Extracellular Vesicles as Multi-Bioactive Complex and mediators of Inter-kingdom communication: Their Versatile Ecosystem Effects

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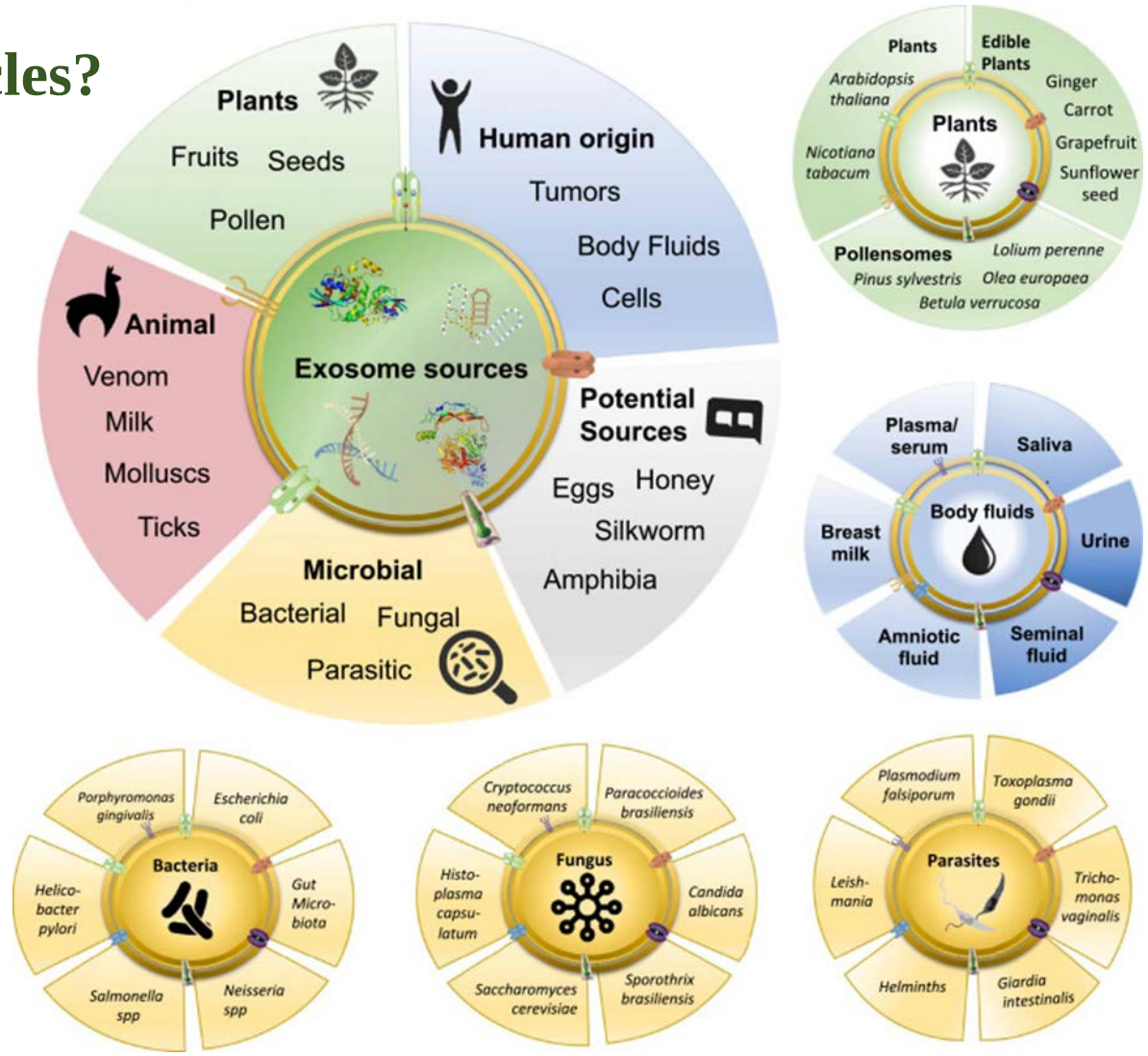
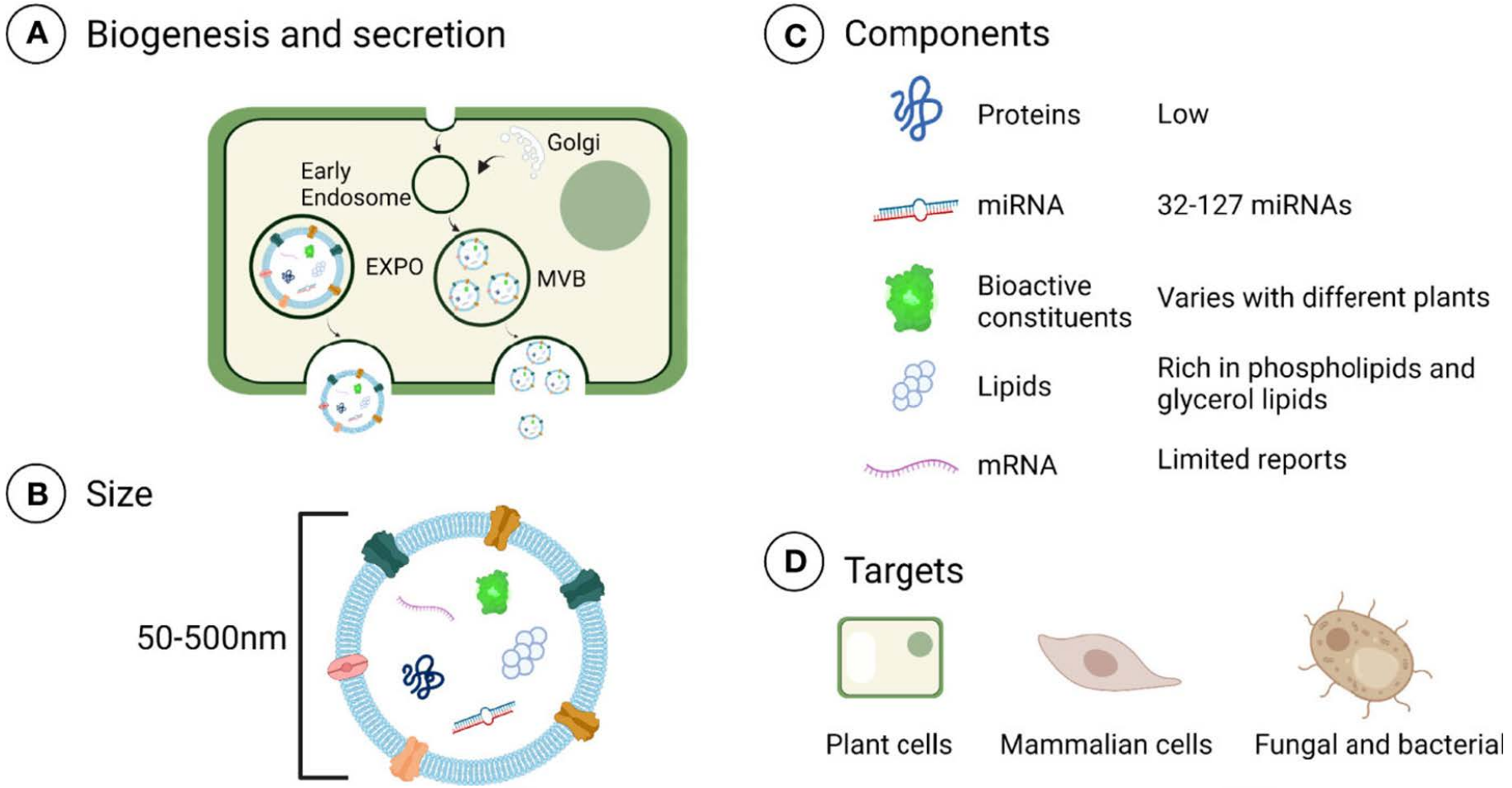
Via Pietro Castellino 111, 80131 Naples, Italy

What are Extracellular Vesicles?



Christina M.A.P. Schuh, Jimena Cuenca, Francisca Alcayaga-Miranda, Maroun Khoury, Exosomes on the border of species and kingdom intercommunication, Translational Research,Volume 210, 2019, Pages 80-98, ISSN 1931-5244, https://doi.org/10.1016/j.trsl.2019.03.008.

