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Cell Anatomy: still alive

Ramón Muñoz Chápuli

Department of Animal Biology, Faculty of Sciences, University of Malaga, E-29071 Malaga, Spain

Classical Cell Biology textbooks usually show substantially similar pictures of the eukaryotic cell. The standard cartoon always includes the nucleus, mitochondria, endoplasmic reticulum, ribosomes and Golgi apparatus floating in a clear and apparently simple cellular milieu. However, novel and more potent imaging techniques have unveiled in the last decade a cell anatomy much more complex than this, arising many questions that remain unanswered. For example, the discovery of nanotubes (the cytoneme) in 1999 revealed a previously unknown system of cell communication (Ramírez-Weber and Kornberg, 1999). Cell nanotubes are long (Fig. 1), thin filaments that connect cells and allow for the exchange of molecules, small organules, or electric signals. The thinner nanotubes (less than 0.7 microns in diameter) carry actin filaments and can operate to transfer portions of membranes between cells. A second, thicker kind of nanotubes also contains microtubules, and they can transport from cell to cell cytoplasm, organelles and large molecules including nucleic acids (Belting and Wittrup, 2008). The physiological role played by nanotubes is still uncertain, but it has been suggested that prions or the HIV can use this way to infect other cells (Gousset et al., 2009; Sowinski et al., 2008).

Other novel structures are the transient clusters of enzymes and other proteins that apparently assemble to accomplish a metabolic function. They were discovered by labeling enzymes with fluorescent dyes, allowing direct observation of their clustering in living cells. These complexes of proteins might improve the efficiency of the metabolic processes acting as «chains of production» of metabolites. An example is the «purinosome», a dynamic assembly of the six enzymes involved in de novo purine biosynthesis. The assembly of the purinosome is controlled by a microtubule network (An et al., 2008; Deng et al., 2012). The «carboxysome», which contains enzymes for carbon fixation in an icosaedric proteinaceous structure (Fig. 2), and the «propanediol metabolosome» would be other examples in prokaryotic cells (Frank et al., 2012). We do not know yet if this spatial organization is the rule for most metabolic processes, nor how the cell machinery controls and regulates the assembly and disassembly of the enzymatic complexes. The term «microcompartment» has recently been proposed as a general suborganellar functional unit shared by prokary-

Corresponding author:
Ramón Muñoz Chápuli. Department of Animal Biology, Faculty of Sciences, University of Malaga, E-29071 Malaga, Spain. Phone: 34-952131853; Fax: 34-952131668. E-mail: chapuli@uma.es

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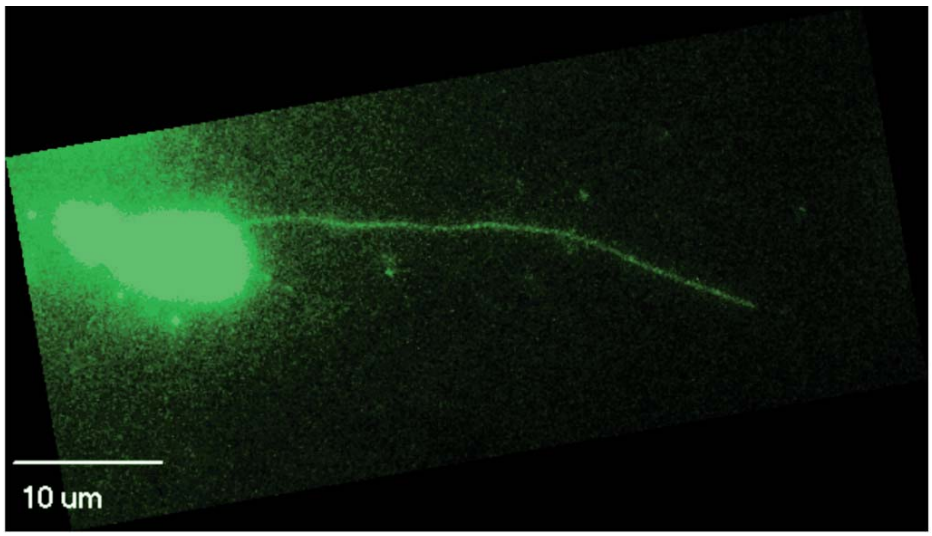

