Membrane-localized Keratin-14 Promotes Invasion*

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Abstract. Metastasis is the main predictor of outcome for patients with cancer, yet the molecular mechanism driving invasive phenotypes is not well understood. Keratin 14 (K14) is a known molecular biomarker that is correlated with poor outcomes in breast cancer patients. In this study, we apply our automated computer model that quantifies the invasive potential of tumors to characterize K14 expression as it relates to invasion. We test the hypothesis that K14 is directly correlated to invasion versus the alternative hypothesis that size is the main predictor. We used two different transgenic mice (PyMT and C3(1)-Tag) as our breast cancer tumor models. Organoids were generated from these mice, and each organoid had a corresponding differential interference contrast image, K14 image, and an invasive potential score generated using our automated system. The parameters assessed include the following: entire K14 expression, peripheral K14 expression (edges of the organoid), central K14 expression (center of the organoid), and organoid size. Peripheral K14 expression showed the strongest correlation with invasion scores for both types of transgenic mice. The results suggest that K14 expression in cells located in the periphery may be an important marker of invasion.

Keywords: Metastasis · Tumor Invasion · Keratin 14 · Spectral Analysis · ...

1 Introduction

Alternative title: Morphological features of organoid invasion are correlated to membrane-localized Keratin-14 expression

- Biology intro (what is our audience). The two different mice models.
- How K14 expression is related to metastasis.
- The use of image analysis for feature extraction, lit review.
- Why spectral score is a good measure for invasion potential.
- Paper outline

* Supported by organization x.

Metastasis stats.
What are organoids.
Quantitative phenotypes.
Hypothesis: a) K14 expression is correlated with organoid invasion.
b) organoid size is correlated with invasion score.
Research questions:

2 Methods

Fig. 0: Make figure showing the 'pipeline'.

- Experimental protocol. Ask Veena to write this part.
  100-300 organoids from 4 mice.
- Image acquisition and organoid periphery. Veena.
  Use ImageJ to mark the periphery of the organoids from DCI microscop images.
- Image segmentation. Andrei to write about convolution kernel.
- Spectral score. Reference Joel's paper. Disclose scripts?

2.1 Database

A total of 4 PyMT and 4 C31T mice were used to generate a total of {} organoids, which were then cultured in collagen I gels for 5 days. At day 5, they were imaged, an average of 16 per sample. Differential interference contrast (DIC) microscopy yielded 1040×1388 pixel images. Microscope optics defined a resolution of 0.51190476 μm per pixel, corresponding to a 532.4×710.5 μm field of view. Images were manually tracked in ImageJ [1] to define the organoid boundaries as pairs of points $\{x_v, y_v\}$ for $v \in [0, V-1]$. The total number of points V depended on the manual tracking, and the spacing between adjacent points was similarly variable.

2.2 Spectral Analysis

3 Results

Start adding figures here.
Q: Are we keeping the large vs. small organoids? Q: should this be split into PyMT section and C31Tag section?

Fig. 1: show each step in the pipeline from DCI to spectral score for 2 organoids (one with low spectral score and one with high spectral score).

Fig. 2: show figures for the convolution kernel used to get peripheral K14 expression.

Fig. 3: Correlation plots PyMT

Fig. 4: Correlation plots C31Tag

Table 1: Summary statistics

4 Discussion

Future directions: Test our method on Patient derived organoids, PDOs.
Does organoid invasion score correlate with patient outcome?

5 Conclusion

References

1. Schneider CA, Rasband WS, Eliceiri KW. NIH Image to ImageJ: 25 years of image analysis. Nature methods. 2012;9(7):671–675.