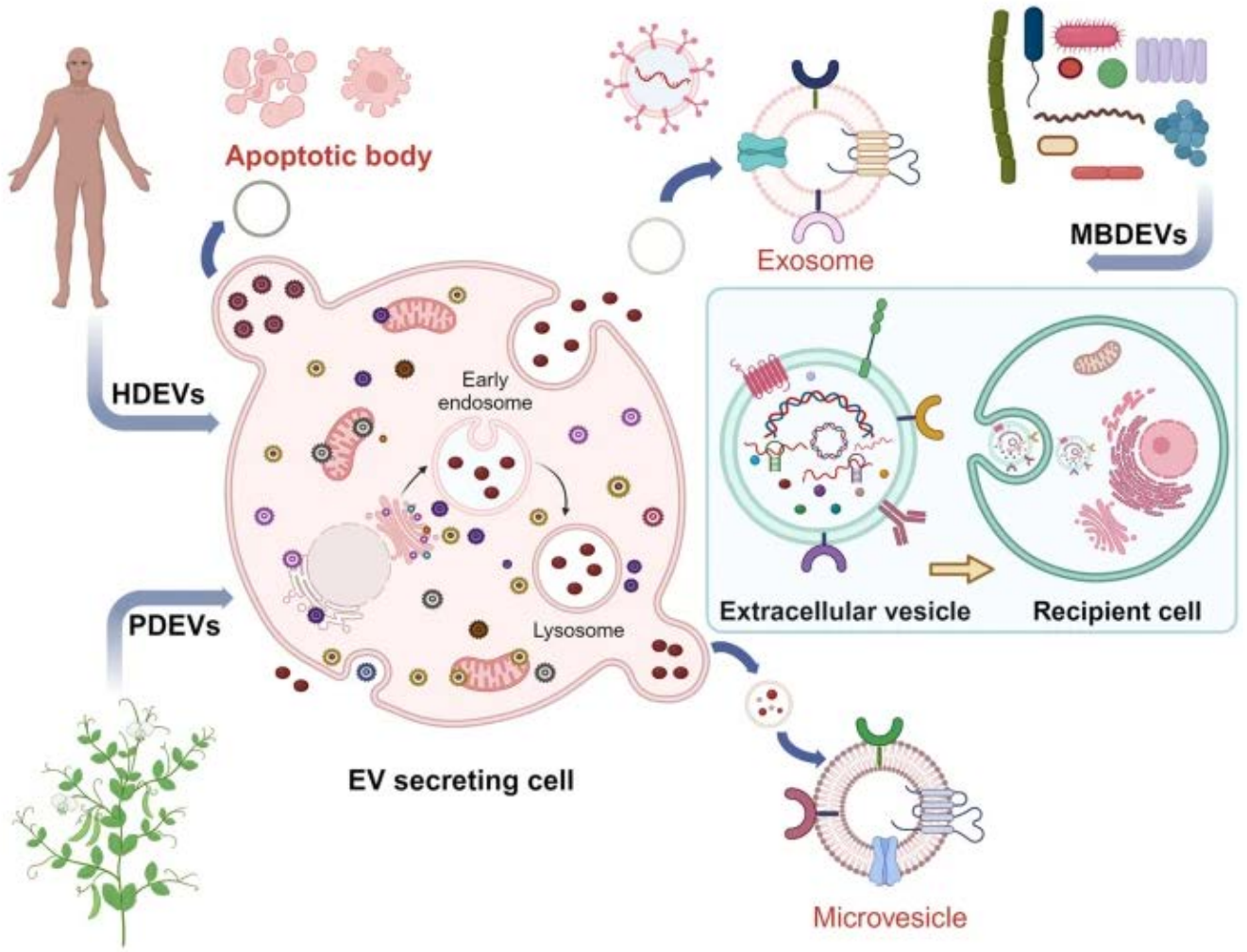
Extracellular Vesicles biogenesis



Zhang Z, Yu Y, Zhu G, et al. The Emerging Role of Plant-Derived Exosomes-Like Nanoparticles in Immune Regulation and Periodontitis Treatment. Frontiers in Immunology. 2022 ;13:896745. DOI: 10.3389/fimmu.2022.896745. PMID: 35757759; PMCID: PMC9231591

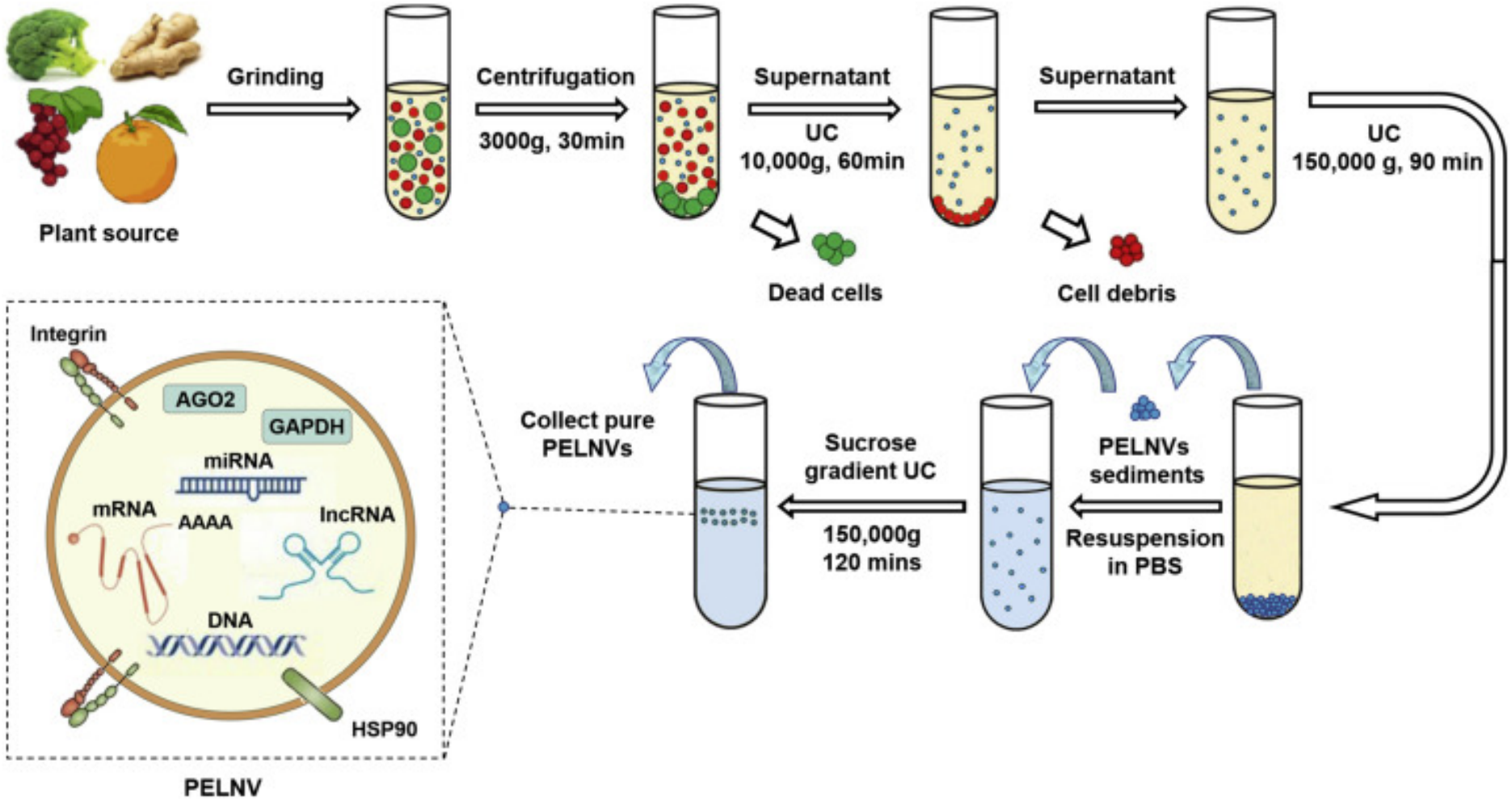
The Biology and Function of Extracellular Vesicles

EVs are emerging as essential mediators of intercellular communication involved in several physiological and pathological conditions. EVs function as a pivotal dialogue mechanism, coordinating cellular responses to environmental stimuli, maintaining homeostasis, and supporting tissue repair and regeneration. EVs also play a significant role in interspecies communication, influencing interactions between microbiota, plants, and animals, and helping ecosystems adapt to changing conditions.



Extracellular vesicles as tools and targets in therapy for diseases. Mudasir A. Kumar, Sadaf K. Baba, Hana Q. Sadida, Sara A. Marzooqi, Jayakumar Jerobin, Faisal H. Altemani, Naseh Algehainy, Mohammad A. Alanazi, Abdul-Badi Abou-Samra, Rakesh Kumar, Ammira S. Al-Shabeeb Akil, Muzafar A. et al.,.

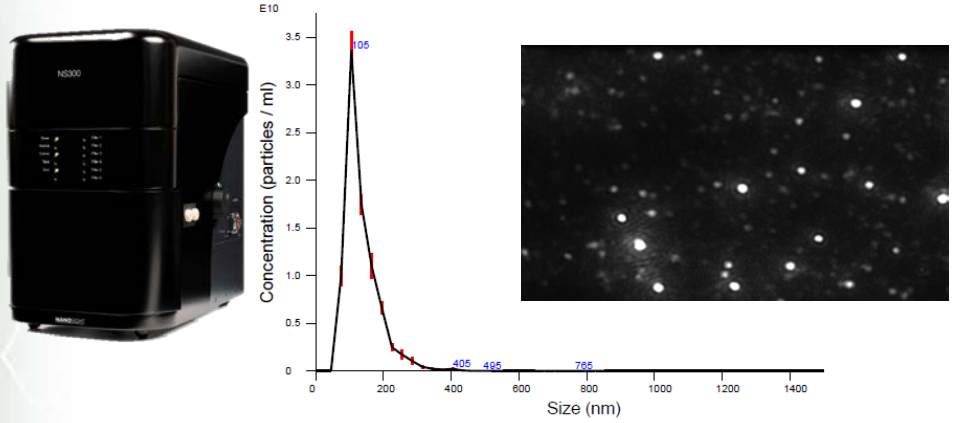
Extracellular Vesicles isolation



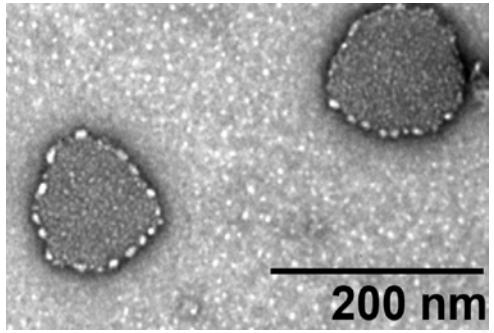
Dad, Haseeb Anwar et al. Plant Exosome-like Nanovesicles: Emerging Therapeutics and Drug Delivery Nanoplatforms Molecular Therapy, Volume 29, Issue 1, 13 – 31

