

Interstitial Cajal-like cells (ICLC) in human atrial myocardium

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Abstract

We present here visual evidence for the existence of a new type of interstitial cells in human atrial myocardium: interstitial Cajal-like cells (ICLC). These cells fulfil the so-called 'platinum standard' (a set of 10 ultrastructural criteria for the positive diagnosis of ICLC). Conventional transmission electron microscopy (TEM), followed by reconstructions from serial photomicrographs, revealed typical ICLC with 2 or 3 long, moniliform processes (several tens of micrometers long and 0.1-0.5 μm thick), emerging from the (small) cell body. Cell processes dichotomously branch and have mitochondria (at the level of dilations), caveolae and Ca^{2+} release units. Cell prolongations establish close spatial relationships between each other, as well as with capillaries, myocardial cells, and other connective tissue cells. Our preliminary data suggest that ICLC exist in rat ventricular myocardium, too.

Keywords: human myocardium • interstitial cells of Cajal • Cajal-like cells • atrium • stromal cells • cell processes • caveolae • ultrastructure • electron microscopy

Motto:

'Identifying ICC outside the gut will, at this moment, require EM and almost in all locations this has not been done to any significant extent.'

Huizinga JD & Faussonne-Pellegrini MS.

About the presence of interstitial cells of Cajal outside the musculature of the gastrointestinal tract, 2005 (ref. [1])

Our knowledge about the extradigestive distribution of interstitial cells with Cajal-phenotype is still in the beginning. However, in 2005, the 'detection pace' of ICLC outside the digestive tract was unexpectedly

high [2–11; see refs. 12–13 for reviews]. In spite of this peak of scientific interest, the myocardial interstitium received little attention, although some indicative data were published before 1900 [ref. 14; see p. 976, this issue].

The study was performed on archived atrial Epon-embedded tissue specimens, previously obtained with informed consent from patients undergoing cardiac surgery. This study was approved by the Bioethics Committee of the "Carol Davila" University of Medicine and Pharmacy, Bucharest, according to generally accepted international standards.

Tissue specimens were fixed in buffered glutaraldehyde 2.5% and then postfixed in buffered OsO_4 1%, dehydrated in ethanols and propylene oxide. Ultrathin sections (50 nm) were collected on Formvar-coated copper grids, stained with uranyl acetate and lead citrate, and observed in a CM 12 Philips electron microscope.

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HUMAN ATRIAL MYOCARDIUM

1

INTERSTITIUM BETWEEN
FOUR MYOCARDIAL CELL BUNDLES

4

m

INTERSTITIAL
CAJAL-LIKE CELL
(ICLC)

ID

ID

Fig. 1. Image gallery of Cajal-like cells from atrial interstitium; TEM (photographic reconstruction), illustrating the long thin processes. Note the characteristic aspect of the processes emerging from the Cajal-like cell body: length, thickness and moniliform appearance. Typical for labyrinthine system of Cajal-like cell processes is the existence of a sinuous traject among at least four cell bundles. Other Cajal-like cells seem to surround blood vessels. This aspect was observed in both transversal or longitudinal sections.

