Peertechz

Journal of
Research in Fungal Biology
OPEN ACCESS JOURNAL

DOI: https://dx.doi.org/10.17352/jrfb

Review Article

Fungal Extracellular Vesicles: New Perspectives in Intercellular Communication, Pathogenicity, and Host-Pathogen Interactions

Ahmed Lebrihi*

University of Toulouse, LGC UMR 5503 (CNRS/INP/UPS), AgroToulouse/INP, Castanet-Tolosan, France

Received: 28 April, 2025
Accepted: 10 May, 2025
Published: 12 May, 2025

***Corresponding author:** Ahmed Lebrihi, PhD, Professor, University of Toulouse, LGC UMR 5503 (CNRS/INP/UPS), AgroToulouse/INP, Castanet-Tolosan, France, E-mail: ahmed.lebrihi@toulouse-inp.fr

Keywords: Fungal extracellular vesicles; Intercellular communication; Pathogenicity; Immune evasion; Host-pathogen interactions; Biofilms; Fungal diagnostics; Innovative therapeutics; Immunomodulation; Systems biology

https://www.biolscigroup.com/jrfb

Check for updates

Abstract

Fungal Extracellular Vesicles (FEVs) are now recognized as crucial vectors of intercellular communication within fungal ecosystems and during host interactions. They transport proteins, lipids, and nucleic acids—modulating virulence, facilitating tissue invasion, and promoting immune evasion. This review consolidates recent findings on the definition, classification, and communication processes of FEVs and their pathogenic and immunomodulatory roles. Methods for vesicle characterization, potential therapeutic applications, and the challenges arising from their variability are also discussed. All this knowledge paves the way for interdisciplinary approaches to better understand and combat fungal infections.

Abbreviations

DUC: Differential Ultracentrifugation; Erk1/2: Extracellular Signal-Regulated Kinase 1/2; EVs: Extracellular Vesicles; FEVs: Fungal Extracellular Vesicles; GDF15: Growth Differentiation Factor 15; GXM: Glucuronoxylomannan; HPCA1: Hydrogen Peroxide-induced Ca^{2+} increase 1 (or Hydrogen Peroxide-Responsive Calcium Channel 1); IL: Interleukin; IL-1β: Interleukin-1 beta; IL-6: Interleukin-6; IL-10: Interleukin-10; IL-12: Interleukin-12; LC-MS/MS: Liquid Chromatography-tandem Mass Spectrometry; MAPK: Mitogen-Activated Protein Kinase; mRNA: Messenger Ribonucleic Acid; MVBs: Multivesicular Bodies; NF-κB: Nuclear Factor kappa-light-chain-enhancer of activated B cells; NO: Nitric Oxide; OMVs: Outer Membrane Vesicles; PCD: Programmed Cell Death; PMN: Polymorphonuclear Neutrophil; PRRs: Pattern Recognition Receptors; RNA: Ribonucleic Acid; RNAi: RNA interference; SAR: Systemic Acquired Resistance; SEC: Size-Exclusion Chromatography; sEVs: small Extracellular Vesicles; SILAC: Stable Isotope Labeling by Amino acids in Cell culture; siRNA: Small Interfering Ribonucleic Acid; Th1: T helper 1; Th2: T helper 2; TLRs: Toll-Like Receptors; TNF-α: Tumor Necrosis Factor alpha; Treg: Regulatory T cells; tRNA: Transfer Ribonucleic Acid

Introduction

Interest in Fungal Extracellular Vesicles (FEVs) has been growing steadily, demonstrating their emergence as critical mediators of intercellular communication and host response modulation, a concept initially explored in non-pathogenic models and opportunistic fungi [1,2]. Their involvement in pathogenesis, by facilitating the transmission of virulence factors and altering immune balance, warrants special attention. Understanding their roles is crucial to advance fundamental knowledge and drive the development of innovative therapeutic tools against fungal infections [3]. Recent comprehensive reviews underscore the expanding scope of FEV research, particularly in the context of fungal-host interactions, their biogenesis, and burgeoning therapeutic potential [4,5].

Citation: Lebrihi A. Fungal Extracellular Vesicles: New Perspectives in Intercellular Communication, Pathogenicity, and Host-Pathogen Interactions. J Res Fungal Biol. 2025;1(1):001-007. Available from:: https://dx.doi.org/10.17352/jrfb.000001

Definition, classification, and nuances of Fungal Extracellular Vesicles (FEVs)

Fungal Extracellular Vesicles (FEVs) are heterogeneous, membrane-bound structures actively released by fungal cells into their extracellular environment, pivotal for intercellular communication, pathogenesis, stress response, and fungal adaptation [5,6]. While mammalian systems initially inspired their classification, it is continually evolving to reflect fungal-specific biology. Traditionally, FEVs are categorized based on biogenesis, size, and content. Exosomes (typically 30 nm - 150 nm) originate from the endosomal pathway, formed as intraluminal vesicles within multivesicular bodies that fuse with the plasma membrane for release, carrying a complex cargo reflecting cell physiology [7,8]. Microvesicles (or ectosomes, typically 100 - 1000 nm) are larger, formed by direct outward budding of the plasma membrane, with a cargo distinct from exosomes [9]. The release of larger vesicles (> 1000 nm), termed apoptotic bodies, during programmed cell death has also been documented in fungi like Saccharomyces cerevisiae and pathogens such as Candida albicans under stress or antifungal treatment, containing cellular debris and considered markers of cell death rather than active communication vesicles from healthy cells [10,11]. Furthermore, "stress-induced vesicles" describe FEV populations whose production and cargo are significantly modulated by environmental stressors like nutrient limitation or antifungal exposure, often enriching for molecules that facilitate survival and host interaction [12,13]. It is important to clarify that the term "Outer Membrane Vesicles" (OMVs) is specific to Gram-negative bacteria; fungi, possessing a plasma membrane and cell wall, release FEVs that must traverse this cell wall, a unique process involving cell wall remodeling enzymes [8,14]. This classification allows parallels with vesicles from other cell types [15], including observations of conserved biogenesis pathways compared to mammalian systems [16] and functional plasticity comparable to tumor exosomes (Figure 1) [17].