Chemical/physical characterization

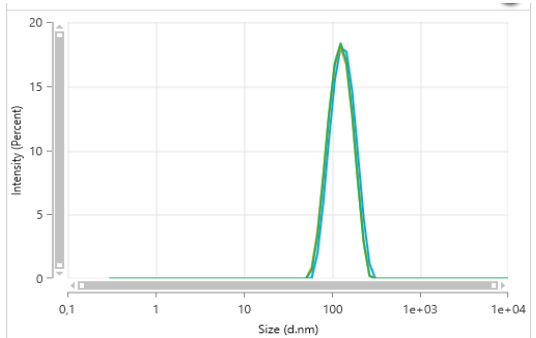
Nanoparticle Tracking Analysis

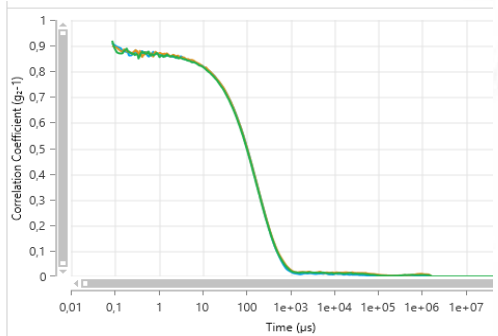


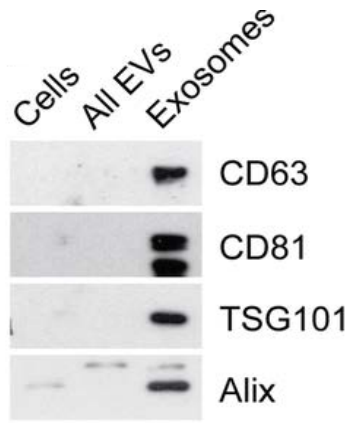
Trasmission Elettron Microscope

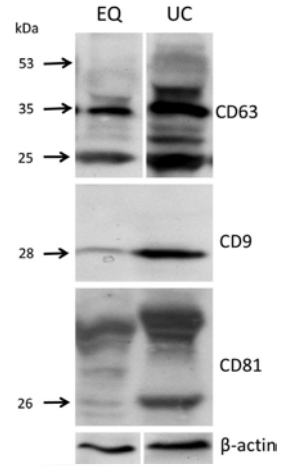


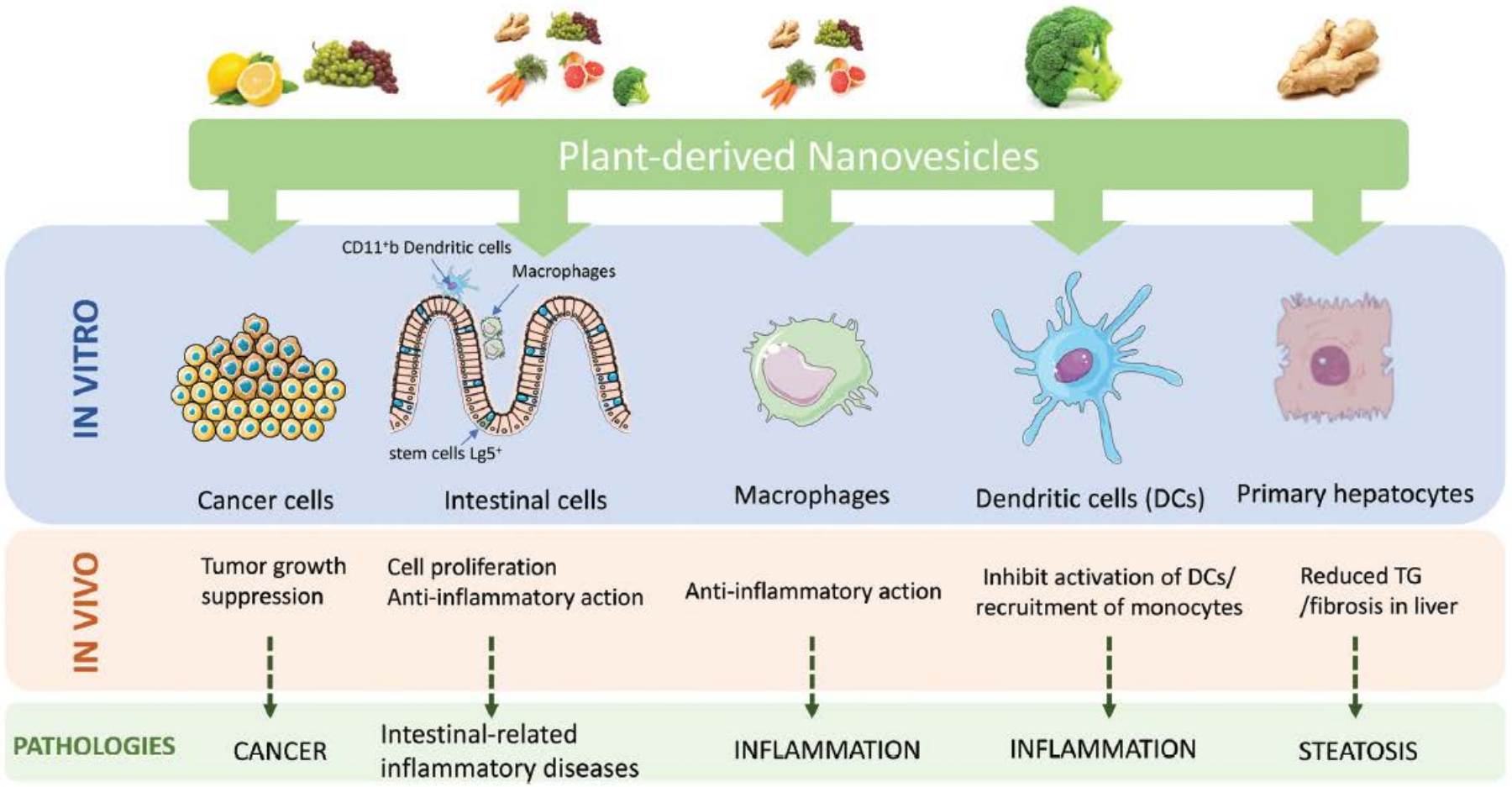
Dynamic Light Scattering







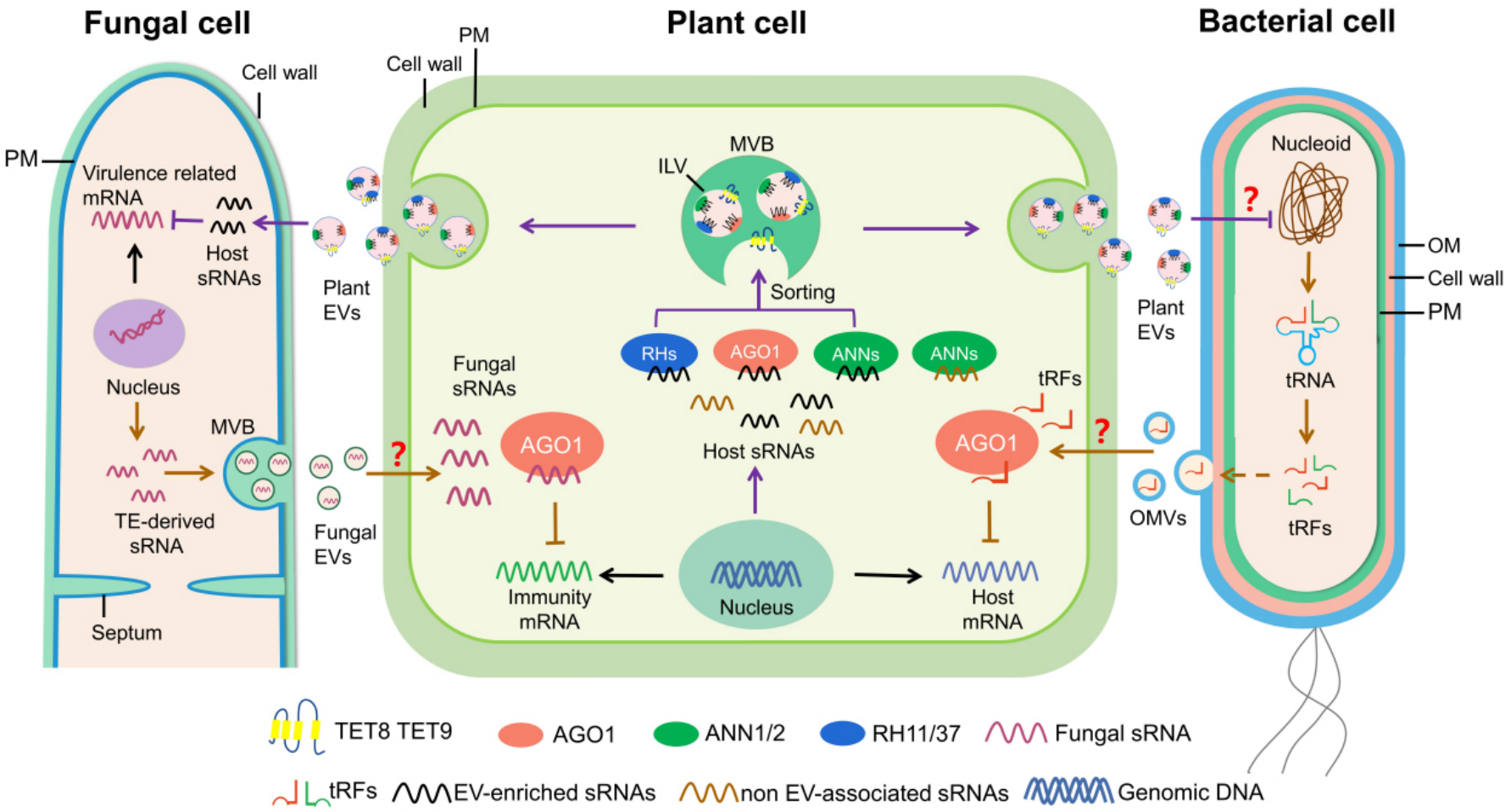




PDEVs demonstrated strong biological properties, such as anti-inflammatory, anticancer, antibacterial, antifungal, and antioxidative effects. They produce these effects through various mechanisms, such as gene regulation, influence on gut microbiota, macrophage activity, gene silencing, and the presence of specific active molecules. These innate therapeutic properties are a promising avenue, whether used alone or in combination with other therapeutic agents.

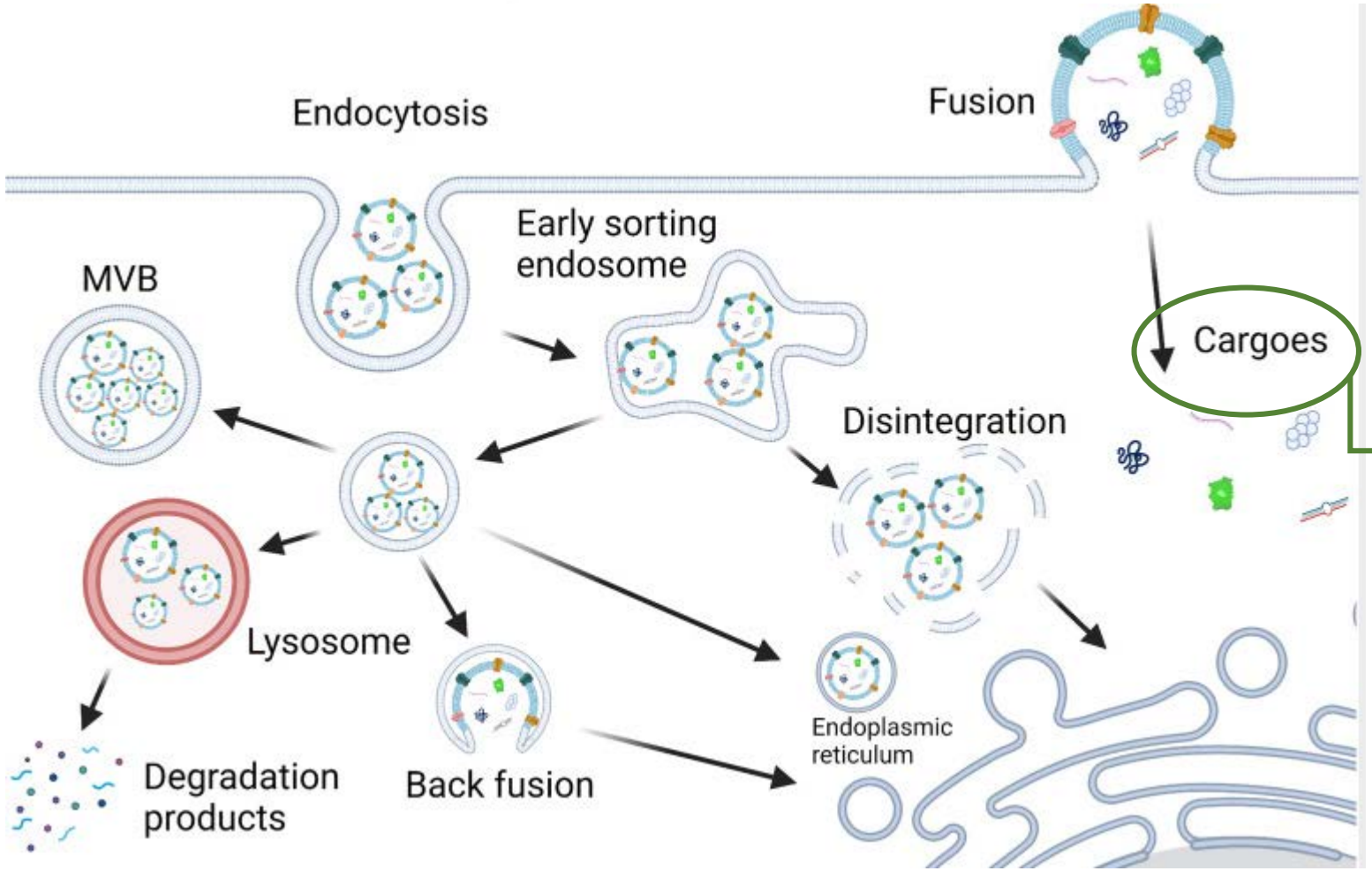
Rome S . Biological properties of plant-derived extracellular vesicles. Food Funct. 2019 Feb 20;10(2):529-538. doi: 10.1039/c8fo02295j.

