Expression of ALDH Isoforms in Colon Tumorigenesis

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INTRODUCTION

- Aldehdyde dehydrogenase (ALDH) has been identified as a reliable biomarker for colorectal cancer (CRC) stem cells
- There are 19 different isoforms of ALDH each of which play a role in balancing the proliferation and differentiation of colorectal stem cells (SC)
- It is not known which isoforms are important for colonic stem cell function
- **Hypothesis: Colonic SC's express unique ALDH isoforms and aberrant expression of these isoforms decreases differentiation and increases growth of SC's in CRC**

References

- Cancer Stud Mol Med Open J. 2015. 2: 87-95.
- Cancer Lett. 2015. 369: 50-57.

MATERIALS & METHODS

- Immunofluorescence staining
- RNA isolation and PCR
- Protein extraction and Western Blot
- Cell culture and cell counts

RESULTS

Stem Cells in Colon Crypt

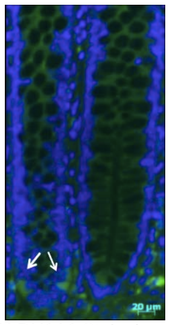

Figure 1: ALDH1A1 Stain, known biomarker for Stem Cells

ALDH2

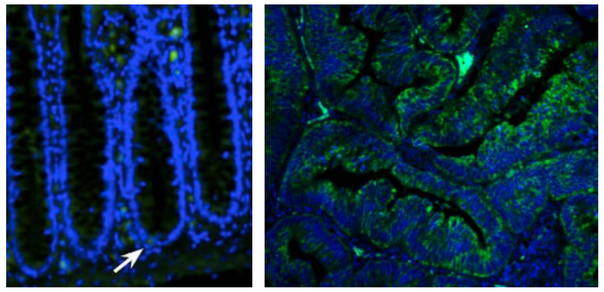

Figure 2. ALDH isoform immunostaining of matched patient samples.

ALDH7

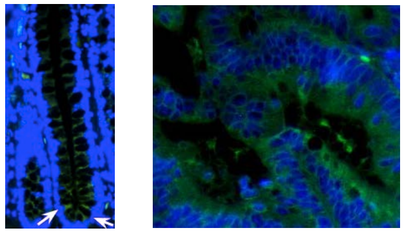

Figure 3: ALDH isoform immunostaining of matched patient samples.

ALDH3A1

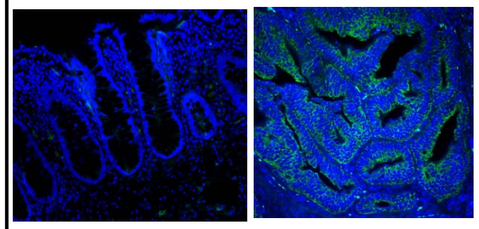

Figure 4: ALDH isoform immunostaining of matched patient samples.

ALDH1A3

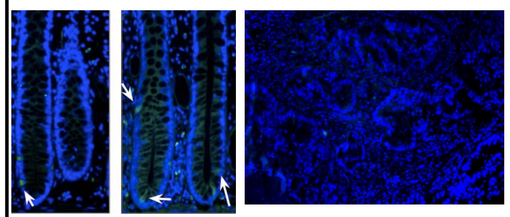

Figure 5: ALDH isoform immunostaining of matched patient samples.

ALDH4A1

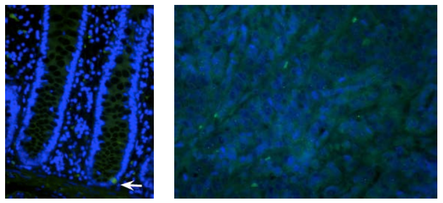

Figure 6: ALDH isoform immunostaining of matched patient samples.

ALDH6A1

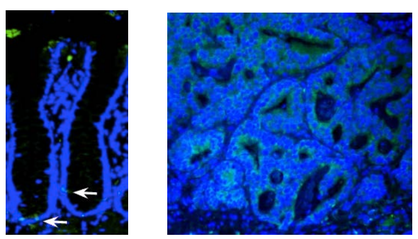

Figure 7: ALDH isoform immunostaining of matched patient samples.

Results from Immunofluorescence Staining

Isoform	Expression in Tumor relative to matched normal sample
ALDH 2	Elevated
ALDH 7A1	Elevated
ALDH 3A1	Elevated
ALDH 1A3	Decreased
ALDH 6A1	Elevated
ALDH 4A1	Unable to tell

LIMITATIONS

- The only limitation that we experienced was the lack of patient samples for Western blot analysis.

CONCLUSIONS

- Variable expression in isoforms; there is a need to look at protein in western blot analysis
- ALDH 2, 7A1 and 3A1 play a role in colon tumorigenesis
- These isoforms will be targets for knockdown analysis

FUTURE WORK

- More complete profile of the target ALDH isoforms
- Quantitative comparison of protein expression through Western blot analysis
- Currently working on growing and expanding ALDH7A1 knockdown clones in HT29 cells to assess protein function in vitro.

CLINICAL IMPLICATIONS

- Understanding how isoforms of ALDH contribute to stem cell overpopulation in colon tumor formation may lead to the development of new more effective treatments for colorectal cancer

ACKNOWLEDGEMENTS

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