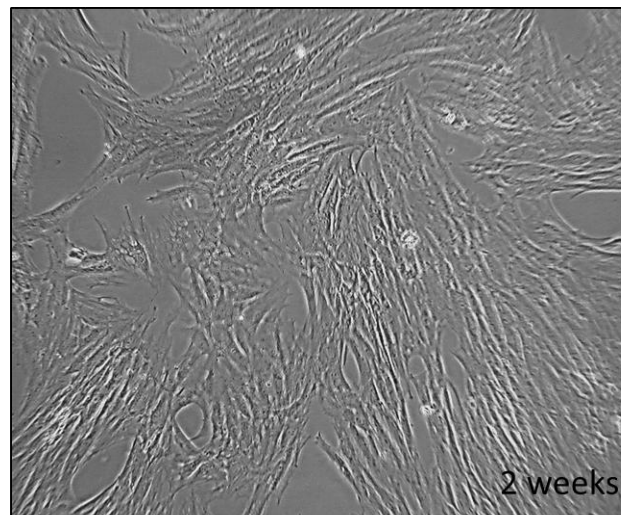
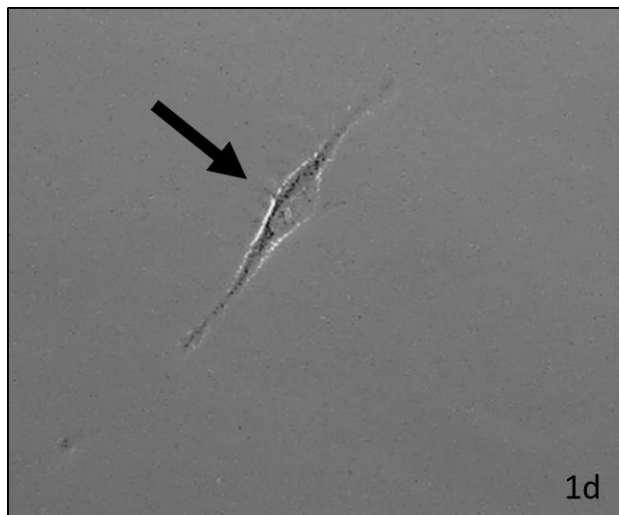
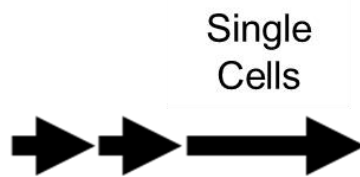
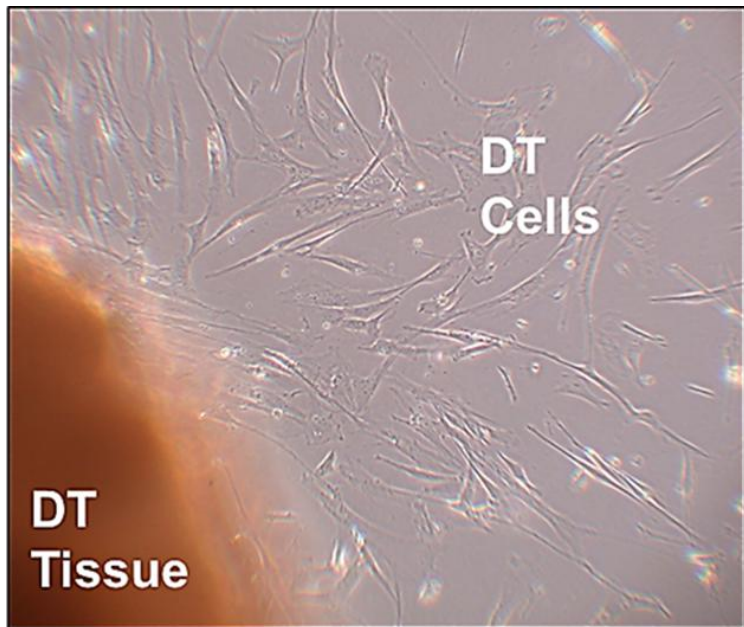
Original Desmoid Tumor Primary Culture