EVs as Biological Shuttles for Target cells



Qiang Cai, ... Hailing Jin. Extracellular vesicles: cross-organismal RNA trafficking in plants, microbes, and mammalian cells

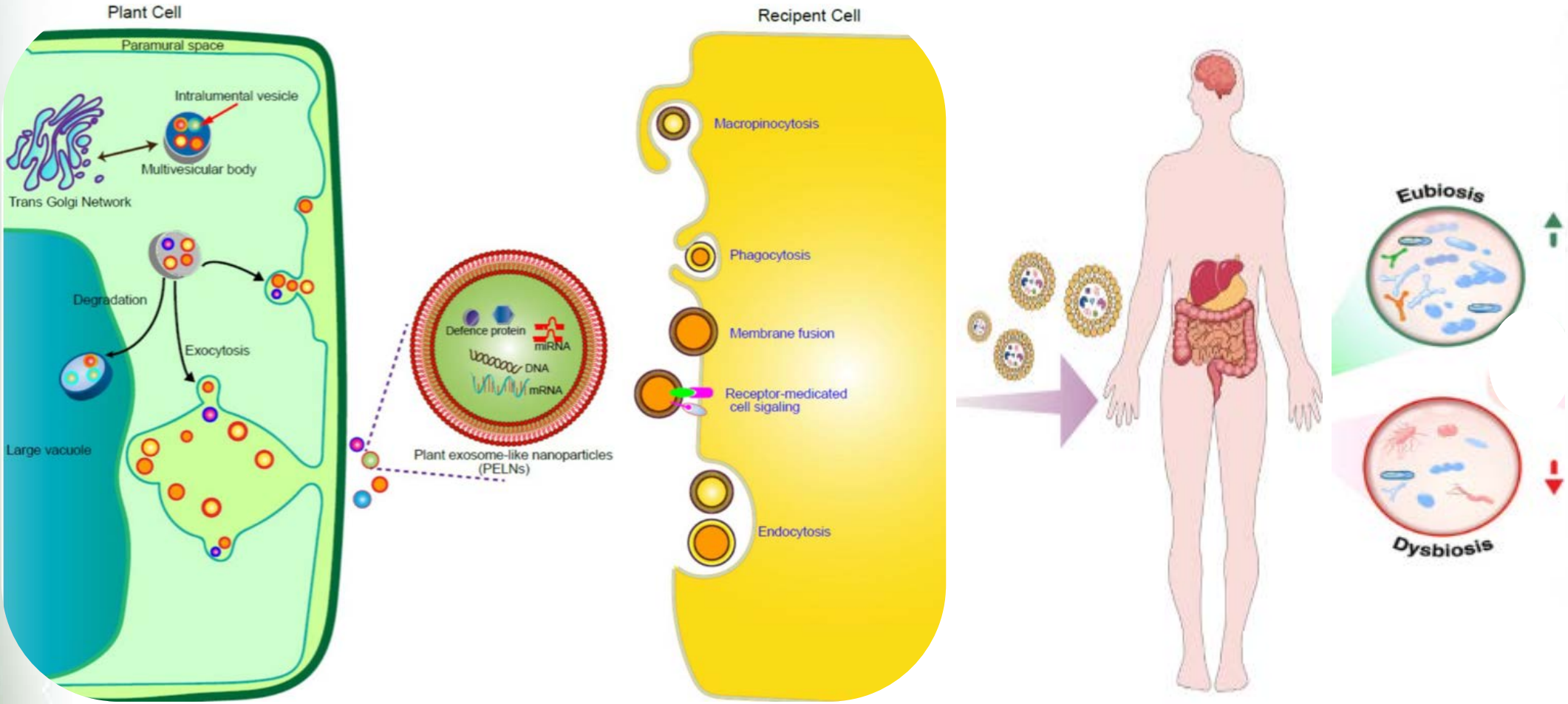
EVs as Biological Shuttles for Target cells



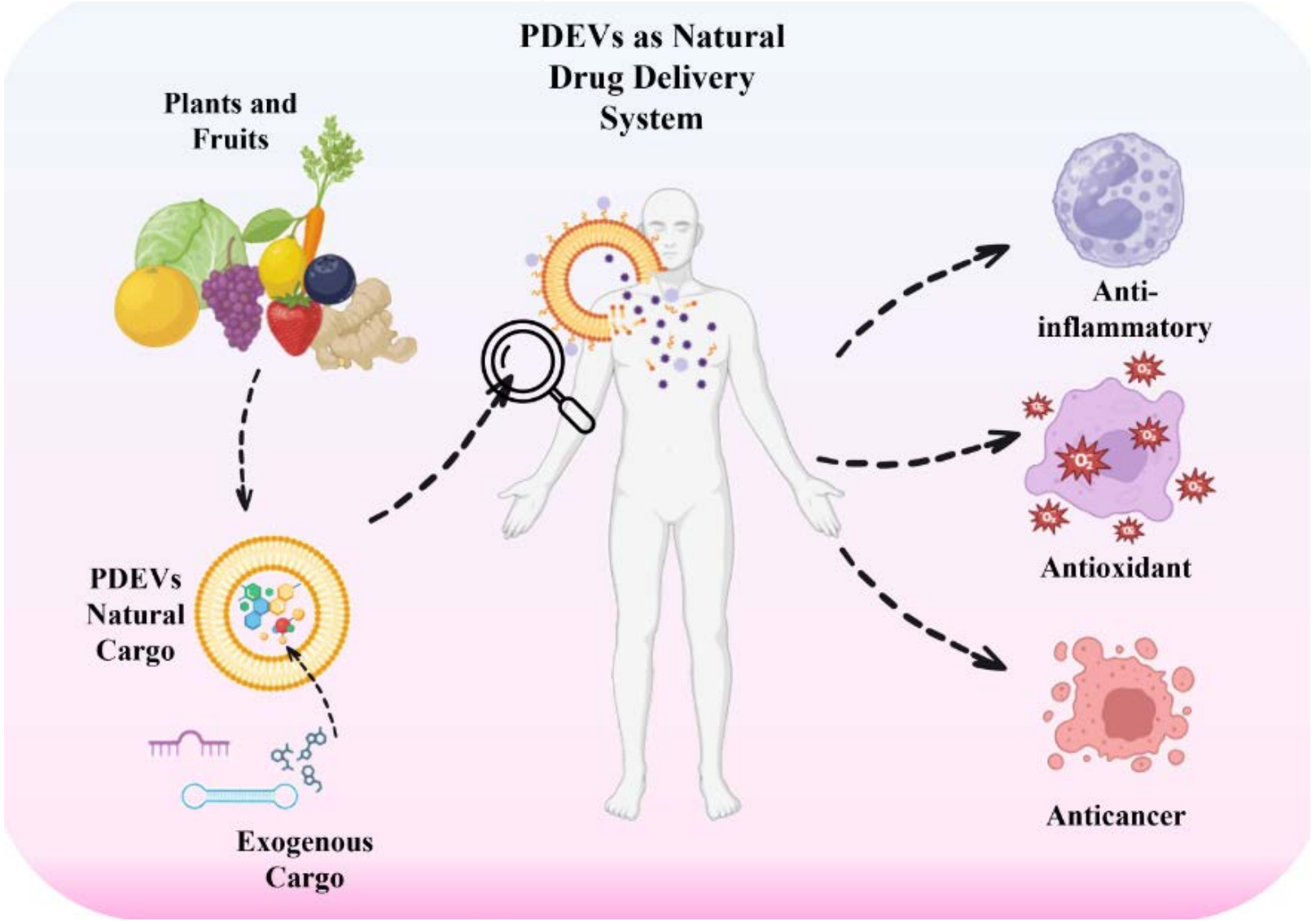
Messengers for Target cells

Zhang Z, Yu Y, Zhu G, et al. The Emerging Role of Plant-Derived Exosomes-Like Nanoparticles in Immune Regulation and Periodontitis Treatment. Frontiers in Immunology. 2022 ;13:896745. DOI: 10.3389/fimmu.2022.896745. PMID: 35757759; PMCID: PMC9231591

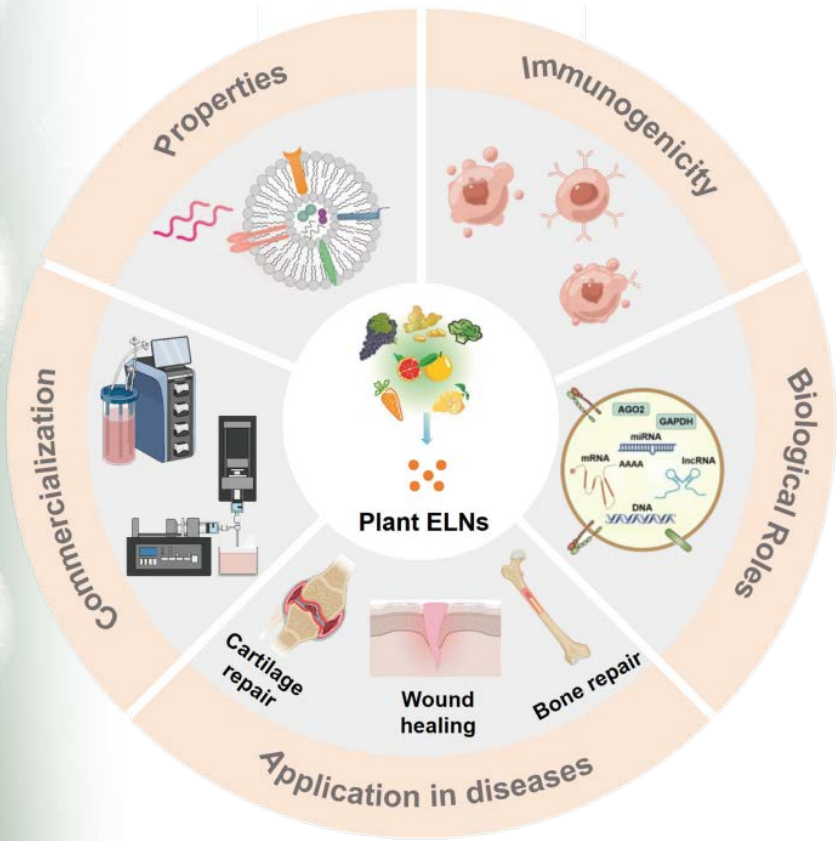
Extracellular Vesicles interaction mechanism



Shafiu A. Umar Shinge, Yin Xiao, Li Duan. New insights of engineering plant exosome-like nanovesicles as a nanoplatform for therapeutics and drug delivery



Calzoni, E.; Bertoldi, A.; Cusumano, G.; Buratta, S.; Urbanelli, L.; Emiliani, C. Plant-Derived Extracellular Vesicles: Natural Nanocarriers for Biotechnological Drugs. Processes 2024, 12, 2938.