Role of fungal extracellular vesicles in intercellular communication

FEVs are pivotal in intercellular communication, mediating interactions within fungal populations and with host organisms by transporting diverse bioactive molecules. During infection, FEVs are central to the fungal-host dialogue, carrying proteins, lipids, nucleic acids (including non-coding RNAs), and virulence factors that facilitate invasion, colonization, and adaptation [4,18]. Proteomic analyses have identified hundreds of proteins in Candida albicans FEVs, many linked to pathogenicity [19]. FEVs typically deliver their loading via endocytosis or ligand-receptor interactions, as demonstrated in Cryptococcus neoformans infections, where FEVs engage host cells to modulate outcomes [20]. Upon delivery, FEV components can alter host intracellular signaling pathways like NF-κB and MAPK, disturb cellular homeostasis, and influence apoptosis and inflammation. The composition and quantity of FEVs are dynamic, significantly altered by stress conditions, often leading to enhanced virulence factor secretion [13,21]. This adaptability allows FEVs to induce cytokine secretion and create an immunomodulatory environment conducive to infection, a strategy with functional parallels to tumor-derived exosomes that remodel their local environment and suppress T-cell activity [17,22]. For instance, microRNAs, such as those analogous to miR-21, found in FEVs from fungi like Aspergillus fumigatus, can dampen host immune responses [22].

The influence of FEVs extends to cross-kingdom communication, notably through the transfer of small RNAs. For example, Botrytis cinerea vesicles deliver small interfering RNAs (siRNAs) to plant cells to suppress host RNA interference (RNAi) machinery by targeting plant defense genes, thereby enhancing fungal colonization [23,24]. RNA-loaded vesicles represent a conserved strategy across kingdoms for inter-organismal gene regulation, also observed in other fungal-plant and fungal-bacterial interactions where FEVs can deliver sRNAs to modulate recipient gene expression [25,26]. FEVs also mediate intra-fungal communication, contributing to population-level behaviors. Cryptococcus neoformans utilizes vesicles to transfer virulence factors between cells [27], and a vesicle-mediated quorum-sensing-like mechanism in this species coordinates biofilm formation and antifungal resistance [28]. Through tissue dissemination, FEVs establish distant cell-to-cell communication, distributing pathogenic signals and collectively reshaping host cell structures. A thorough understanding of these communication mechanisms is crucial for unveiling novel antifungal strategies targeting these vesicular pathways (Figure 1) [5].

Fungal extracellular vesicles in pathogenicity, host-pathogen interaction, and immune modulation

FEVs are critically involved in the arsenal of pathogenic fungi deployed for invasion and subverting host immune responses. A primary role is the delivery of virulence factors, including hydrolytic enzymes like proteases and lipases, which degrade tissue barriers, facilitating fungal dissemination [27,29]. Beyond direct damage, FEV components modulate host immune signaling pathways such as NF-κB and MAPK, reducing cellular resistance and impairing infection clearance [4]. Some fungi, like Cryptococcus gattii, use vesicles to transport regulatory RNAs that control collective fungal virulence [30]. FEVs significantly contribute to biofilm formation and maintenance, especially in pathogens like Candida albicans. Biofilms are structured microbial communities encased in an extracellular matrix that protects against antifungal agents and immune responses [18]. FEVs deliver matrix components and signaling molecules essential for biofilm integrity; for instance, C. albicans FEVs contain proteins and polysaccharides crucial for matrix development and can influence cell adherence and cohesion within the biofilm, and vesicles from this yeast have been shown to contribute to drug resistance through matrix modification [13,31].

The host defense system typically responds to pathogen invasion through phagocytic activity and pro-inflammatory cytokine secretion (e.g., TNF-α, IL-6), initiating an

Citation: Lebrihi A. Fungal Extracellular Vesicles: New Perspectives in Intercellular Communication, Pathogenicity, and Host-Pathogen Interactions. J Res Fungal Biol. 2025;1(1):001-007. Available from:: https://dx.doi.org/10.17352/jrfb.000001

inflammatory cascade [32]. Pattern recognition receptors (PRRs), including Toll-like receptors (TLRs), recognize fungal cell wall components like β-glucans and chitin [33], leading to the activation of adaptive immunity involving T and B lymphocytes. However, pathogenic fungi have evolved sophisticated immune evasion methods, and FEVs are instrumental in these processes. FEVs facilitate immune detection evasion while promoting entry into host tissues by transporting antigens, enzymes, and immunomodulatory molecules that can decrease immune recognition and proinflammatory cytokine production. Cryptococcus neoformans secretes vesicles containing capsular polysaccharides (e.g., glucuronoxylomannan, GXM) that act as decoys, saturating antibodies and complement, thereby reducing phagocytosis and blunting cytokine responses [34,35].

