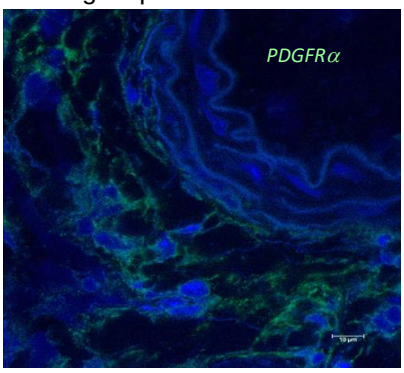
TELOCYTE IDENTITY – A DISTINCT CELL OR A DIFFERENT PHENOTYPE

Principal Investigator - Mihaela Gherghiceanu [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 and and on publicly available transcriptomic and proteomic 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.

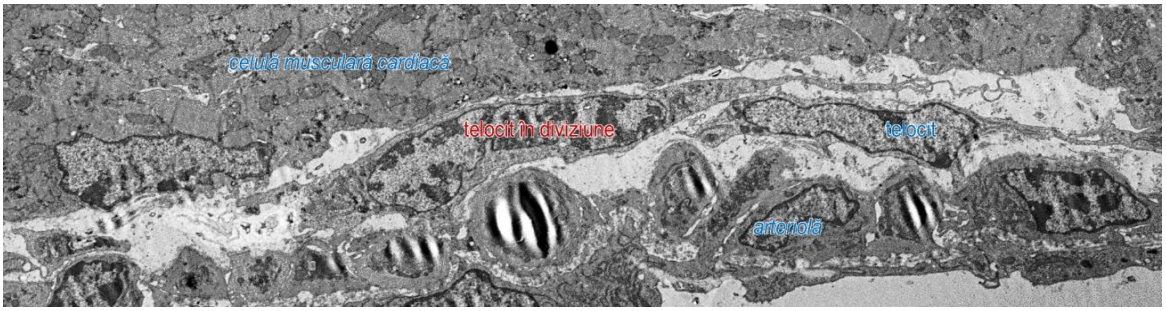


Confocal microscopy. PDGFRα (green) labels telocytes in the perivascular space of an adult mouse heart.

In this study we analyzed open access databases (The Human Protein Atlas, UniProt; STRING) to shortlist possible specific markers for heart TCs. The likely candidates were CD34, CD90, PDGFRα, Foxl1, Tcf21 and Nkx2-5, due to their proven involvement in heart development. For most of these proteins we could not detect a specific signal. Encouragingly, interstitial cells in the adult mouse heart were positive for PDGFRα staining. These cells localize in the perivascular space, a region that can be more easily characterized by electron microscopy. The fact that anti-PDGFRα only stains certain interstitial cells, but does not stain capilaries, cardiac muscle or all other types of interstitial cells, makes it a promising candidate as a specific TC marker.

This result is in agreement with our analysis of the mouse heart transcriptome (Tabula muris), which shows that PDGFRα is expressed in 46.2% of generic fibroblast cells. Further studies are needed to validate **PDGFRα as a TC-specific marker**.

In our ultrastructural study of the developing mouse heart we found that TCs appear only after the formation of the epicardium (E14.5), with a likely origin in the proepicardium. TCs are abundant in the one-day old mouse heart when they actively divide, thus contributing to the cardiac hyperplasia of the post-natal period. Notably, we observed TCs undergoing division in the newborn mouse heart, when dividing cardiomyocytes and Schwann cells can also be observed.



Transmission electron microscopy image showing a telocyte undergoing cell division (telophase), localized between an arteriole and cardiomyocytes in the 1-day old mouse heart.

Our study indicates that TCs are resident cardiac cells, sharing a common origin in the proepicardium with other cardiac cells. Furthermore, cardiac TCs have high tissue specificity and PDGFRα can be used as a specific marker for this cell type.