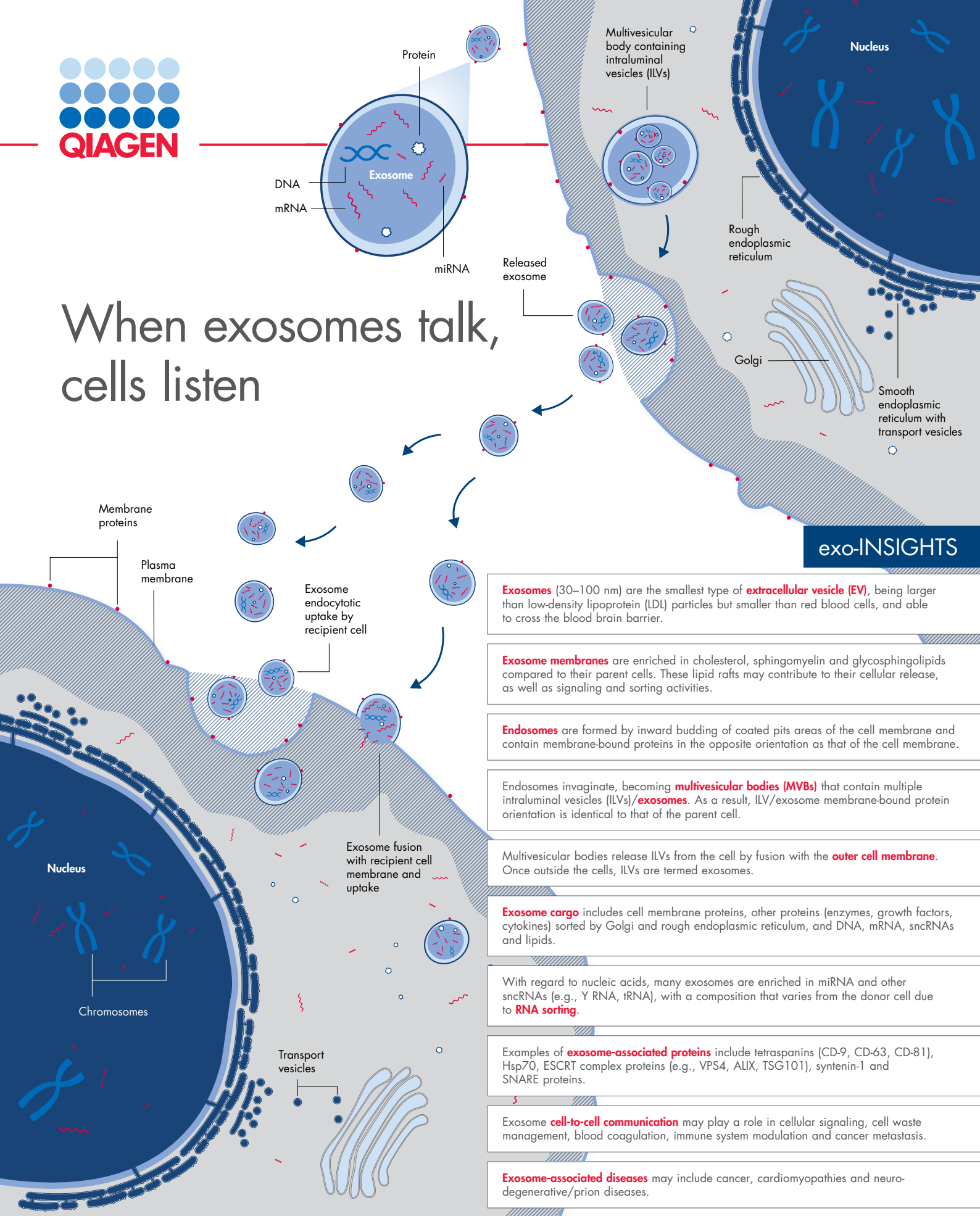
When exosomes talk, cells listen



exo-INSIGHTS

Exosomes (30–100 nm) are the smallest type of **extracellular vesicle (EV)**, being larger than low-density lipoprotein (LDL) particles but smaller than red blood cells, and able to cross the blood brain barrier.