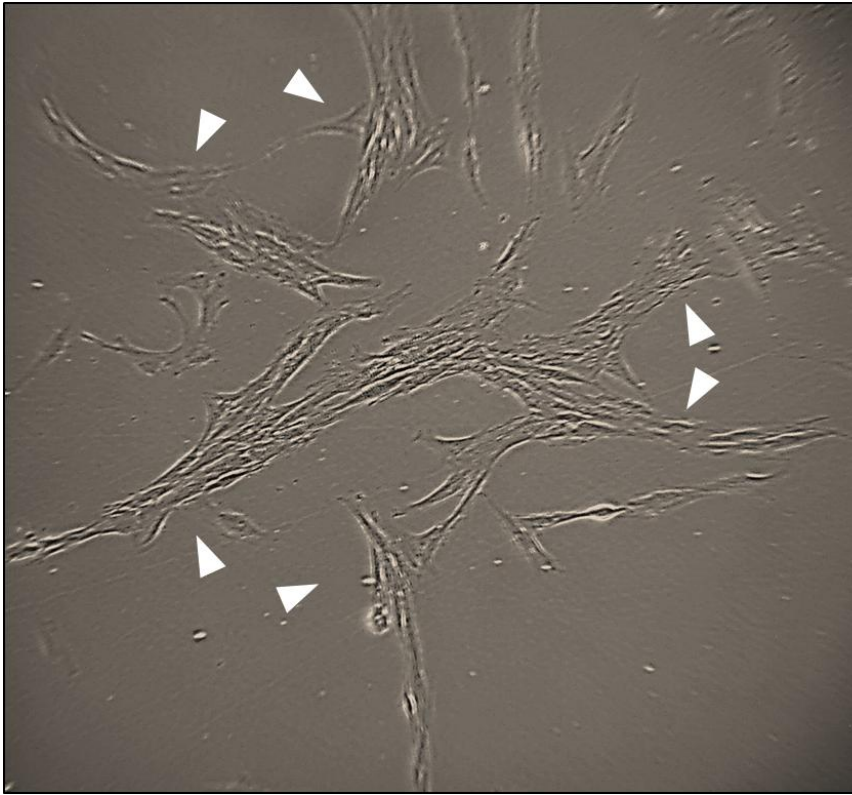
T41A

Aim: Establish single cell-derived clones to study desmoid tumor heterogeneity

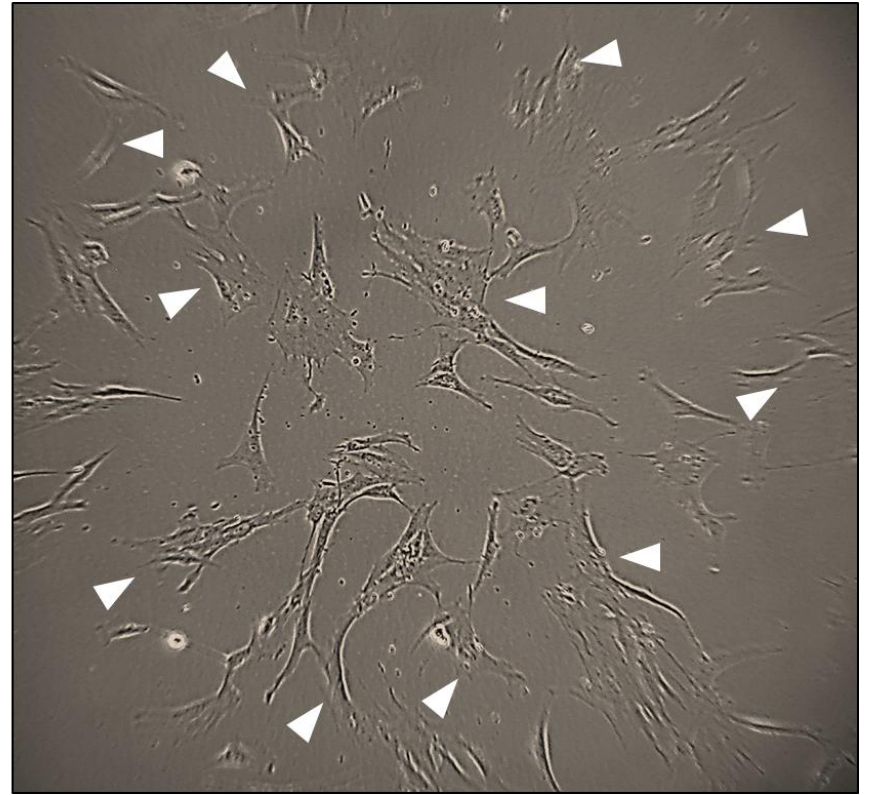




Clones from the same sample display differential growth morphology

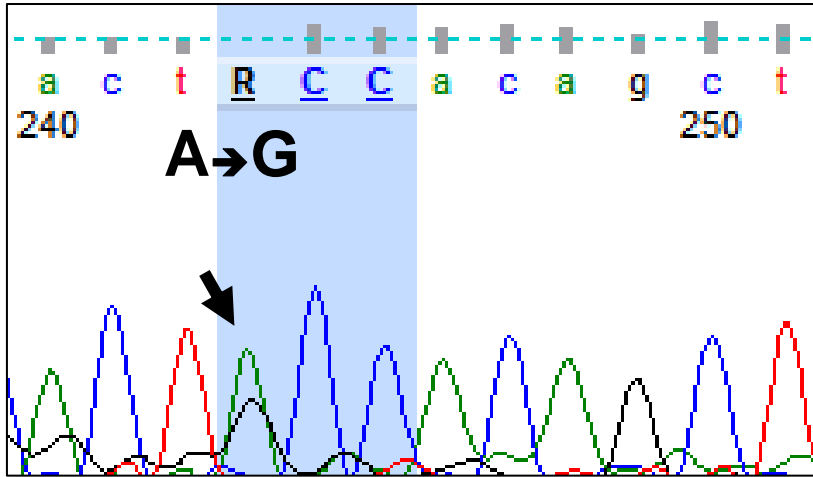


**Branched Growth
(Clones 1 and 2)**

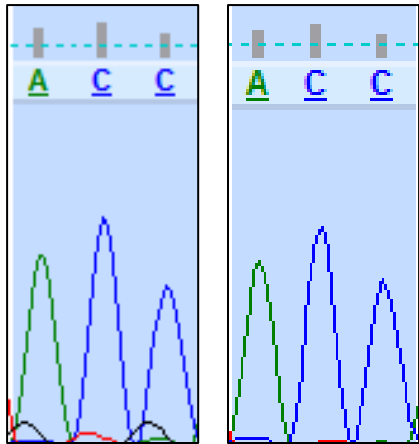


**Spreading Out Growth
(Clones 3 and 4)**

Original Desmoid Tumor Primary Culture

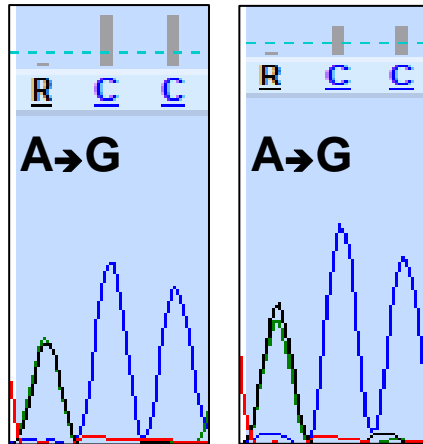


Clones 1 and 2
(wildtype)



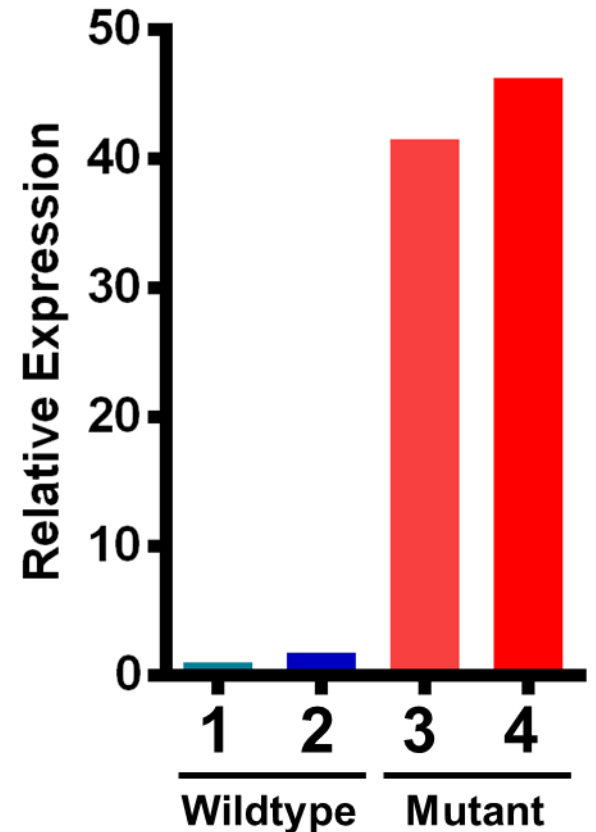
Branched
Growth

Clones 3 and 4
(T41A mutant)



Spreading Out
Growth

β -catenin Activity
(*AXIN2* Expression)



Conclusions

- Primary cultures of desmoid tumors can contain a **heterogeneous mixture** of normal (wild-type) and mutant cells.
- We can establish colonies out of **single mutant cells and single normal cells** from the same desmoid tumor sample:
 - Study differences in characteristics and behavior **between** mutant and normal cells.
 - Study differences in characteristics and behavior **within** mutant cells or normal cells.
- We can modify **growth conditions** for individual mutant clones to understand what influences their growth (factors, inhibitors, other cells/clones).

Acknowledgements

Dr. Benjamin Alman

Raymond Poon



My Students

Magdalene Au

Jessica Liu

Jillian Loree

Angela Ma

Tansy Zhao



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