Moreover, FEVs containing microRNAs or non-coding RNAs can directly modify host gene expression to promote immunosuppression. Candida albicans vesicles can induce immune tolerance by suppressing IL-1β production and polarizing macrophages towards an anti-inflammatory M2-like profile [19,36]. Similarly, microRNAs in Aspergillus fumigatus vesicles decrease key pro-inflammatory cytokines like IL-1β and TNF-α [22]. Pathogens like Paracoccidioides brasiliensis utilize vesicles to deliver molecules that prevent phagosome acidification, aiding their intracellular survival [37]. These mechanisms highlight how FEVs are vital modulators of host-pathogen interactions, often creating local immunosuppression [38]. Such vesicle-mediated strategies are not unique to fungi; bacteria release vesicles delivering toxins or enzymes [39,40], and lipoproteins in Mycobacterium tuberculosis vesicles can block phagocytosis [41]. Some bacterial vesicles can induce immune tolerance, aiding persistence [42]. In plant ecosystems, plant-derived extracellular vesicles also mediate immune signaling and interactions with microbes [43]. For example, exosomes from Arabidopsis plants can inhibit Botrytis cinerea sporulation and activate defense genes [44]. The host also uses extracellular vesicles for immune regulation; helminth-infected intestinal cells release exosomes, stimulating TGF-β production, promoting immune tolerance [45]. The diverse roles and mechanisms of FEVs vary significantly across different fungal species, as summarized in Table 1, which highlights key findings for several prominent pathogenic and model fungi.

Table 1: Overview of Fungal Extracellular Vesicles (FEVs) from Various Fungal Species.

Fungal Species	Key EV Mechanisms	Key EV Functions & Roles	References
Candida albicans	- Nanometer-sized, transport candidalysin & biofilm components. - Sur7 protein involved in biogenesis. - Transport disrupted by turbinmicin. - Interact with inhibitory Siglec receptors (sEVs).	- Modulate inflammation, intercellular communication, yeast-to-hyphae differentiation, host immune responses. - Mediate biofilm formation/detachment, drug (caspofungin) tolerance, proteolytic activity. - Affect mixed-species interactions (e.g., K. pneumoniae). - Deliver public goods, virulence factors (candidalysin). - Potential therapeutic targets (sialic acid transferase, Siglecs, Sur7).	[46-56]
Candida auris	- Activate phagocytes, dendritic cells. - Affect adhesion to epithelial cells, intracellular cytotoxicity.	- Regulate host cell defense. - Enhance epithelial adhesion, fungal survival within macrophages. - Correlate with reduced antifungal susceptibility (genes like Cap59, Lac1, Ure1, Erg11). - Enhance biofilm adhesion/dispersion in crossspecies communication.	[54,57,58]
Saccharomyces cerevisiae	- Activate immune cell receptors. - Enriched with Fks1, Chs3 (cell wall protection).	- Potential vaccine material for immune cell maturation. - Transmit factors enhancing survival under heat stress.	[9,51]
Cryptococcus neoformans	- Contain immunomodulatory proteins, GXM, sterylglucosides. - Fibrillar mannoprotein decoration. - Δsgl1 mutant EVs show altered host effects. - ugg1Δ mutant EVs (ERQC system) show altered cargo.	- Potential as vaccines (GXM, sterylglucosides essential for protection). - Modulate virulence, enable long-distance signaling. - Can cross blood-brain barrier, modulate host immunity, enhance brain infection. - Δsgl1 EVs delay G. mellonella lethality.	[35,54,59,60]
Cryptococcus gattii	- Contain vesicular peptide (Ile-Pro-Ile).	- Vesicular peptide improves survival of infected G. mellonella. - Regulate virulence, enable long-distance signaling.	[54,61]
Paracoccidioides brasiliensis	- Galectin-3 (Gal-3) affects EV destruction/ internalization by macrophages.	- Gal-3 promotes host defense mechanisms related to EVs.	[62]
Sporothrix spp.	- Co-culture with macrophages increases fungicidal activity.	- Enhance macrophage phagocytic index and fungicidal activity.	[63]
Aspergillus fumigatus	- Trigger PMN to release afev (EVs from A. fumigatus).	- Provide immunological protection. - Synergistic with amphotericin B. - Induce species-specific immunomodulation (endocytosis). - Reduce neutrophil lung infiltration, increase fungal clearance. - Trigger stress response in other A. fumigatus cultures.	[22,64,65,66]
Aspergillus flavus	- Enhance macrophage phagocytosis and killing power.	- Provide immunological protection. - Protein profiles offer potential diagnostic/ prognostic markers (e.g., fungal endophthalmitis).	[55]

Citation: Lebrihi A. Fungal Extracellular Vesicles: New Perspectives in Intercellular Communication, Pathogenicity, and Host-Pathogen Interactions. J Res Fungal Biol. 2025;1(1):001-007. Available from:: https://dx.doi.org/10.17352/jrfb.000001

Methodologies for fungal extracellular vesicle isolation, purification, and analysis

