Interstitial Cells of Cajal and the Promise of Single Cell Molecular Analysis

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Editorial

The interstitial cells of Cajal (ICC) are pacemaker cells organized in networks located in all layers of the intestines [1,2]. Together with the myenteric neurons and the smooth muscle cells, they comprise the machinery that controls the peristaltic movements [3,4]. However, the individual contribution of smooth muscle and ICC to the different motility patterns present throughout the GI tract is not completely described [5]. This task has proven difficult because of the overlapping mechanisms to produce motility in the gut, as well as the close embryonic and anatomic relationship of ICC and myocytes, which underlies the myocyte-like differentiation of ICC after several days in culture [6] impeding the generation of pure ICC cultures and the performance of “bulk” molecular analyses.

Recent attempts to purify ICC and define their transcriptomic differences with myocytes have identified genes that can be used to discern between the anatomically distinct populations of ICC and myocytes at the molecular level [7,8]; unfortunately, the required FACS enrichment of ICC to obtain a transcript library hampers the identification of ICC subtypes with physiological functions. The existence of these subtypes has been suggested previously in W/W (v) embryos and anatomic relationship of ICC and myocites, which underlies the myocyte-like differentiation of ICC after several days in culture [6] impeding the generation of pure ICC cultures and the performance of “bulk” molecular analyses.

The electrical activity of ICC originates from the interplay between pumps and channels, generating their oscillating pacemaker activity. Although most of the conductances in ICC are known, there are “orphan” conductances that have not a particular gene associated to them. Such is the case of the maxi channel, which has proven elusive to identify as shown by knockdown studies performed in fibroblasts [18].

In summary, the study of ICC physiology as well as the study of GI motility can tremendously benefit from the implementation and use of the single cell molecular analysis tools available today. The accumulated knowledge in the field has produced many unique experimental settings and approaches which, combined with the use of more precise molecular tools, opens possibilities for solving questions that have stood for more than 100 years.

References

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