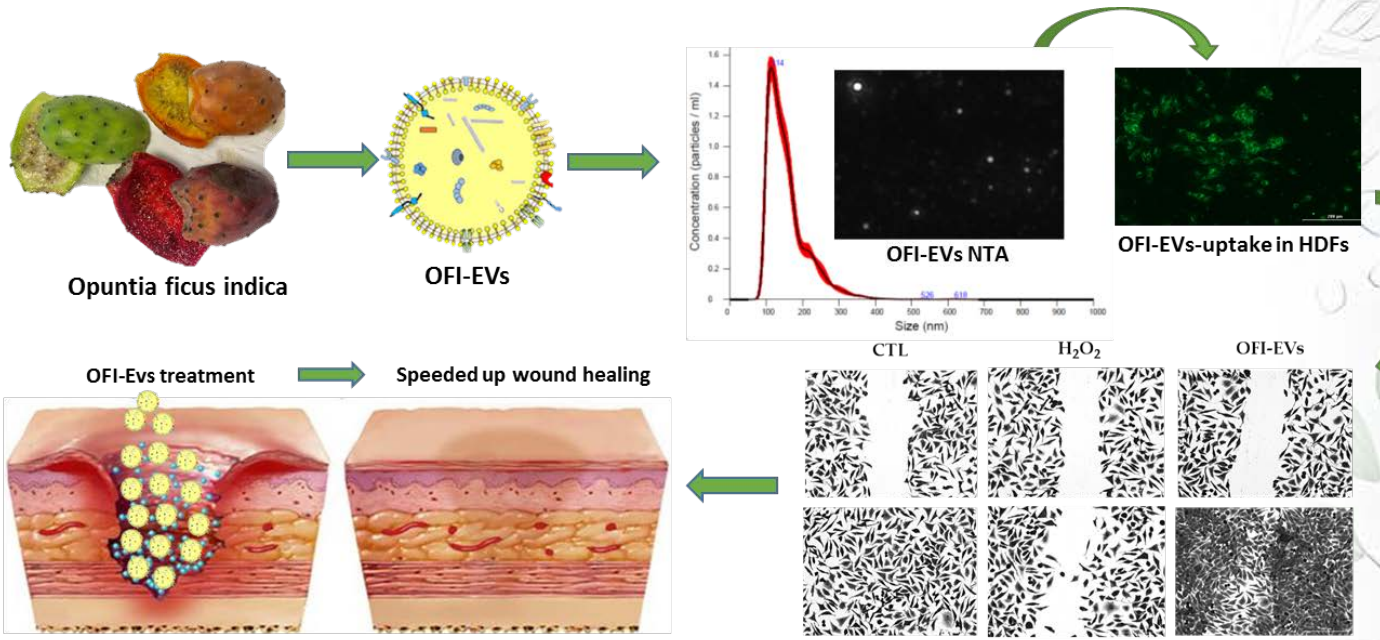
International Journal of *Molecular Sciences*

MDPI

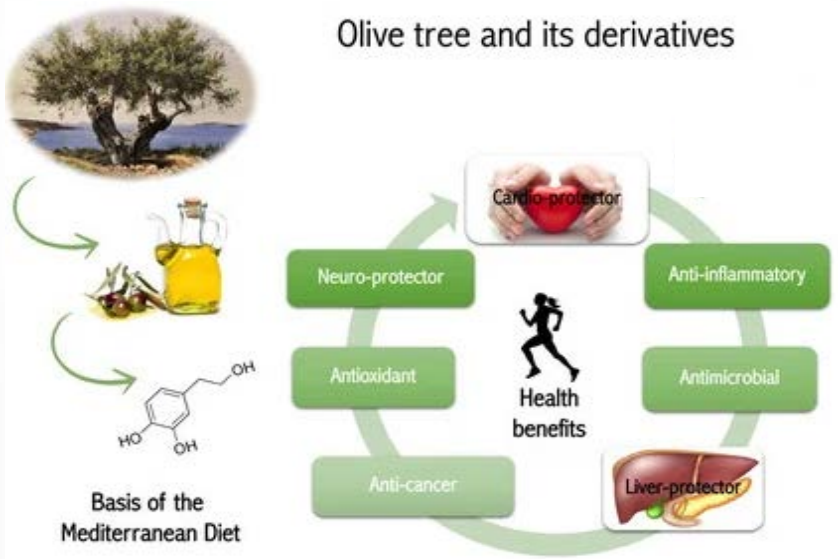
Article

Extracellular Vesicles Derived from *Opuntia ficus-indica* Fruit (OFI-EVs) Speed up the Normal Wound Healing Processes by Modulating Cellular Responses

Anna Valentino [1,2,*,†], Raffaele Conte [1,2,†], Dalila Bousta [3], Hicham Bekkari [4], Anna Di Salle [1,2], Anna Calarco [1,2,5,*] and Gianfranco Peluso [1,2,5]

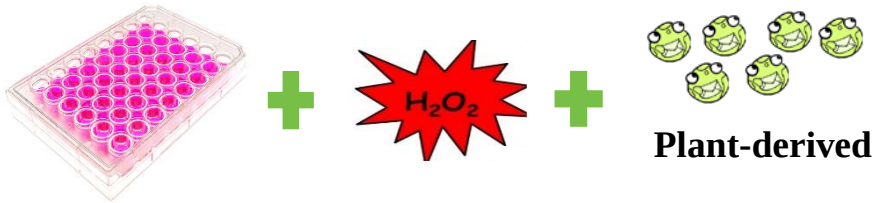


Valentino A, Conte R, Bousta D, Bekkari H, Di Salle A, Calarco A, Peluso G. Extracellular Vesicles Derived from *Opuntia ficus-indica* Fruit (OFI-EVs) Speed Up the Normal Wound Healing Processes by Modulating Cellular Responses. Int J Mol Sci. 2024 Jun 28;25(13):7103. doi: 10.3390/ijms25137103.



