

Snapshots of mammary gland interstitial cells: methylene-blue vital staining and c-kit immunopositivity

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Abstract

We show here that methylene-blue supravital staining of specimens from normal human mammary-gland reveals (selectively) interstitial (stromal) cells, with 2–3 long (20–80 μ m), thin, moniliform processes. Such cells appear c-kit/CD117 positive, either by immunohistochemistry (IHC) or immunofluorescence (IF). Since these features (affinity for methylene blue, c-kit positivity, and characteristic processes) define archetypal interstitial cells of Cajal (ICC) in light microscopy, our results suggest the existence of Cajal-like cells in the interstitium of human normal mammary gland.

Keywords: human mammary-gland • methylene-blue vital staining • CD117 • interstitial cells of Cajal • Cajal-like cells • cell processes • stromal cells

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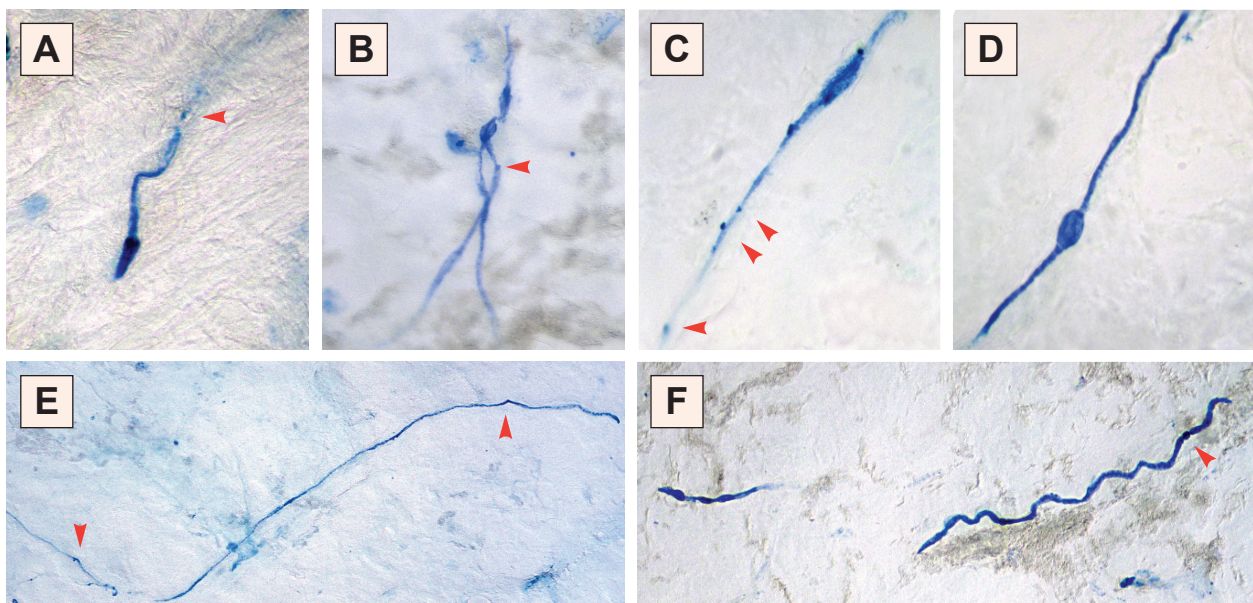


Fig. 1A–F. Methylene blue supravital staining of normal human mammary-gland specimens. Note selective Prussian-blue color of some interstitial cells, with one or two very long, moniliform processes. Initial magnification: 20x (A, B), 100x (C, D), 10x (E, F).

Recent studies in our laboratory, looking for Cajal-like cells outside the gastrointestinal tract, revealed the presence of such cells in human pancreas, myometrium and fallopian tube [1-3]. We provide here evidence for the existence in the interstitium of inactive human mammary gland of cells with similar features to the

cells described by Ramon y Cajal, in other organs, more than a century ago.

Techniques used for supravital methylene-blue staining [2], IHC, on fresh and paraffin-embedded tissue [1], and indirect IF [3] have been described in detail elsewhere. An electron microscopy study is under way.

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Our snapshots deal with the 'hot diagnostic topics' of Cajal-like cells: positioning in interstitium, affinity for methylene blue (Fig. 1), c-kit positivity, and typical long cellular processes (Fig.2). Despite the fact that the positive expression of c-kit in normal breast tissue has been reported [4], the affinity of stromal cells for methylene blue has not been tested (according to biomedical journal literature from MEDLINE /Pubmed).

