Figure 1. Schematic of the “tree” built to allow for all possible choices from a toy consensus string, ‘CA/TN.’

Twelve total binding sites, and eleven unique binding sites, were identified within the promoter region, from the 128 possible binding sites. Eight binding sites were identified with at least one capital letter, corresponding to strong preference for that nucleotide over its partner (e.g., preference for “A” in “A/t”).

These results suggest a possible novel mechanism of cell fate determinant regulation. Prospero is vital to stem cell fate determination, particularly in the neural system (Choksi et al., 2006; Spana and Doe, 1995; Doe et al., 1991

proliferate and differentiate appropriately, allowing for development of a tumor, which is often compared to a wound that does not heal (Dvorak, 1986). Disrupted lateral inhibition due to altered Notch signaling may allow for rampant proliferation of one cell type rather than a controlled cell fate distribution (Arnold et al., 2015). In fact, Notch dysregulation has been implicated in several cancers (Nickoloff et al., 2003). Null mutation of in neural cells was linked with tumorigenesis when these cells were transplanted to the abdomen (Caussinas and Gonzales, 2005). Furthermore, the disruption of Prospero-mediated expression of stem cell genes and differentiation genes induced excessive cell proliferation (Choksi et al., 2006). Interestingly, vertebrate homolog of Pros, Prospero homeobox 1 (PROX1) is considered a tumor suppressor in the context of some cancers, and a progressive factor in others (Lu et al., 2012). Together, these findings implicate a role for Prospero and Notch in cancer, and beg further elucidation of possible interactive roles.

Figure 2. Schematic of lateral inhibition regulated by Notch in the intestine. Briefly, reduced Notch activity in one cell (blue) is associated with increased production of the ligand, Delta. Production of this ligand induces heightened Notch activity and reduced ligand production in neighboring cells (red). This forms a positive feedback loop, and initially small differences in Notch levels are amplified, resulting in opposite cell fate. From Sancho et al., 2015 (Figure 2).

Several studies have demonstrated that Prospero is a downstream target of Notch (Hayashi et al., 2008

Notch signaling is limited. As a notable exception, Charlton-Perkins et al. (2011) report that in the retinal system the transcription factors Prospero and Pax2 regulate cell fate via the Notch pathway in the retinal system. However, the authors propose that Pros acts indirectly on the Notch pathway by increasing pERK levels, thereby activating Delta and reducing Notch expression. In contrast to this model, the current results suggest a direct action of Pros on the promoter region.

Further computational, statistical, and empirical investigation is needed to determine the validity of this direct action by Prospero on Notch signaling. First, the statistical significance of this event (i.e., eleven unique 7-mers found in a 1000 nucleotide sequence from a list of 128 possible 7-mers) should be determined. Furthermore, the same code may be applied to examine individual components of the Notch pathway, including pERK and Delta, to determine whether binding sites are distributed across elements of the signaling pathway. If both these measures prove promising, lab work may confirm the existence of Pros binding sites in the promoter region. For instance, DNA footprinting may be used to examine the regions of DNA that are bound versus unbound

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