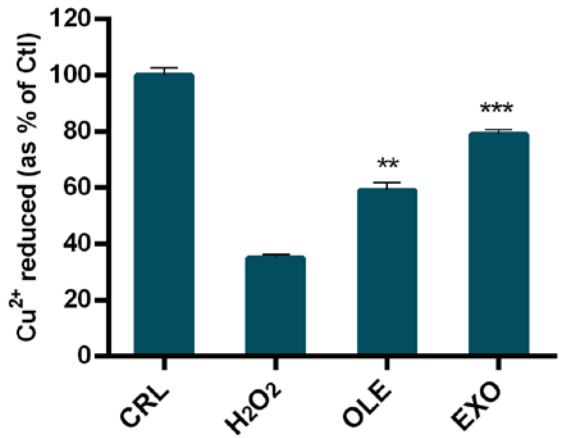
Biological assay

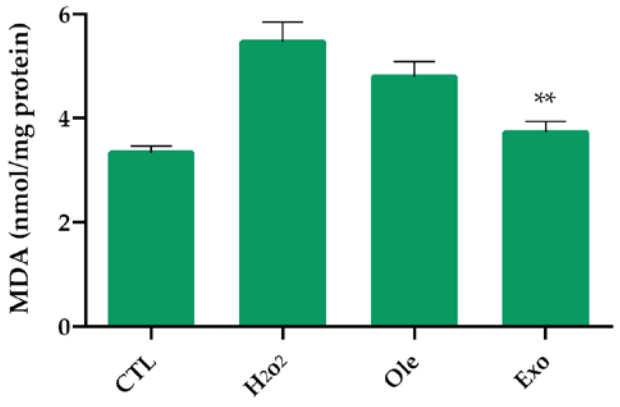
Cellular model: RAW 264.7

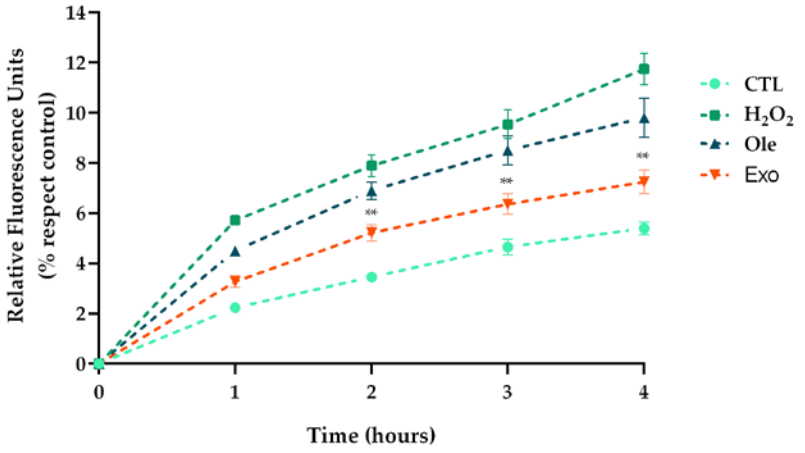


Plant-derived EVs

Results



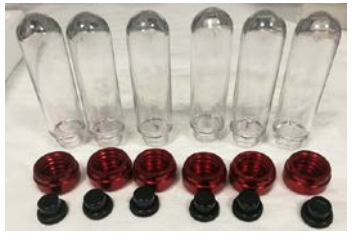


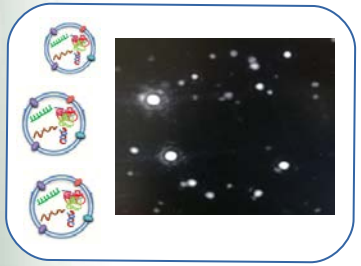


Tomato EVs

EVs derived from peel and pulp tomato

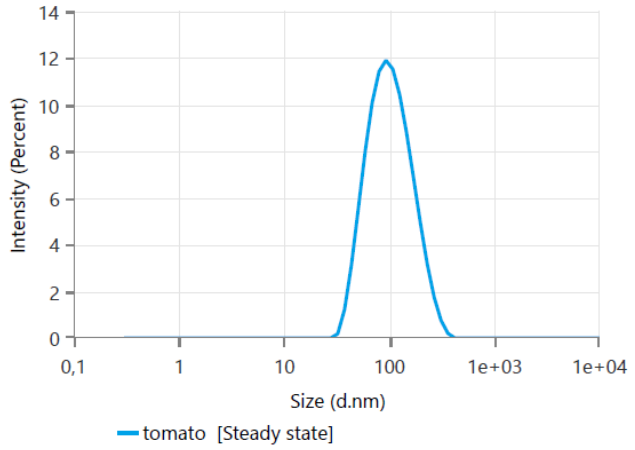
Differential centrifugation

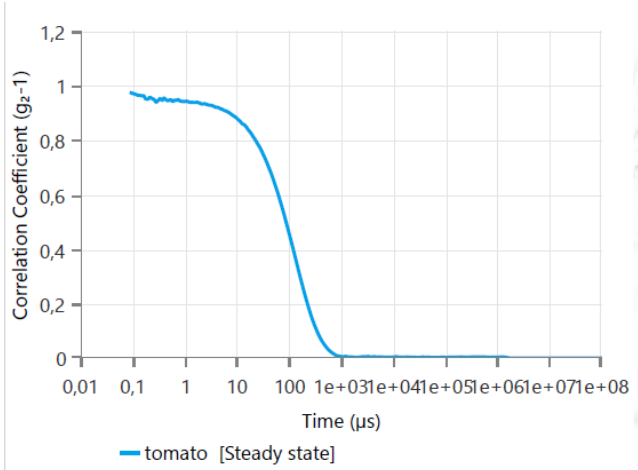




Tomato-derived EVs

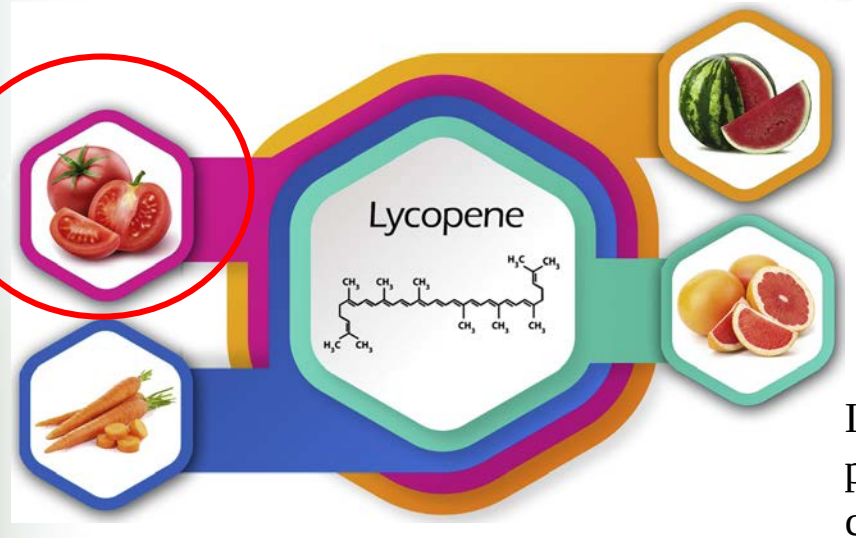
DLS

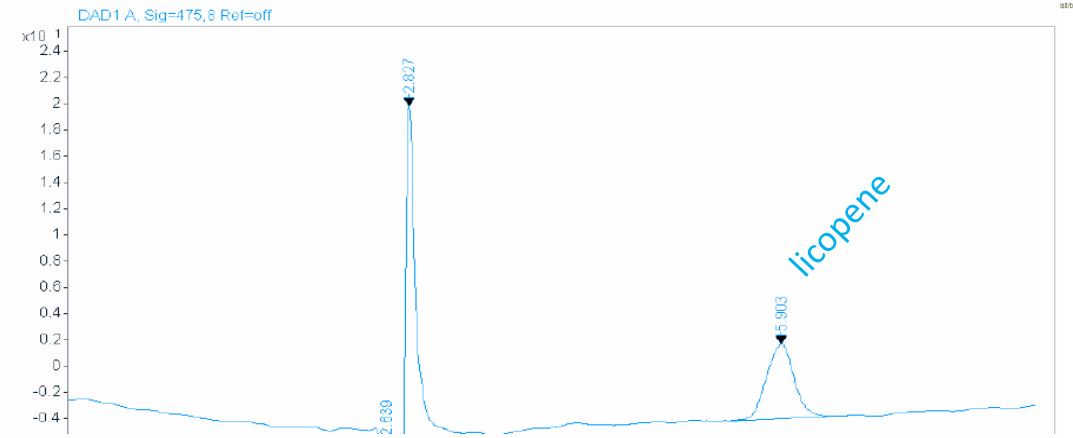




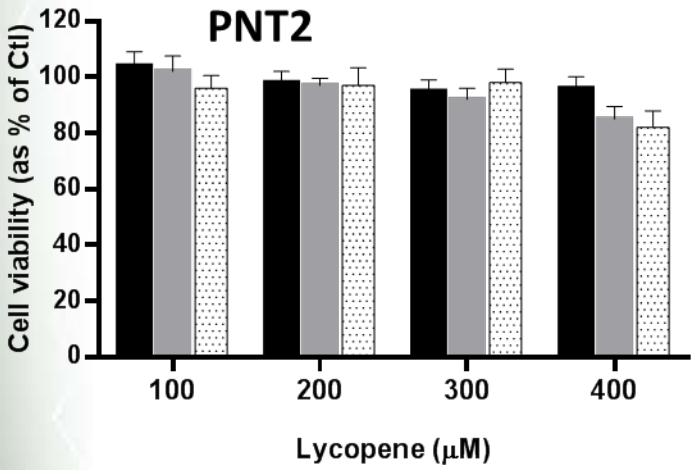
Statistics Table

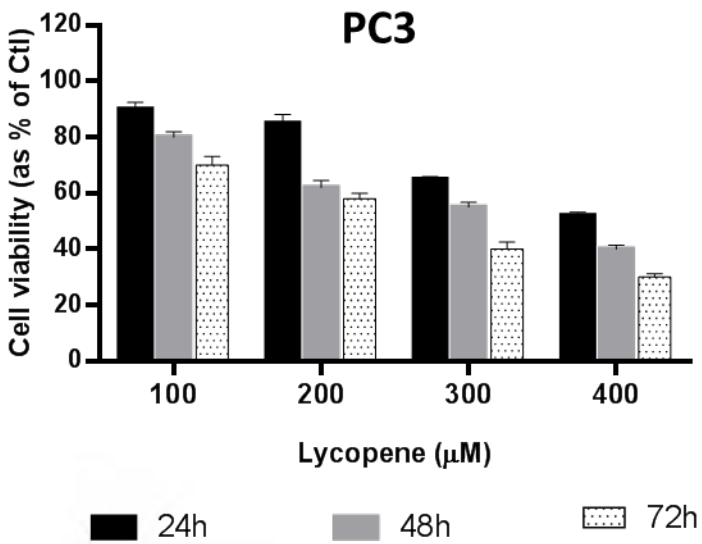
Name	Mean	Standard Deviation	RSD	Minimum	Maximum
Z-Average (nm)	91,04	-	-	91,04	91,04
Polydispersity Index (PI)	0,1795	-	-	0,1795	0,1795
Peak One Mean by Intensity (nm)	111,4	-	-	111,4	111,4
Peak One Area by Intensity (%)	100	-	-	100	100

