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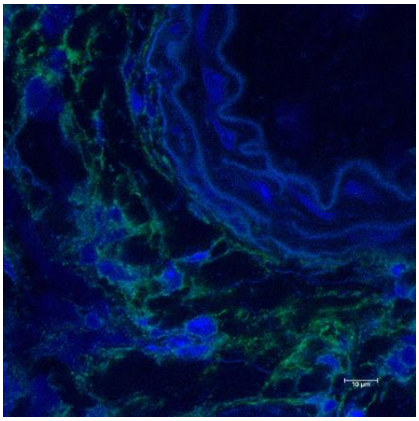
TELOCYTE IDENTITY – A DISTINCT CELL OR A DIFFERENT PHENOTYPE [TIDY]

Executive Summary

Telocytes (TCs) were discovered and characterized by electron microscopy in 2005. Initially, these newly described interstitial cells were named “Cajal-like interstitial cells”. However, in 2010 the groups led by Prof. L.M. Popescu and Prof. M.S. Faussone-Pellegrini suggested renaming these cells to *telocytes*, to avoid confusion with the gut-specific Cajal cells.
TCs have since been identified in a plethora of tissue types and organs, almost exclusively by electron microscopy, recognized by their distinctive morphology, with very long and very thin extensions, named *telopodes*. Although TCs are relatively large cells (reaching up to 100 μm in length), their extensions are remarkably thin, often under 100 nm in diameter, making them practically invisible by conventional bright-field microscopy. Unfortunately, although a number of studies have attempted to find one or more molecular markers for these cells, such specific proteins have proven elusive. Moreover, this specific area of investigation is plagued with controversy, as some published literature reviews on TCs incorrectly interpret and/or reference original studies on the molecular identity of TCs.
Based on previously published experimental data from other groups and from our own analysis of publicly available transcriptomic data, this study aims to test the specificity of various likely molecular candidates, with the aim of finding a specific marker that allows the differentiation of TCs from other cells in the fibroblast family.



Confocal microscopy. PDGFRα (green) labels telocytes in the perivascular space.

In Phase 1 this study focused on the analysis of publicly available protein databases (The Human Protein Atlas, UniProt; STRING) and of the previously published literature, with the aim of shortlisting likely molecular markers, initially for heart tissue. The likely candidates were CD34, CD90, PDGFRα, Foxl1, but Tcf21 and Nkx2-5 were also considered, due to their proven involvement in heart development. Of these, PDGFRα, Foxl1, Tcf21 and Nkx2-5 were finally selected for experimental testing.
Labeling of adult mouse cardiac tissue for these proteins showed that Foxl1 and Nkx2-5 have very low or absent levels of expression (Tcf21 expression will be further analyzed in the next phase of this study), whereas CD34 and CD90 are not specific to a single cell type. Despite these setbacks, **PDGFRα** labeling was successful, allowing localization of a cell population forming elaborate networks of extensions in the perivascular space of arteries. Importantly PDGFRα is not present around capilaries, on cardiac muscle cells or on other interstitial cells from the deep myocardium, suggesting high specificity to a particular type of interstitial cell. This particular distribution matches electron microscopy observations of TCs.
Indeed transcriptomic data from mouse cardiac tissue (Tabula muris), confirms PDGFRα is expressed in 46.2% of cardiac cells classified as fibroblasts.

This result remains to be confirmed by further immunolabeling, using more precise techniques, such as immuno-electron microscopy and/or correlative light and electron microscopy. Such techniques will confirm if labeled cells have the expected ultrastructural characteristics of TCs.