It is still unclear how interstitial cells give rise to signals toward their major potential targets since, apparently, there is no close spatial relationship with either epithelial or myoepithelial cells. One may speculate that the spatial distribution may change during lactation. Since the stroma seems to be a crucial target in mammary gland carcinogenesis [5], including phyllodes tumors [6], further characterization of the interstitial Cajal-like cells might have (major) clinical relevance.

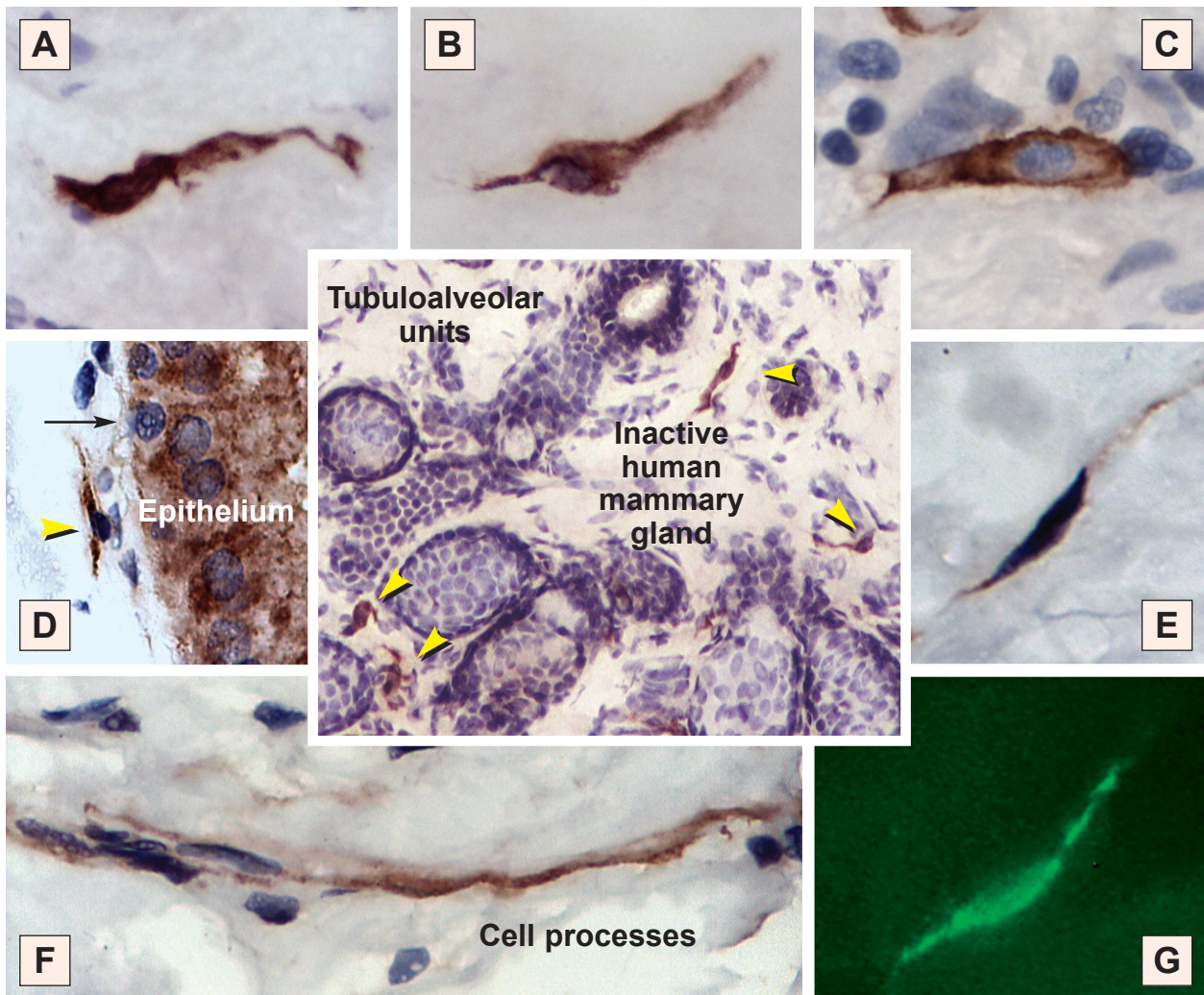


Fig. 2. A–F, IHC, and G, indirect IF for c-kit. A, B, fresh specimens, cryosections. C–F, fixed, paraffin embedded sections. Counterstaining: Mayer haematoxylin. Note in the central image the location of c-kit positive cells, in the interstitium located at a given distance from ductolobular units, excluding epithelial or myoepithelial lineage; yellow arrowheads = c-kit positive interstitial cells; arrow = lymphocyte that has entered the epithelium.

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