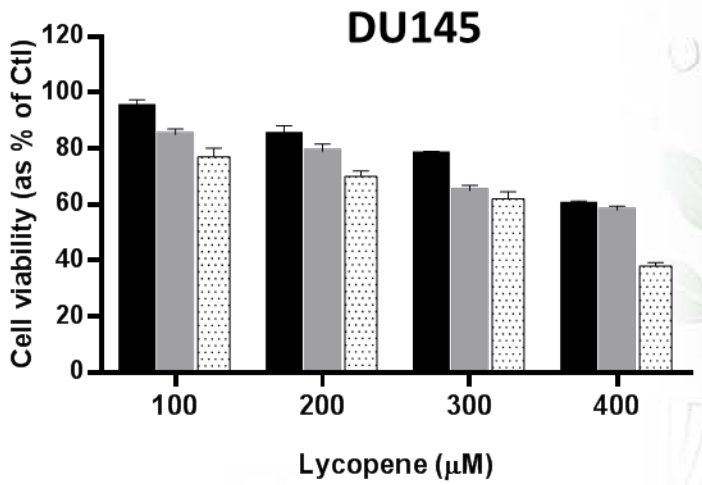




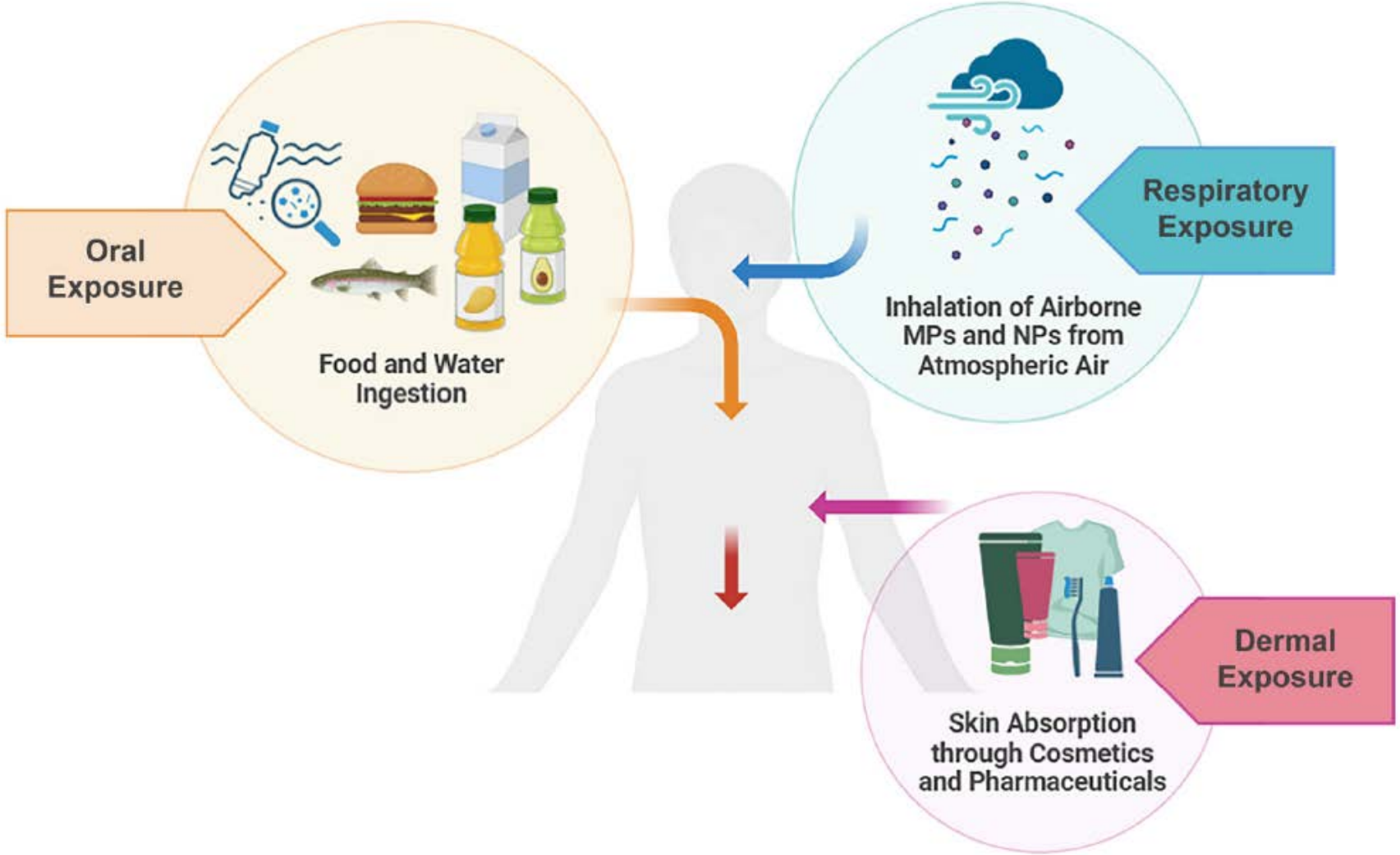
It is widely known that lycopene effectively suppresses the progression, proliferation, arrests the cell cycle and induces apoptosis of prostate cancer cells both in vivo and in vitro.





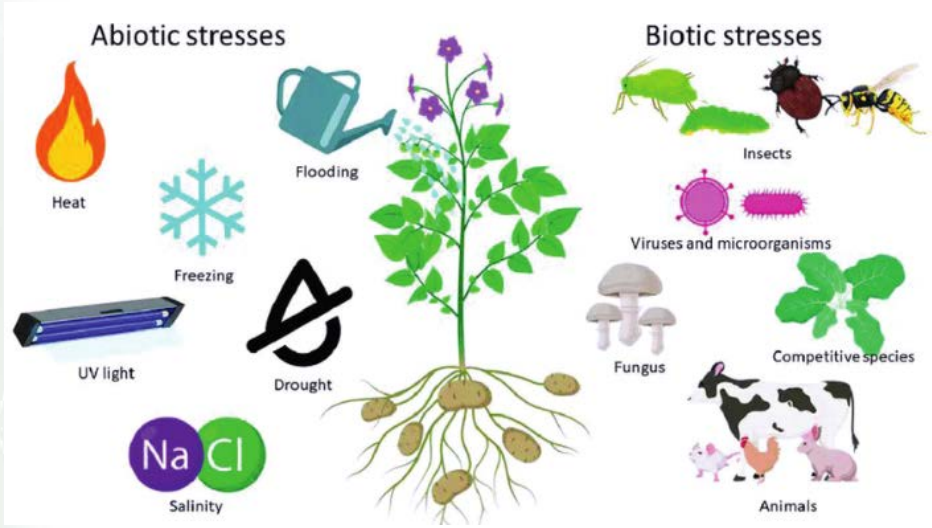


Extracellular Vesicles and Environmental Risks



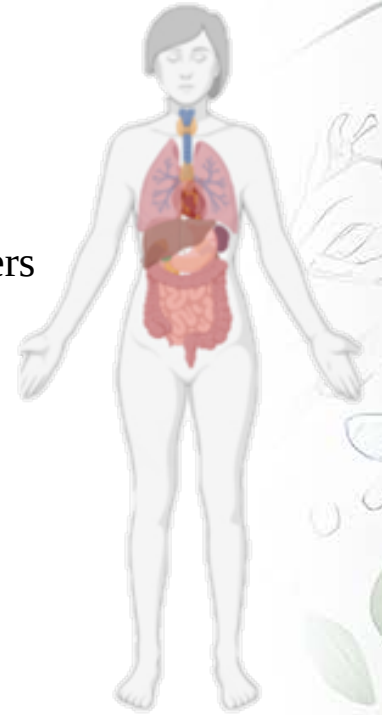
Calzoni, E.; Montegiove, N.; Cesaretti, A.; Bertoldi, A.; Cusumano, G.; Gigliotti, G.; Emiliani, C. Microplastic and Extracellular Vesicle Interactions: Recent Studies on Human Health and Environment Risks. *Biophysica* **2024**, *4*, 724-746. https://doi.org/10.3390/biophysica4040047

Environment and Health



Environmental stress modify the EVs molecular cargo

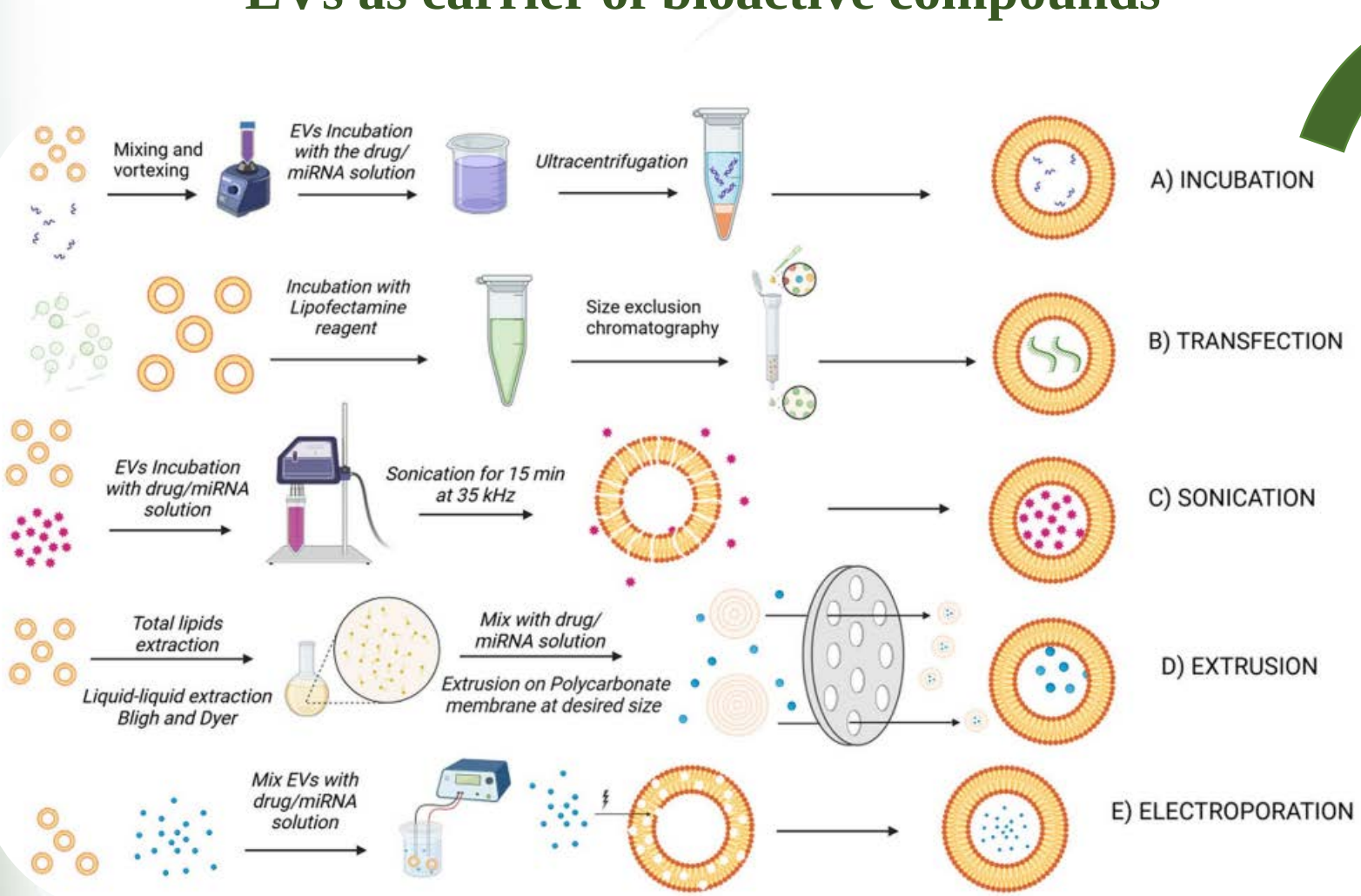
Negative messengers



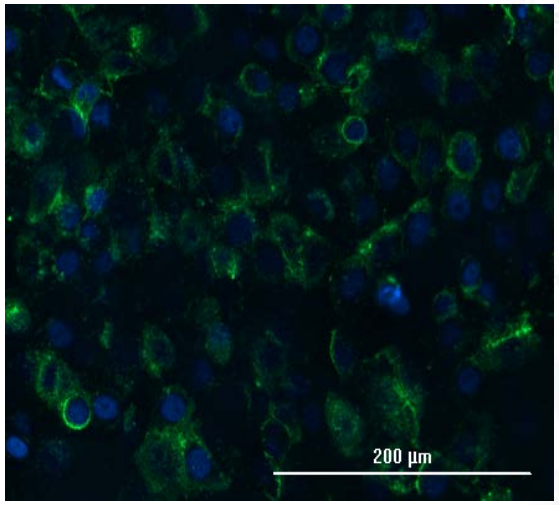
Human Health

The role of EVs in these complex dialogues will open new avenues for therapeutic strategies aimed at restoring ecological balance and enhancing health resilience, since it is becoming increasingly evident that these nano-vesicles play important roles in the global ecosystem.