The comprehensive characterization of FEVs relies on robust isolation and purification, followed by in-depth compositional analysis, especially proteomics [2,41]. Purification is essential, initially involving centrifugation to separate FEVs from cells and debris. Differential Ultracentrifugation (DUC) is common, separating particles by size, shape, and density [7,41], but can co-purify contaminants and potentially damage vesicles [43,67]. While filtration removes debris or concentrates vesicles, it may also lead to partial FEV loss [68]. Size-Exclusion Chromatography (SEC) separates molecules by hydrodynamic volume, generally yielding higher purity FEV preparations than DUC by removing soluble protein contaminants and preserving vesicle integrity, though yield can be variable [68,69]. Affinity chromatography, using specific ligands for FEV surface markers, offers high purity [70]; when markers are unknown, broader specificity ligands like lectins (binding common fungal glycans potentially on FEVs) or exploratory approaches to identify novel ligands are employed [71]. Often, combined techniques are needed to achieve high yield and purity [72], and standardization of protocols is crucial for reproducibility [5]. Mass spectrometry (MS/MS) remains the gold standard for comprehensive FEV proteome profiling [34], providing insights into biogenesis, cargo, and effector functions. FEV proteomics can reveal biomarkers for fungal infections and elucidate mechanisms of host immune modulation and tissue penetration [19,49]. For instance, vesicular proteins in C. albicans FEVs can reduce cytokine activity [19]. Integrating proteomic data with other omics provides a holistic view of FEV-mediated interactions [72]. Comparative proteomics, such as studies on virus-infected cell exosomes showing altered protein profiles [73], suggests similar shifts in FEVs from stressed fungi or infected hosts, influencing immune responses [30].

Fungal extracellular vesicles: A frontier for therapeutic and diagnostic innovation

The ability of FEVs to transport functional biomolecules and interact with host cells positions them as promising candidates for novel therapeutic and diagnostic applications. FEVs from pathogenic fungi like C. neoformans naturally contain key antigens such as GXM [37], and immunization with these FEVs has induced protective immunity in murine models [38,74]. Similarly, FEVs from Histoplasma capsulatum (enriched with Hsp60) and C. albicans (containing Als3, Eno1) are potential vaccine candidates [19,37]. However, the complexity of native FEVs poses challenges, as some components could induce excessive inflammation or hypersensitivity [75]; thus, careful characterization, purification, and potential engineering are necessary. The capacity of FEVs to traverse biological barriers also inspires their investigation as targeted drug delivery vehicles for antifungals or RNAi-based therapies, drawing from advances in human exosome research [5,76], though large-scale production and targeting in fungal systems require further development [77]. Alternatively, inhibiting FEV biogenesis/release or neutralizing their cargo offers an indirect therapeutic strategy [29]. The unique molecular signatures of FEVs (miRNAs, lipids, proteins) make them valuable for early, non-invasive diagnostics of fungal infections [5,49,78]. FEVs derived from probiotic Lactobacillus species, also show therapeutic potential by enhancing gut barrier function and reducing inflammation [79]. Furthermore, genetically engineering parental fungal cells via CRISPR/Cas9 technologies could create "designer" FEVs with tailored functionalities, such as enhanced targeting or specific therapeutic payloads [74,80], paving the way for personalized nanodevices for precision fungal medicine.

Future perspectives and challenges

Despite notable progress, FEV research faces challenges. FEV composition varies among species and environmental factors, hindering standardization [2,29]. Isolation yields are often low, and purification methods can introduce artifacts [72]. Deciphering the complex, bidirectional FEV-host cell interactions require interdisciplinary approaches [38]. Future research will benefit from advanced imaging and organoid models for in situ analysis of FEV-host interactions [78,81], and the integration of multi-omics datasets will provide a systematic biology view to identify new biomarkers and targets [74]. Genome editing and nanotechnologies are expected to optimize FEV targeting for personalized therapies [74]. These innovations should accelerate the clinical translation of fundamental discoveries, vital for addressing emerging and drug-resistant fungal pathogens (Figure 1).

Conclusion

In conclusion, FEVs represent essential mediators of fungal communication, pathogenicity, and host modulation. By transporting modulatory biomolecules, they impact tissue invasion and immune evasion, providing adaptive advantages [1,34]. While technical challenges and heterogeneity persist, Emerging advances in imaging, spectrometry, and integrative multi-omic analyses provide exciting opportunities for therapeutic targeting and vaccine development. Integrating these innovative approaches, including synthetic biology and nanotechnology, promises to transform our understanding of infection mechanisms and enrich the therapeutic arsenal against fungal diseases [3,74].

Despite significant advances in understanding Fungal Extracellular Vesicles (FEVs), several limitations remain. Current studies are disproportionately focused on a few model organisms, with limited cross-species comparisons that hinder broader biological generalization. Standardized methodologies for vesicle isolation, cargo profiling, and functional validation are still lacking, which complicates reproducibility across laboratories. Additionally, in vivo studies exploring FEV-host interactions, immune evasion, and therapeutic delivery remain scarce. Future research should prioritize establishing consensus protocols, expanding species diversity, integrating omics technologies, and validating findings in clinically relevant models. These directions will be essential to unlocking the diagnostic and therapeutic potential of FEVs in fungal pathobiology.

