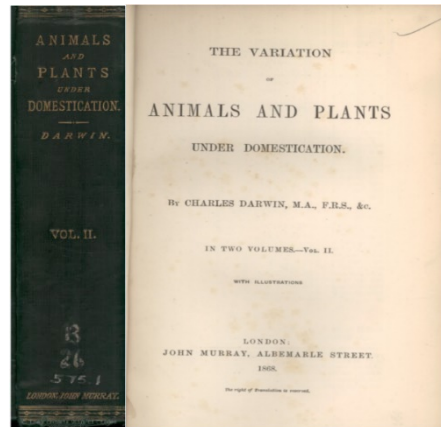


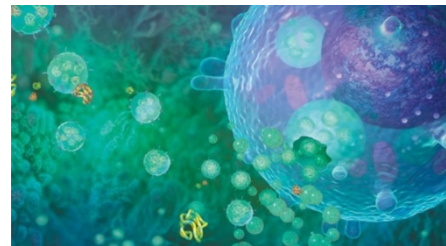
evMANIFESTO

As a part of his pangenesis theory in *Animals and Plants under Domistiation* (1868), Charles Darwin hypothesized that every cell type in the body generates “minute size” *gemmules* that contain molecules and serve to communicate them to other cell types. This seminal intuition fell unnoticed for 150 years (at most the tiny particles released by cells were discarded as debris without biological significance) until the latest days, when contemporary readers may recognize extracellular vesicles (EVs) in Darwin’s *gemmules*^{1,2}.



In the last years intensive research at the convergence of biology and nanotechnology³ has abruptly brought EVs under the limelight as the universal agents of intercellular and inter-organismal communication, in both normal and pathological processes. By virtue of their bioactive cargoes, EVs represent an appealing cell-free strategy for the treatment of a range of pathologies and are multiplex biomarkers, paving the way to non- invasive fluid biopsy. EV engineering with therapeutic agents is expected to foster a sweeping paradigm-shift in medicine applications of nanoparticles: from the synthetic mainstream - which after two decades of intense efforts and funding seems to have reached a dead end⁴ - to biogenic nanoparticles 3.0 “made by cells for cells” with unsurpassed circulation and targeting abilities, personalization and sustainability.

Indeed, EVs are poised to reshape our perspective on life sciences, environment and public health, but research is at the very beginning with several outstanding questions and technical challenges ahead. Nevertheless, companies all over the world are starting to massively invest in the field. According to the *Exosome Diagnostic and Therapeutic Market Report*, published by Allied Market Research (exosomes are among the most promising subpopulation of EVs in terms of clinical applications), the global market is expected to garner 329 M€ by 2022, registering a CAGR (Compound annual growth rate) of 37.8% during the period 2016-2022⁵. The diagnostic segment dominated the market in 2015, and it is expected to continue its dominance throughout the forecast period. Cancer applications hold two-fifths share of the world exosome diagnostic and therapeutic market.



Five EIC - FET OPEN funded projects having EVs as central common focus are to date running in parallel. They are INDEX (www.indexproject.eu), VES4US (ves4us.eu), evFOUNDRY (www.evfoundry.eu), GLADIATOR

(www.fet-gladiator.eu) and MINDGAP (<http://www.biomark.isepp.pt/mindgap/>). We intuited and agreed that this singular situation deserved an action point. Therefore, the projects started an active networking, with the aim of effectively promoting cross-fertilization and maximizing the outcomes. The key

¹ Darwin, C. (1868), *The Variation of Animals and Plants under Domestication* (1st ed.), London: John Murray. doi: 10.1017/CBO9780511709517

² Margolis L, Sadovsky Y (2019) The biology of extracellular vesicles: The known unknowns. *PLoS Biol* 17(7): e3000363. <https://doi.org/10.1371/journal.pbio.3000363>

³ Wang et al. (2019) “The State of Exosomes Research: A Global Visualized Analysis,” *BioMed Research International*, vol. 2019. <https://doi.org/10.1155/2019/1495130>

⁴ Chan et al. (2016) Analysis of nanoparticle delivery to tumours *Nature Review Materials* n.16014. doi:10.1038/natrevmats.2016.14

⁵ *Exosome Diagnostic and Therapeutic Market by Application (Diagnostic and Therapeutic), Product (Instrument, Reagent and Software) and End-User (Cancer Institute, Hospital, Diagnostic Center, and Others) - Global Opportunity Analysis and Industry Forecasts, 2014-2022 - Allied Market Research*

researchers heading these projects have started elaborating a **road map** for the next years and the first action was to commit to meet once a year in a **Clustering Event**. The first was held in Palermo (Italy) November 6th, hosted by VES4US project. 51 researchers registered, 34 organizations from 15 countries were present to the event; a collection of the "raw" documents of the day can be found here:

(https://drive.google.com/drive/folders/1Uhn1OE-pYX9ePeCM6Cj532DT-yfYu_zh?usp=sharing). The next event will be held in November 2020 in Portugal, hosted by MINDGAP.

The emerging field of EV-based research and its industrial/clinical translation will significantly profit from the outcomes of these 5 EIC FET Open innovative projects. The new knowledge created will influence not only the biomedical landscape, but also may have applications in other sectors like Original Equipment Manufacturers (OEMs), cosmetics and nutraceuticals, shaping the future both within and outside the European Union.

The second action is this extracellular vesicle Manifesto - **evMANIFESTO**, which aims at **highlighting the current EU effort in EV research within the FET program and the urgency of introducing and securing more firmly the EV-related theme as a cornerstone in the research agenda in EU**.

With this regard, INDEX, VES4US, evFOUNDRY, GLADIATOR and MINDGAP commit themselves towards:

- the gain of scientific knowledge, exploiting the project outcomes and promoting networking and cross-fertilization within, but not limited to, the EV community,
- the training of a highly qualified workforce to meet the future needs of the European society,
- the establishment, optimization, validation and sharing of good research practices for reproducible and standardized EV studies and projects,
- dissemination, communication and publicising activities aimed at promulgating EV-related findings and innovations to scientific communities, key stakeholders and to the general public,
- the developing of a knowledge-based economy.

This commitment will sustain the placing of Europe at the front row of EV research and, more generally, in the key sector of frontier bio(nano)technology.

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