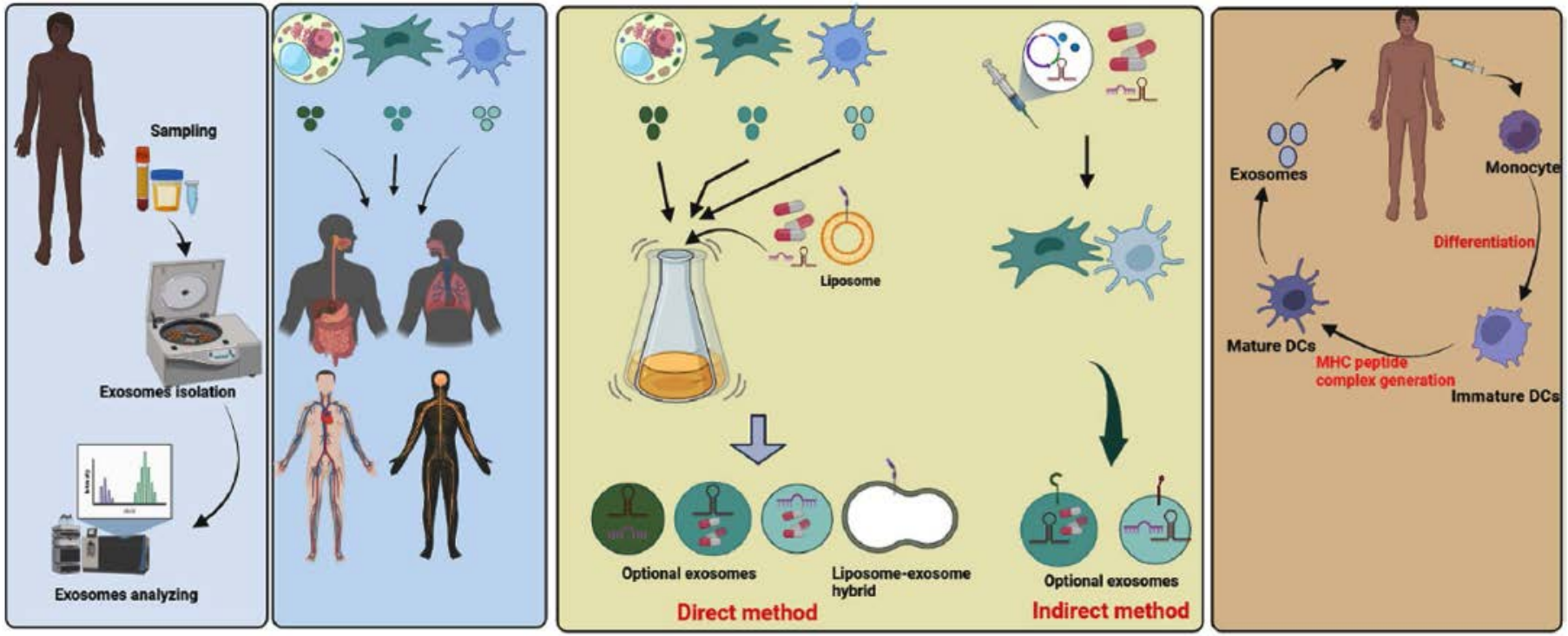
EVs as carrier of bioactive compounds



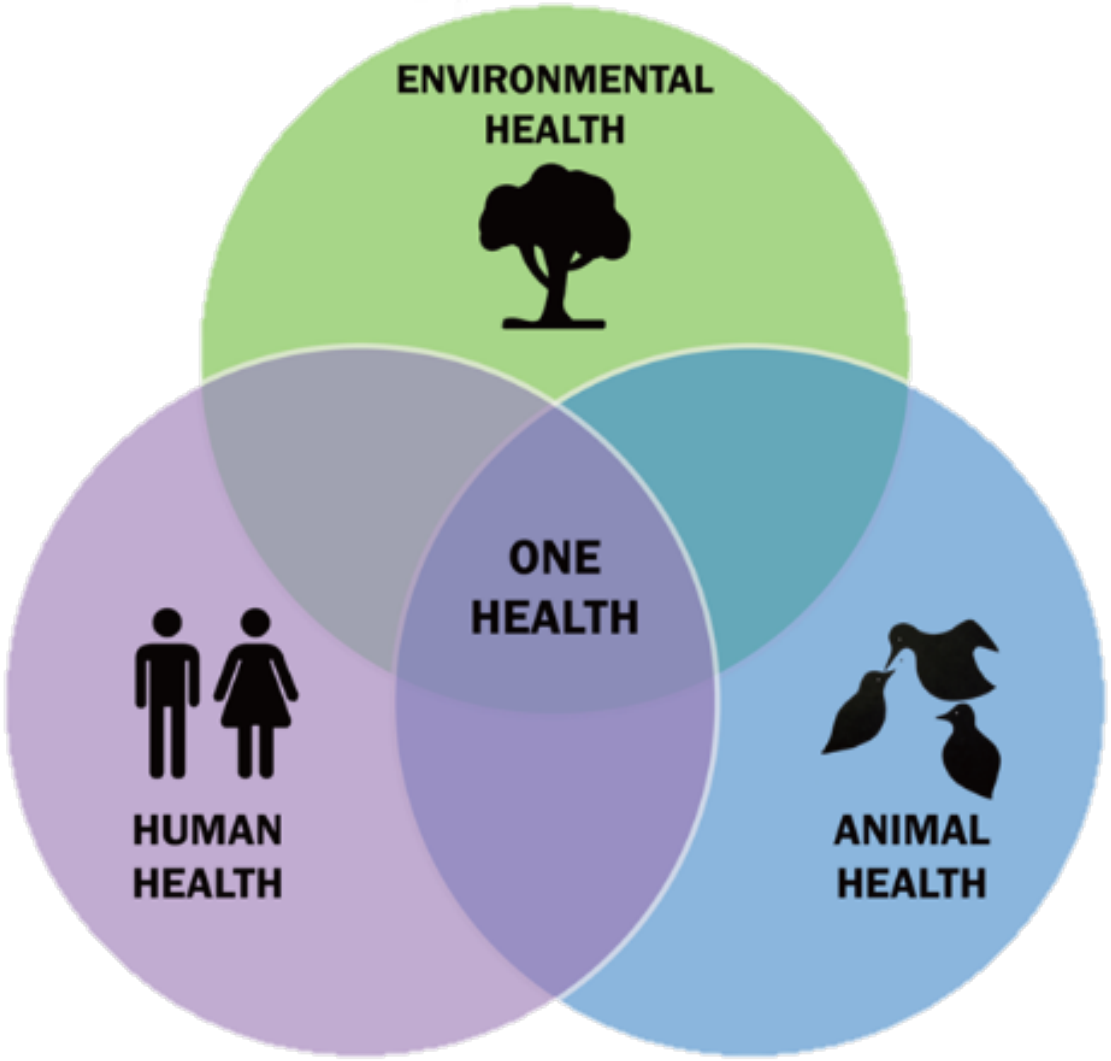
Fluorescent Probe : curcumin



Langellotto, M.D., Rassu, G., Serri, C. *et al.* Plant-derived extracellular vesicles: a synergetic combination of a drug delivery system and a source of natural bioactive compounds. *Drug Deliv. and Transl. Res.* **15**, 831–845 (2025).



Clinical application of EVs. In clinical studies, exosomes are used as biomarkers, cell-free therapy (exosomal therapy). Exosomes of both animal and plant origin are promising vectors for drug delivery systems, proteins and bioactive molecules. In the direct method, exosomes are loaded with therapeutic agents, while through indirect methods, appropriate cells are genetically engineered or co-cultured with therapeutic agents to produce artificial exosomes.



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CNR IRET Conference

Rome, February 18th-19th, 2025

CNR IRET

International Journal of *Molecular Sciences*

Article

Plasma Exosomal microRNA Profile Reveals miRNA 148a-3p Downregulation in the Mucosal-Dominant Variant of Pemphigus Vulgaris

Anna Valentino [1,2,†], Stefania Leuci [3,†], Umberto Galderisi [4], Gianrico Spagnuolo [3], Michele Davide Mignogna [3], Gianfranco Peluso [1,5,*] and Anna Calarco [1,5]

International Journal of *Molecular Sciences* — MDPI

Article

Extracellular Vesicles Derived from *Opuntia ficus-indica* Fruit (OFI-EVs) Speed up the Normal Wound Healing Processes by Modulating Cellular Responses

Anna Valentino [1,2,*,†], Raffaele Conte [1,2,†], Dalila Bousta [3], Hicham Bekkari [4], Anna Di Salle [1,2], Anna Calarco [1,2,5,*] and Gianfranco Peluso [1,2,5]

gels — MDPI

Review

Stimuli-Responsive Nanocomposite Hydrogels for Oral Diseases

Raffaele Conte [1,2,*], Anna Valentino [1,2], Silvia Romano [1], Sabrina Margarucci [1], Orsolina Petillo [1] and Anna Calarco [1,2,3]

Volume 15, Issue 3, 152418 (1-8)

International Journal of Nano Dimension (IJND)

https://dx.doi.org/10.57647/j.ijnd.2024.1503.18

Nanotechnology advancements transforming molecular diagnostics: Applications in precision healthcare

Raffaele Conte[1,*], Roberta Foggia[2], Anna Valentino[1], Anna Di Salle[1], Fahd Kandsi[3], Anna Calarco[1]

Volume 15, Issue 4, 152432 (1-9)

International Journal of Nano Dimension (IJND)

https://dx.doi.org/10.57647/j.ijnd.2024.1504.32

Microfluidic approach for the synthesis of silver nanoparticles (AgNPs) as promising antimicrobial agent

Raffaele Conte[1,2,*], Anna Valentino[1,2], Silvia Romano[1,3], Sorur Yazdanpanah[1,4], Fatima Ez-Zahra Amrati[5], Fahd Kandsi[6], Anna Calarco[1,2,7]

gels

Review

Smart Nanocomposite Hydrogels as Next-Generation Therapeutic and Diagnostic Solutions

Anna Valentino [1,2,†], Sorur Yazdanpanah [1,3,†], Raffaele Conte [1,2,*], Anna Calarco [1,2,4,*] and Gianfranco Peluso [1,2,4]

International Journal of *Molecular Sciences* — MDPI

Article

Thermo-Responsive Hydrogel Containing Microfluidic Chitosan Nanoparticles Loaded with *Opuntia ficus-indica* Extract for Periodontitis Treatment

Raffaele Conte [1,2,*,†], Anna Valentino [1,2,†], Ilenia De Luca [1], Gemilson Soares Pontes [3,4], Anna Calarco [1,2,*] and Pierfrancesco Cerruti [5]

International Journal of *Molecular Sciences*

Review

Marine-Derived Polysaccharide Hydrogels as Delivery Platforms for Natural Bioactive Compounds

Fabrizia Sepe [1,†], Anna Valentino [1,2,†], Loredana Marcolongo [1], Orsolina Petillo [1,*], Raffaele Conte [1,2,*], Sabrina Margarucci [1], Gianfranco Peluso [1,3] and Anna Calarco [1,2]

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Thank you!