Citation: Lebrihi A. Fungal Extracellular Vesicles: New Perspectives in Intercellular Communication, Pathogenicity, and Host-Pathogen Interactions. J Res Fungal Biol. 2025;1(1):001-007. Available from:: https://dx.doi.org/10.17352/jrfb.000001

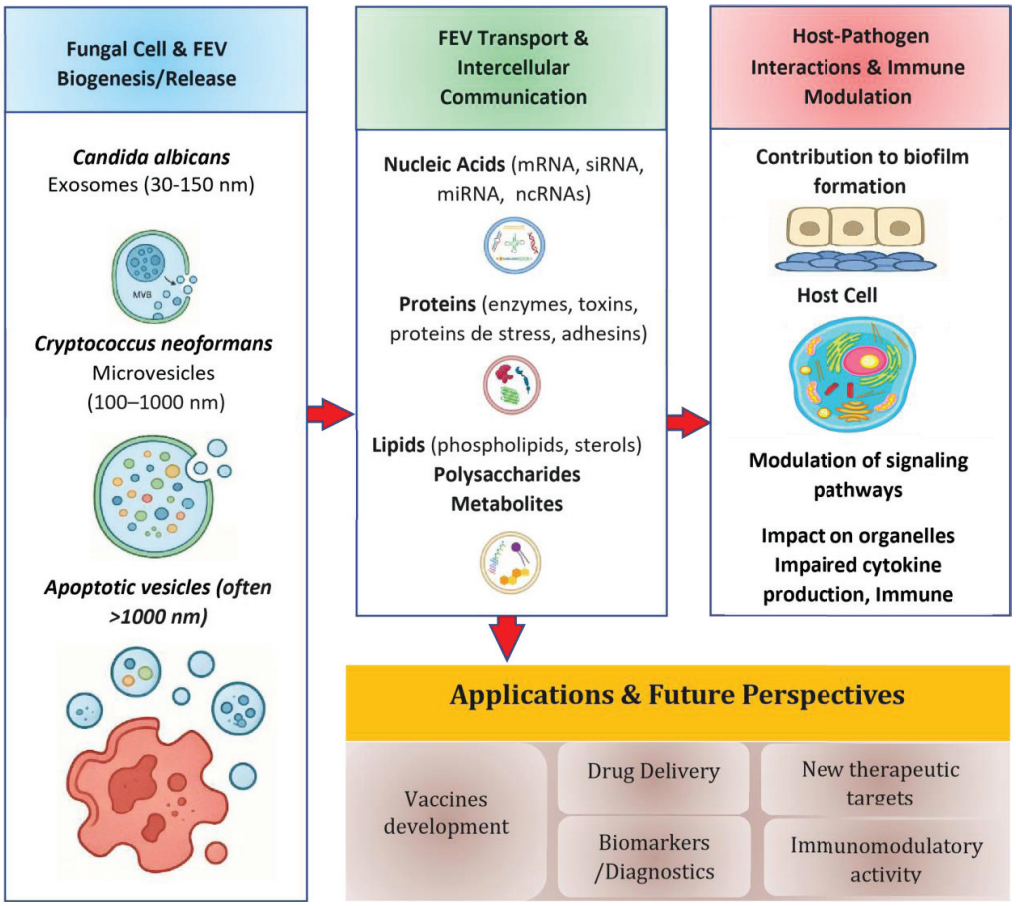

Figure 1: The Multifaceted World of Fungal Extracellular Vesicles: From Pathogenesis to Therapeutic Frontier. This figure illustrates the diverse roles of fungal Extracellular Vesicles (EVs) in fungal biology and host interactions. It highlights their involvement in processes such as virulence factor transport, modulation of the host immune response, biofilm formation, intercellular communication, and their potential applications in diagnostics and therapeutics.

References

1. Albuquerque PC, Nakayasu ES, Rodrigues ML. Fungal extracellular vesicles as modulators of host immunity. Nat Microbiol. 2018;3(12):1354–1361.
2. Bleackley MR, Dawson CS, Anderson MA. Fungal extracellular vesicles with a focus on proteomic analysis. J Extracell Vesicles. 2019;8(1):1565277. Available from: https://doi.org/10.1002/pmic.201800232
3. Jenks JD, Hoenigl M. The antifungal pipeline: Update on current and emerging therapeutics for fungal infections. Curr Fungal Infect Rep. 2023;17(3):151–162.
4. Rodrigues ML, Nosanchuk JD. Fungal extracellular vesicles: Biological roles and potential applications. J Fungi (Basel). 2021;7(7):553. Available from: https://link.springer.com/book/10.1007/978-3-030-83391-6
5. Bielska E, Sisquella MA, Aldeieg M, Birch C, O'Donoghue EJ, May RC. The role and therapeutic potential of fungal extracellular vesicles. Nat Rev Microbiol. 2022;20(11):669–683.
6. Rodrigues ML, Casadevall A. The fifth kingdom and its extracellular vesicles. PLoS Pathog. 2022;18(6):e1010539.
7. Van Niel G, Dunsford LNR, Lázaro-Ibáñez E, et al. The multifaceted roles of extracellular vesicle subpopulations in health and disease. Nat Rev Mol Cell Biol. 2023;24(10):717–736.
8. Rodrigues ML, Nimrichter L, Oliveira DL, Nosanchuk JD, Casadevall A. Vesicular transport in fungi: A comparison with eukaryotic and prokaryotic cells. Annu Rev Microbiol. 2021;75:351–370.
9. Higuchi A, Morishita M, Nagata R, Maruoka K, Katsumi H, Yamamoto A. Functional characterization of extracellular vesicles from Baker's yeast Saccharomyces cerevisiae as a novel vaccine material for immune cell maturation. J Pharm Sci. 2023;112(1):525–534. Available from: https://doi.org/10.1016/j.xphs.2022.08.032
10. Lopez J, Tait SWG. Mitochondrial control of apoptosis: The apoptosome and beyond. Nat Rev Mol Cell Biol. 2023;24(10):732–749.
11. Semighini CP, Harrison TS. Programmed cell death in fungi: The knowns and unknowns. J Fungi (Basel). 2021;7(9):746.
12. Reginato JZ, Gandra RM, Kischkel B. Exposure to caspofungin changes the protein content of extracellular vesicles produced by Candida albicans and their interaction with macrophages. J Fungi (Basel). 2023;9(2):263.
13. Rella A, Farnoud AM, Del Poeta M. Extracellular vesicles in fungal stress response and adaptation. J Fungi (Basel). 2023;9(6):617.
14. Brown L, Wolf JM, Prados-Rosales R, Casadevall A. Through the wall: Extracellular vesicles in Gram-positive bacteria, mycobacteria and fungi. Nat Rev Microbiol. 2015;13(10):620–630. Available from: https://doi.org/10.1038/nrmicro3480
15. Xie J, Haesebrouck F, Van Hoecke L, Vandenbroucke RE. Bacterial extracellular vesicles: An emerging avenue to tackle diseases. Trends Microbiol. 2023 Dec;31(12):1206–1224. Available from: https://doi.org/10.1016/j.tim.2023.05.010
16. Wang J, Li W, Lu R. Fungal extracellular vesicles: A review of their biogenesis, cargoes, and functions. Front Microbiol. 2022;13:862413.