Exosome membranes are enriched in cholesterol, sphingomyelin and glycosphingolipids compared to their parent cells. These lipid rafts may contribute to their cellular release, as well as signaling and sorting activities.

Endosomes are formed by inward budding of coated pits areas of the cell membrane and contain membrane-bound proteins in the opposite orientation as that of the cell membrane.

Endosomes invaginate, becoming **multivesicular bodies (MVBs)** that contain multiple intraluminal vesicles (ILVs)/**exosomes**. As a result, ILV/exosome membrane-bound protein orientation is identical to that of the parent cell.

Multivesicular bodies release ILVs from the cell by fusion with the **outer cell membrane**. Once outside the cells, ILVs are termed exosomes.

Exosome cargo includes cell membrane proteins, other proteins (enzymes, growth factors, cytokines) sorted by Golgi and rough endoplasmic reticulum, and DNA, mRNA, sncRNAs and lipids.

With regard to nucleic acids, many exosomes are enriched in miRNA and other sncRNAs (e.g., Y RNA, tRNA), with a composition that varies from the donor cell due to **RNA sorting**.

Examples of **exosome-associated proteins** include tetraspanins (CD-9, CD-63, CD-81), Hsp70, ESCRT complex proteins (e.g., VPS4, ALIX, TSG101), syntenin-1 and SNARE proteins.

Exosome **cell-to-cell communication** may play a role in cellular signaling, cell waste management, blood coagulation, immune system modulation and cancer metastasis.

Exosome-associated diseases may include cancer, cardiomyopathies and neuro-degenerative/prion diseases.

Exosomes demystified

Exosomes are small (30–100 nm) membrane-bound vesicles released by cells into interstitial fluids that serve as a means of intercellular communication (1–3). Through uptake by both neighboring and distantly located cells, exosomes have the potential to initiate systemic changes in the physiology, phenotype and function of their recipient cells (2, 3).

Exosomes are primarily enriched in small noncoding RNAs, including miRNAs, full-length transfer RNAs and Y RNAs. The RNA-binding protein YBX1 plays a role in sorting small noncoding RNAs into exosomes (4). Exosomes can also contain mRNA and DNA (5).

The DNA, RNA and proteins contained within exosomes are consistent with the health of their cell-of-origin. Transfer of these molecules by exosomes into recipient cells has the potential, therefore, to impact the health and pathology of recipient cells, either positively (if from healthy cells) or negatively (if from diseased or cancerous cells) (2). Some studies suggest that exosomes administered in vivo may reduce apoptosis, as well as affect inflammation, cancer growth, neurodegenerative diseases and myocardial viability (2).

Exosomes are currently being investigated as potential therapeutic delivery systems to treat disease and cancer (2). Additionally, analysis of exosomal nucleic acids derived by liquid biopsy are being researched as potential diagnostic biomarkers in cancer and other diseases (6–7).

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Easy-to-use QIAGEN technologies for exosome and exosomal RNA isolation from various sample types

exoEasy® Maxi Kit (cat no. 76064) – Membrane affinity-based spin-column kit for isolation of intact functional exosomes and other extracellular vesicles using serum/plasma or cell culture supernatant

exoRNeasy® Kits (cat no. 77023, 77044 and 77064) – Membrane affinity-based spin-column kits for highly specific RNA isolation from exosomes and other extracellular vesicles using serum/plasma, cell culture supernatant, urine or cerebrospinal fluid

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Selected publications using QIAGEN exoEasy, exoRNeasy and miRCURY Kits:

1. Teng, Y. et al. (2017) MVP-mediated exosomal sorting of miR-193a promotes colon cancer progression. Nat. Commun. **8**,14448.
2. Wang, X., et al. (2017) Unique molecular profile of exosomes derived from primary human proximal tubular epithelial cells under diseased conditions. J. Extracell. Vesicles **6**, 1314073.
3. Reithmair, M., et al. (2017) Cellular and extracellular miRNAs are blood-compartment-specific diagnostic targets in sepsis. J. Cell Mol. Med. **21**, 2403–2411.
4. Helwa, I., et al. (2017) A comparative study of serum exosome isolation using differential ultracentrifugation and three commercial reagents. PLoS ONE **12**, e0170628.

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