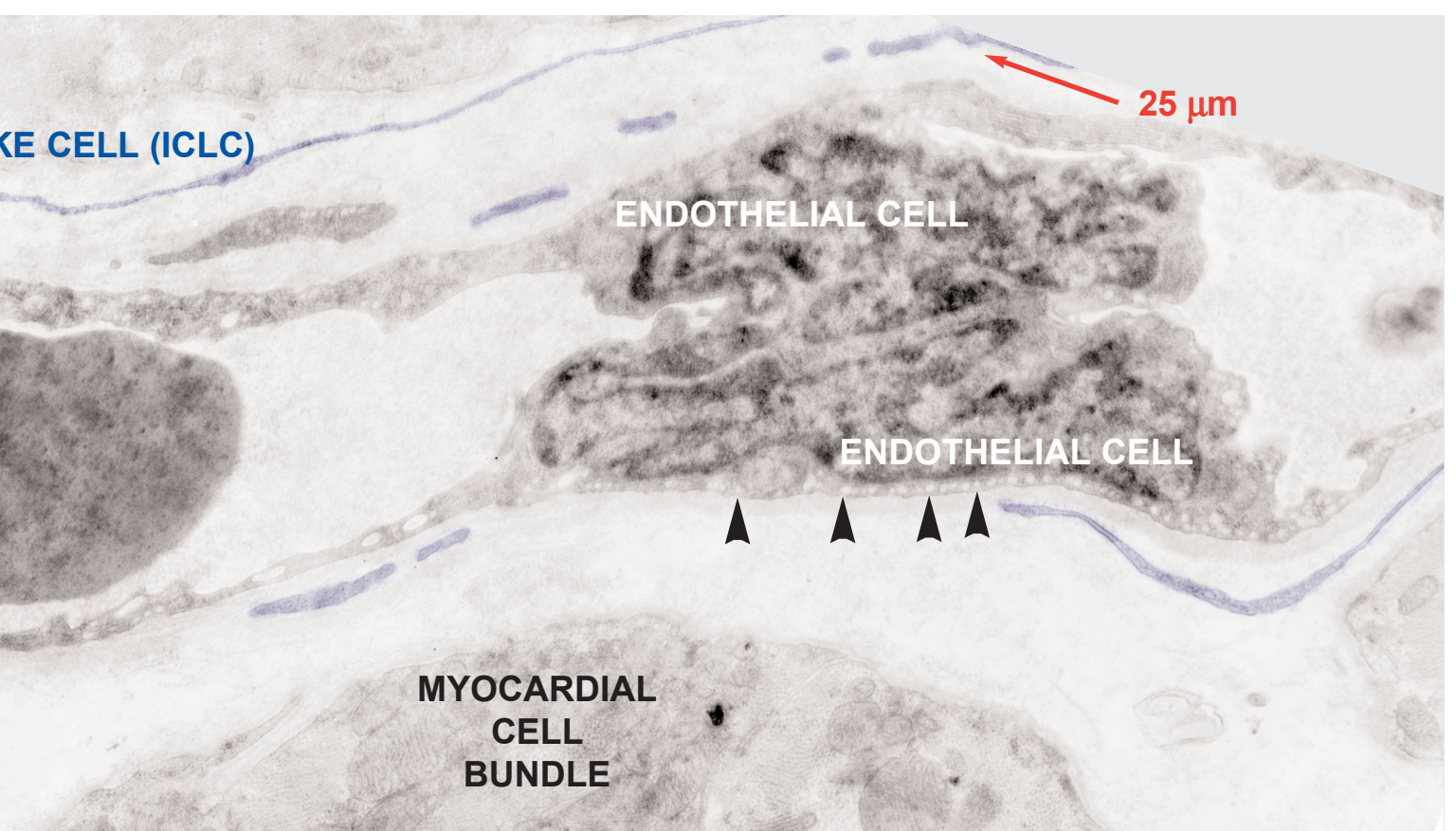
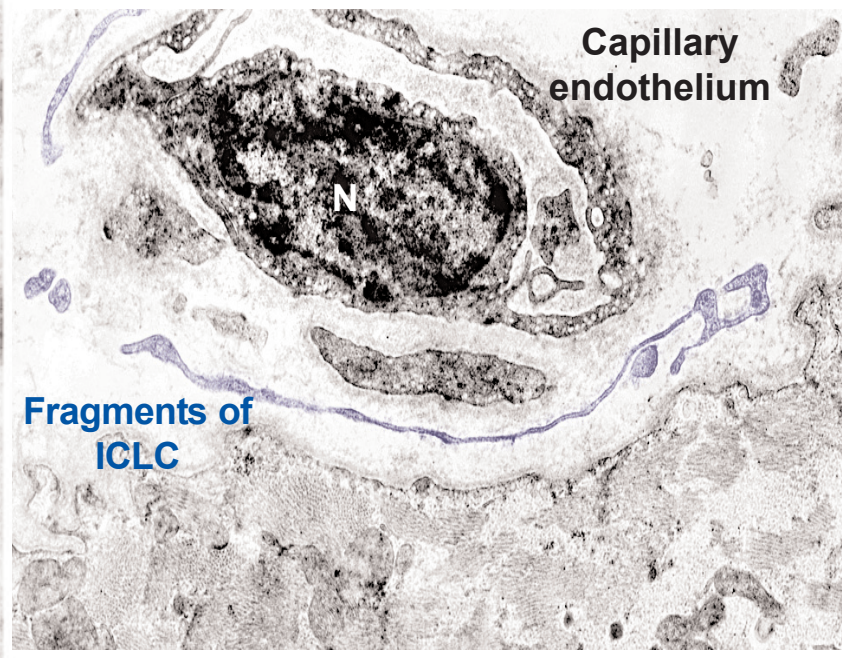
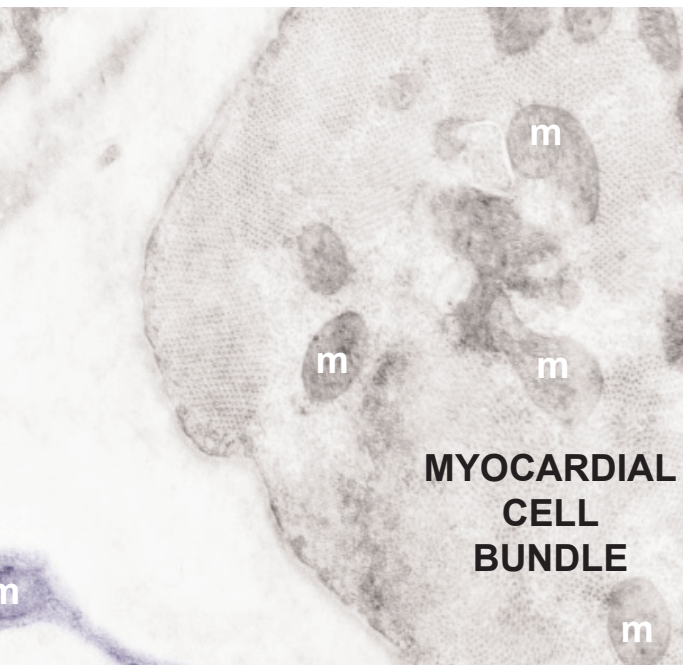
Abbreviations and symbols: arrowheads = plasmalemmal vesicles/caveolae; ID = intercalated disks; m = mitochondria; N = nucleus.