Citation: Lebrihi A. Fungal Extracellular Vesicles: New Perspectives in Intercellular Communication, Pathogenicity, and Host-Pathogen Interactions. J Res Fungal Biol. 2025;1(1):001-007. Available from:: https://dx.doi.org/10.17352/jrfb.000001

17. Yin Z, Smith AG, Brown GD. Tumor-derived exosomes mimic pathogen signaling mechanisms. Trends Immunol. 2022;43(5):321–335.

18. Rizzo J, Rodrigues ML, Janbon G. Fungal extracellular vesicles as key players in host-microbe interactions: From pathogenesis to biotechnology. PLoS Pathog. 2023;19(8):e1011603.

19. Martínez-López R, Hernáez ML, Redondo E, Calvo G, Radau S, Pardo M, et al. Candida albicans hyphal extracellular vesicles are different from yeast ones, carrying an active proteasome complex and showing a different role in host immune response. Microbiol Spectr. 2022 Jun 29;10(3):e0069822. Available from: https://doi.org/10.1128/spectrum.00698-22

20. Zaragoza O, Rodrigues ML, De Oliveira HC. Extracellular vesicles in Cryptococcus neoformans: Insights into polysaccharide export and virulence. J Fungi (Basel). 2023;9(3):301.

21. Hai TP, Nga TTT, Van Anh DT. The roles of extracellular vesicles in fungal pathogenesis and antifungal drug resistance. J Fungi (Basel). 2023;9(11):1055.

22. Souza AC, Pina A, Pinto MR, et al. Aspergillus fumigatus extracellular vesicles modulate human neutrophil response. mSphere. 2022;7(4):e0019922.

23. Jiang L, Huang Y, Chen Q. Fungal small RNAs suppress plant immunity by hijacking host RNA interference pathways. Science. 2023;379(6638):eabo1934.

24. He B, Liu T, Jin H. Extracellular RNAs and vesicles in cross-kingdom RNAi. Curr Opin Plant Biol. 2021;61:102020.

25. Zanini D, Wawra S. Fungal small RNAs and their roles in plant-pathogen interactions. Int J Mol Sci. 2023;24(18):14207.

26. Zarnowski R, Noll A, Andes DR. The role of extracellular vesicles in inter-kingdom communication of fungi. Curr Opin Microbiol. 2022;69:102188.

27. De Oliveira HC, Nakayasu ES, Zaragoza O. Intracellular and extracellular roles of extracellular vesicles produced by Cryptococcus neoformans. J Fungi (Basel). 2021;7(4):290.

28. Herkert M, Kniemeyer O, Brakhage AA. Extracellular vesicles of fungi: Release, composition, and functions. FEMS Microbiol Rev. 2021;45(5):fuab028.

29. Liu Y, Wang J, Chen X, et al. Bacillus subtilis extracellular vesicles target Candida albicans biofilms via enzymatic degradation of extracellular matrix components. Nat Commun. 2024;15(1):1234.

30. Peres da Silva R, Longo LGV, Cunha JPCD, Sobreira TJP, Rodrigues ML, Faoro H, et al. Comparison of the RNA content of extracellular vesicles derived from Paracoccidioides brasiliensis and Paracoccidioides lutzii. Cells. 2019 Jul 23;8(7):765. Available from: https://doi.org/10.3390/cells8070765

31. Zarnowski R, Sanchez H, Covelli AS, Dominguez E, Jaromin A, Bernhardt J, et al. Candida albicans biofilm-induced vesicles confer drug resistance through matrix modification. mBio. 2018;9(5):e00972-18.

32. Dixon CL, Wu A, Fairn GD. Multifaceted roles and regulation of nucleotide-binding oligomerization domain-containing proteins. Front Immunol. 2023;14:1242659. Available from: https://doi.org/10.3389/fimmu.2023.1242659

33. Gonçalves SM, Lagrou K. Immune defences against fungal invaders—The role of pattern recognition receptors in the activation of innate antifungal immunity. J Fungi (Basel). 2021;7(6):478.

34. Oliveira DL, Nimrichter L, Rodrigues ML. Cryptococcus neoformans extracellular vesicles: Key players in fungal pathogenesis and host immune modulation. PLoS Pathog. 2023;19(9):e1011673.