Fig. 1. Cytoneme. Taken from: http://en.wikipedia.org/wiki/File:Cytoneme.tif

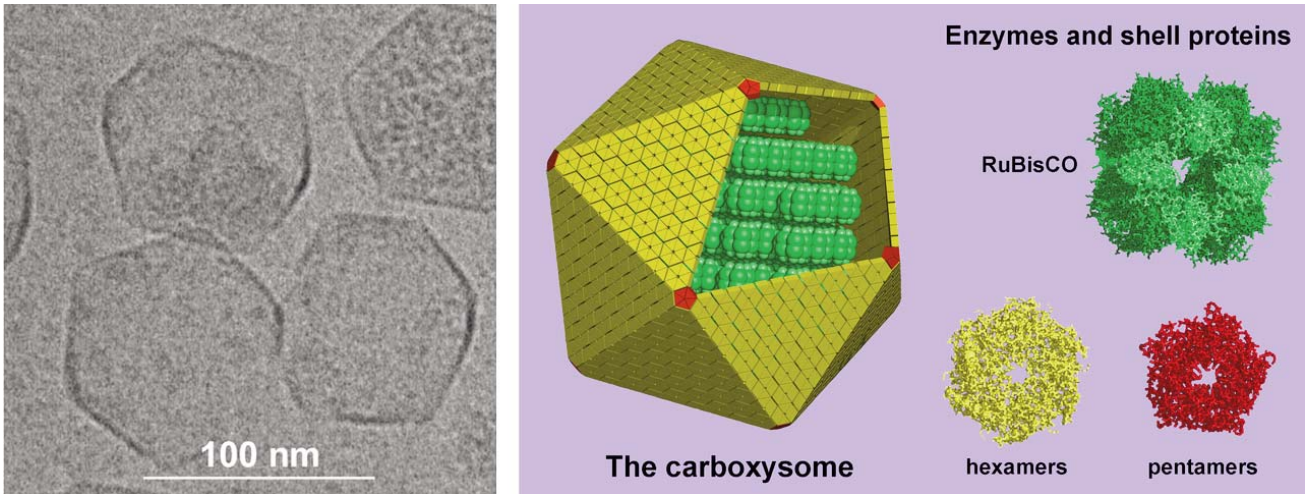

Fig. 2. Carboxysome. Taken from: http://en.wikipedia.org/wiki/File:Carboxysome.png

otic and eukaryotic cells (Holthuis and Ungermann, 2012).

Other cell microstructures that are catching the attention of the scientists are the exosomes or microvesicles, secretory vesicles 40-100 nanometers in diameter. First considered as a way to release «rubbish» out of the cell, the evidence about exosomes carrying and delivering mRNA and miRNA to other neighbouring cells revealed an unsuspected role for cell communication (Chen et al., 2010). In this way, cells of the immune system may modulate immune response (Li et al., 2006). A database of the molecules identified in exosomes is available in the web (http://www.exocarta.org). Exosomes could be used in cell therapy for delivering of mRNAs towards a mutant cell to correct a genetic defect, or to supply a therapeutically relevant protein. On the other hand, exosomes released by tumor cells and isolated from blood or urine can be used as a novel diagnostic tool.

The same technique of fluorescent enzyme labeling for intracellular localization allowed for the discovery of the «cell serpents» (aka «cytoophidia»), long filaments (up to 5-6 microns long) that apparently serve as scaffolds for enzyme spatial organization (Liu, 2011). These enigmatic structures have been identified in bacteria, yeast, fruit flies and mammals. All the cytoophidia contain the enzyme cytidine 5'-triphosphate (CTP) synthase, probably associated to other proteins. CTP is an essential component of nucleic acids, an energy transporter and a cofactor for some metabolic reactions. The physiological significance of cytoophidia remains unknown.

All these discoveries show that cell anatomy is far from being completely known. As remarked in a recent review (Kwok, 2011), supposedly old-fashion techniques such as conventional electron microscopy have been crucial for the discovery or the study of some of these suborganellar structures. On the other hand, the refinements of new techniques, such as live cell imaging microscopy, two-photon excitation microscopy, FRET and others (see Schmolze et al., 2011 for a review), have allowed cell researchers to have a closer look inside the cell, and even to detect interactions at the protein-protein level. Cell anatomy is still alive, providing us with unsuspected views and arising many new questions.

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