INTERSTITIAL CAJAL-LIKE CELL

CAPILLARY
(longitudinal section)

ERYTHROCYTE

Fragments of
INTERSTITIAL CAJAL-LIKE CELL (ICLC)



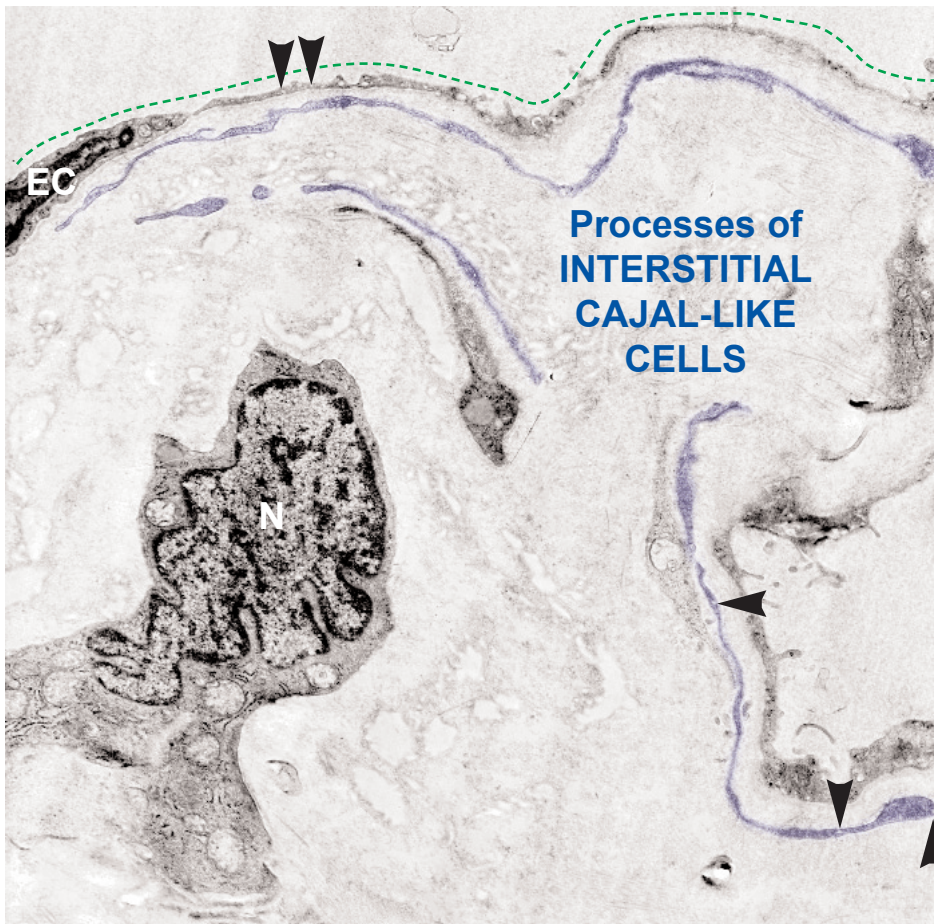
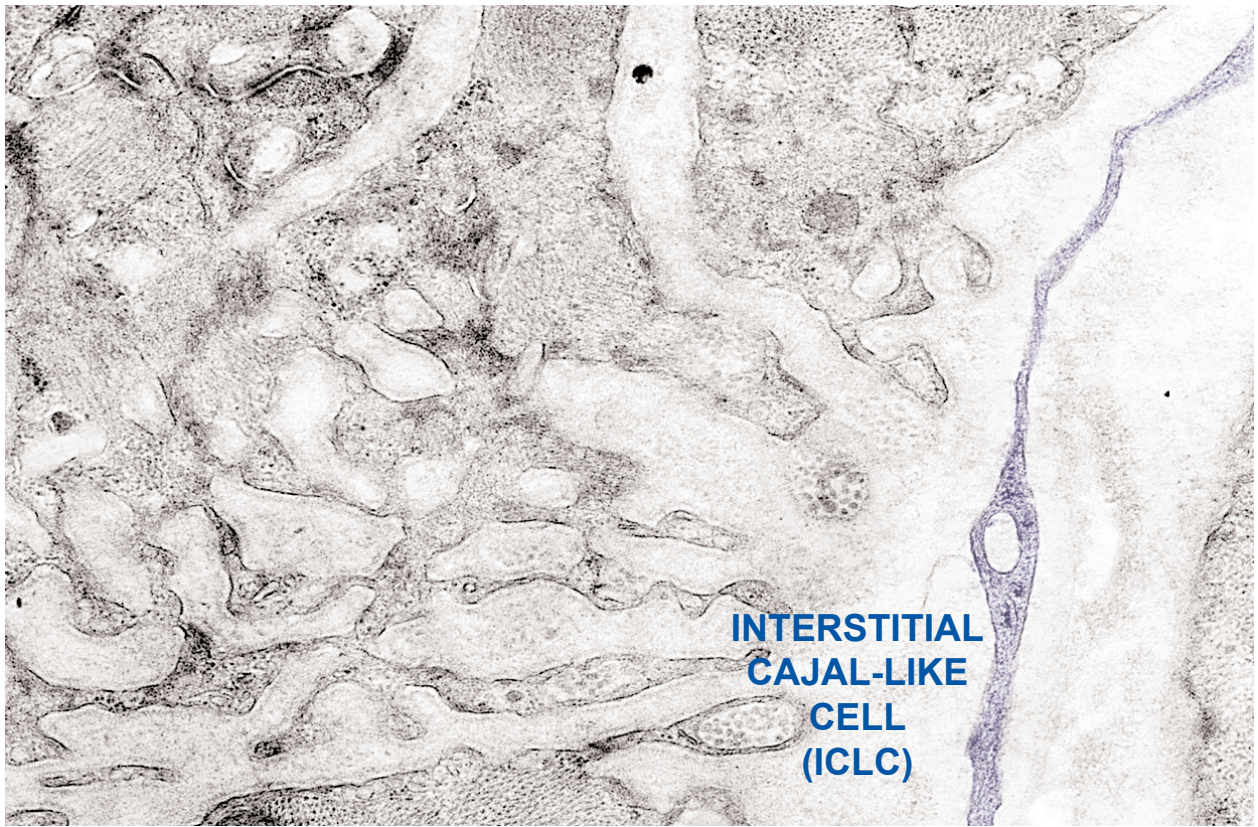