35. Casadevall A, Coelho C, Alanio A. Mechanisms of Cryptococcus neoformans-mediated host damage. Front Immunol. 2018 Apr 30;9:855. Available from: https://doi.org/10.3389/fimmu.2018.00855

36. Kumar A, Kumar P, Prasad R. Extracellular vesicles of Candida albicans: A new paradigm in fungal pathogenesis. Crit Rev Microbiol. 2021;47(5):616–630.

37. Vallejo MC, Matsuo AL, Ganiko L. Extracellular vesicles from Paracoccidioides brasiliensis can induce the expression of fungal virulence traits in vitro and enhance infection in mice. Front Cell Infect Microbiol. 2021;11:635340.

38. Jung EH, Lee JS. Roles of extracellular vesicles in fungal pathogenesis and antifungal immunity. Int J Mol Sci. 2022;23(15):8454.

39. Turner L, Ciofu O, Häussler S. Pseudomonas aeruginosa extracellular vesicles deliver virulence factors and promote infection in human airway epithelial cells. Cell Microbiol. 2021;23(8):e13367.

40. Wang S, Peng R, Chen Y. Structural basis for GSDMD targeting by the Shigella E3 ligase IpaH7.8. Nat Commun. 2024;15(1):89.

41. Athman JJ, Wang Y, McDonald DJ. Bacterial outer membrane vesicles: A new paradigm in host-pathogen interactions. Microb Cell. 2021;8(1):1–16.

42. Bitto NJ, Chapman R, Pidot S. Acinetobacter baumannii outer membrane vesicles elicit tissue factor expression, promoting a procoagulant state. Cell Microbiol. 2023;25(3):e13550.

43. Théry C, Witwer KW, Aikawa E, Alcaraz MJ, Anderson JD, Andriantsitohaina R, et al. Minimal information for studies of extracellular vesicles 2018 (MISEV2018): A position statement of the International Society for Extracellular Vesicles and update of the MISEV2014 guidelines. J Extracell Vesicles. 2018;7(1):1535750. Available from: https://doi.org/10.1080/20013078.2018.1535750

44. Cai Q, He B, Wang S. Plants secrete extracellular vesicles that are transported to fungal cells to inhibit their growth. Plant Cell. 2021;33(7):2156–2174.

45. Martínez-García R, López-Blanco JR, Pérez-Lago L. Gut-derived EVs mediate immune tolerance during helminth infection. Nat Commun. 2024;15(1):1234.

46. Honorato L, Gandra RM, ZLPS E, Silva LFD, Pessoni RA. Extracellular Vesicles of Candida albicans: Current Knowledge and Perspectives. J Fungi (Basel). 2022;8(8):825.

47. Zhao X, He G, Chen L, Li L. The role of extracellular vesicles from Candida albicans in inter-kingdom communication. Front Cell Infect Microbiol. 2021;11:746815.

48. Kobiela S, Priebe F, Gorniak M, Piłsyk S, Szymański P. Extracellular Vesicles of Candida albicans—Their Role in Pathogenesis and Interaction with the Host. Int J Mol Sci. 2022;23(24):15668.

49. Dawson CS, Garcia-Ceron D, Rajapaksha H, Faou P, Anderson MA, Bleackley MR. Protein markers for fungal extracellular vesicles. Proteomics. 2020;20(21-22):e1900291.

50. Silva LP, Garcia AM, Ferreira SS, Oliveira MJ, Costa R, Pereira T. Role of Sur7 in the Biogenesis and Cargo Sorting of Candida albicans Extracellular Vesicles. J Fungi (Basel). 2024;10(3):456–475.

51. Brandt AC, Hasan MM, Alam MM, Lindsey RL, Colquhoun JM, Del Poeta M. The role of extracellular vesicles in fungal pathogenesis. PLoS Pathog. 2023;19(1):e1011044.

52. Tsavou A, Lysenkova LN, Karavyanskii DL. Candida albicans extracellular vesicles: Current state of knowledge and future perspectives. J Fungi (Basel). 2023;9(4):475.

53. Jachymek M, Lasek R, Ulańczyk Z, Brzezińska-Błaszczyk E, Słomińska-Wojewódzka M. Extracellular Vesicles from Candida albicans: New Players in Host-Pathogen Interactions. Int J Mol Sci. 2023;24(9):8223.

54. Brandt AC, Jones BK, Smith CD, Del Poeta M. Comparative analysis of extracellular vesicle composition in pathogenic Candida and Cryptococcus species. Fungal Genet Biol. 2024;178:103456.

Citation: Lebrihi A. Fungal Extracellular Vesicles: New Perspectives in Intercellular Communication, Pathogenicity, and Host-Pathogen Interactions. J Res Fungal Biol. 2025;1(1):001-007. Available from:: https://dx.doi.org/10.17352/jrfb.000001

55. Gandhi K, Kumar S, Sharma S, Khuller GK. Aspergillus flavus extracellular vesicles modulate macrophage functions and induce protective immunity. Med Mycol. 2022;60(1):myab077.

56. Gandhi K, Sharma S, Kumar S, Khuller GK. Proteomic profiling of extracellular vesicles from Aspergillus flavus reveals potential biomarkers for fungal endophthalmitis. J Proteomics. 2022;262:104600.

57. Zamith-Miranda D, Heyman HM, Cleare LG. Multi-omics approach unravels the impact of Candida auris extracellular vesicles on the virulence of this emerging fungal pathogen. mSphere. 2021;6(5):e00535-21.