Fig. 2. Human atrial myocardium TEM. Different cell-body shapes of Cajal-type cells may be observed. Note the characteristic aspects of processes: length, unequal thickness and the nature of the surrounding area (capillaries or myocardial cell bundles). N = nucleus, EC = endothelial endocardial cell, dotted line = endocardium profile, arrowheads = caveolae/plasmalemmal vesicles.

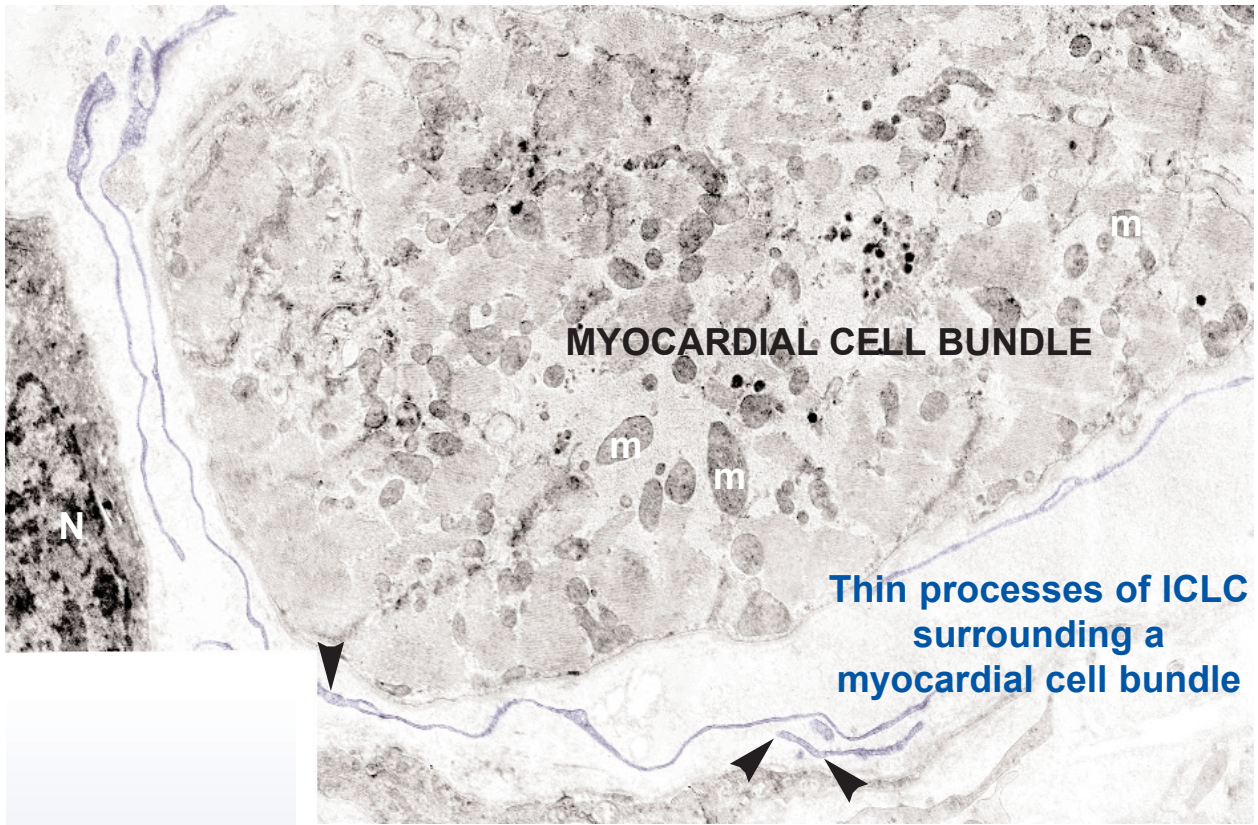
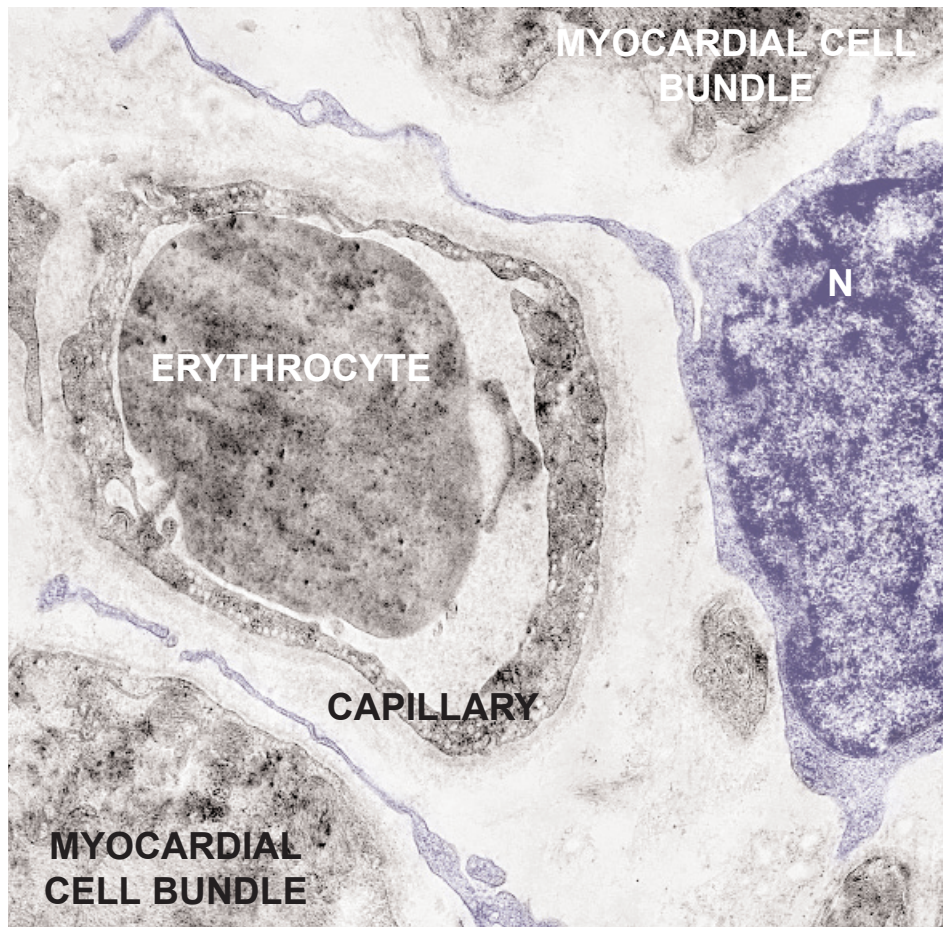


Fig. 3. Human atrial myocardium TEM. When present near endocardial endothelial cells, the Cajal-like cell processes seem to follow the shape of endocardial layer. Near the working cells, sometimes, the labyrinthic system of Cajal-like cells is very well developed. Arrowheads = caveolae.



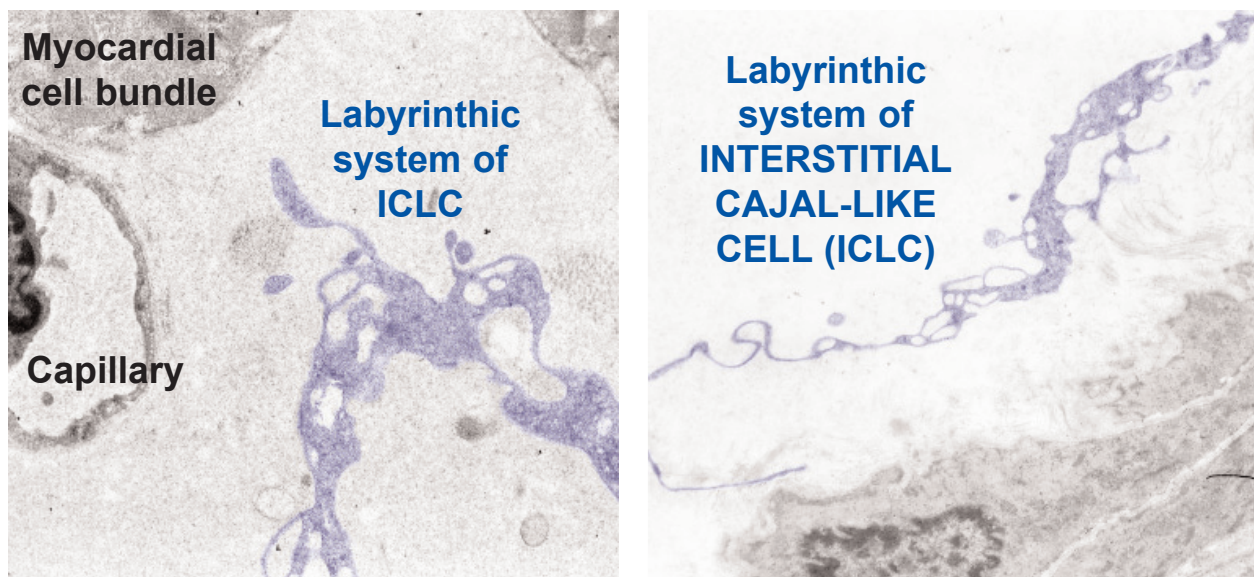


Fig. 4. Rat ventricular myocardium TEM. A striking ultrastructural match with cells of human origin was observed concerning the extent of the labyrinthic system.

Digitally colored TEM images have been obtained from human atrial ultrathin-sections showing several cells which fulfil the ultrastructural requirements imposed by the 'platinum standard' [5] for diagnosis of Cajal-like cells. Emphasis was laid on: a) presence of typical long cellular processes (number, length, thickness, aspect, branching, labyrinthic system, and b) identification of the target (ultra)structures of ICLC processes: capillaries, myocardial cell bundles, connective tissue cells or other ICLC (Fig. 1–3).

In order to check the presence of Cajal-like type cells in ventricular interstitium, ultrathin sections of rat tissue specimens were examined by TEM. Data presented in Fig. 4 show a very similar morphological profile with human interstitial atrial cells. Even though not mentioned (1972 was too early!), the presence of such cells was previously recorded in electron micrographs of 7 days old rats [see fig. 9 in ref. 15].

Further characterization of cardiac ICLC by immunocytochemistry, immunofluorescence, (non-)conventional light microscopy, cell culture and electrophysiology is underway.

Acknowledgements

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