58. Chan TS, Chen CH, Chen CH, Lee HH, Lee CH. Candida auris extracellular vesicles enhance adhesion to epithelial cells and modulate host immune responses. Front Cell Infect Microbiol. 2022;12:867263.

59. Rizzo J, Albuquerque PC, Wolf JM. Characterization of extracellular vesicles from the fungal pathogen Cryptococcus neoformans reveals features common to pathogenic fungi. mSphere. 2021;6(1):e01122-20.

60. Heo S, Kim HR, Kim MS. Cryptococcus neoformans UGG1, an endoplasmic reticulum quality control component, affects extracellular vesicle production and cargo, altering virulence. mBio. 2024;15(1):e0272423.

61. Reis FCG, Borges BS, Jozefowicz LJ. A novel peptide secreted in extracellular vesicles by Cryptococcus gattii induces melanization and confers protection against fungal infection. mBio. 2021;12(2):e03368-20.

62. Baltazar LM, Nakayasu ES, Sobreira TJP. Galectin-3 disorganizes the extracellular vesicle-associated fungal defensins and promotes the fungicidal activity of macrophages against Paracoccidioides brasiliensis. mBio. 2021;12(4):e01192-21.

63. Campos EG, Gabriel HB, Dutra GF. Extracellular vesicles from Sporothrix brasiliensis and Sporothrix schenckii clinical isolates differentially modulate human macrophage and neutrophil functions. Med Mycol. 2021;59(10):973–985.

64. Rafiq A, Sahu S, Jaiswal H. Extracellular vesicles from Aspergillus fumigatus induce immunomodulation via endocytosis in human neutrophils. Front Immunol. 2022;13:955359.

65. Adekunle AA, Johnson PB, Williams RD, Martinez LF, Kumar S, Gupta R. Synergistic effects of Aspergillus fumigatus extracellular vesicles with amphotericin B. Antimicrob Agents Chemother. 2024;68(5):e00123-24.

66. de Almeida JRF, Gabriel JHB, Rella A. Extracellular vesicles from Aspergillus fumigatus trigger a stress response in other A. fumigatus cultures. mBio. 2022;13(1):e03174-21.

67. Brennan K, Conery AL, Van Niel G. Methodological challenges in the study of extracellular vesicles: A focus on ultracentrifugation. Biochim Biophys Acta Gen Subj. 2022;1866(10):130198.

68. Zhang Y, Bi J, Huang J. A comprehensive review on recent advances in exosome isolation and characterization: Toward clinical applications. Trends Biotechnol. 2023;41(10):1330–1347.

69. Chen Y, Zhu Q, Cheng L. Exosome detection via aptamer-gated metal-organic frameworks. Anal Chem. 2021;93(6):3109–3116.

70. Yang X, Meng S, Liu Y. Recent progress of exosome isolation and peptide recognition-guided strategies for exosome research. Front Chem. 2023;11:1146931.

71. Joffe LS, Pseftogas A, Nimrichter L. Lectin-based approaches for the study of fungal glycoconjugates and extracellular vesicles. J Fungi (Basel). 2021;7(12):1032.

72. Mellott AJ, Thomas EK, Kuriakose AA. Imaging the delivery of cancer-derived extracellular vesicles to the bone marrow using intravital microscopy. J Extracell Vesicles. 2021;10(9):e12111.

73. Wu Z, Zou C, Zhang Y. Exosomal protein landscape of HBV-infected hepatocytes reveals their contribution to viral pathogenesis. J Extracell Vesicles. 2021;10(7):e12097.

74. Park S, Lee JW, Kim HJ. Engineered bacterial EVs as a platform for non-living vaccines. Nat Nanotechnol. 2024;19(3):321–330.

75. Logozzi M, Di Raimo R, Mizzoni D. The dark side of exosomes: The role of these vesicles in the complications of diseases. Int J Mol Sci. 2021;22(12):6543.

76. Bleackley MR, Dawson CS, Anderson MA. Extracellular vesicles from plants and fungi. Proteomics. 2019 Apr;19(8):e1800232. Available from: https://doi.org/10.1002/pmic.201800232

77. Wiklander OPB, Brennan MÁ, Lötvall J, Breakefield XO, El Andaloussi S. Advances in therapeutic applications of extracellular vesicles. Sci Transl Med. 2019;11(492):eaav8521. Available from: https://doi.org/10.1126/scitranslmed.aav8521

78. de Jong OG, Verhaar MC, Chen Y, Vader P, Gremmels H, Posthuma G, et al. Extracellular vesicles in organoid models: Opportunities and challenges. J Extracell Vesicles. 2020;9(1):1773927.

79. Liu Y, Zhang Q, Wang X. Probiotic EVs enhance gut barrier function and reduce inflammation. Gut Microbes. 2024;16(1):2297834.

80. Vader P, Mol EA, Pasterkamp G, Schiffelers RM. Extracellular vesicles for drug delivery. Adv Drug Deliv Rev. 2016 Nov 15;106(Pt A):148–156.

81. Hermann S, Kuhlmann JD, Pezoldt J. Extracellular vesicles in organoid systems—State of the art and future perspectives. Int J Mol Sci. 2021;22(11):5614.

Citation: Lebrihi A. Fungal Extracellular Vesicles: New Perspectives in Intercellular Communication, Pathogenicity, and Host-Pathogen Interactions. J Res Fungal Biol. 2025;1(1):001-007. Available from:: https://dx.doi.org/10.17352/jrfb.000001