International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2024: 7.101

Idioblasts in the Human Body: Comparative Anatomy and Cytology and Their Role in Longevity and Health Mechanisms

Alexandre Tavartkiladze[1,2], Russel J. Reiter[3], Dinara Kasradze[2]

[1]Tbilisi State Medical University, Tbilisi, Georgia

[2]Institute for Personalized Medicine, Tbilisi, Georgia;

[3]Department of Cellular & Structural Biology, University of Texas Health Science Center, San Antonio, USA

(Correspondence: Alexandre Tavartkiladze)

Abstract: ***In classical plant anatomy, idioblasts are solitary or clustered cells that differ sharply from surrounding tissue in morphology and chemical content. They frequently accumulate high concentrations of secondary metabolites (e.g., tannins, alkaloids, crystals) and are strategically localized to protect long-lived organs against herbivores, pathogens, and abiotic stress [1-4]. Although the term "idioblast" is not used in human histology, a convergent design principle appears in the form of discrete secretory and detoxifying cells- goblet cells, Paneth cells, periportal hepatocytes, club (Clara) cells, and tissue-resident macrophages- that function as focal reservoirs and control points for potent bioactive molecules [5-12]. This review develops the concept of "idioblast-like" cells in humans by outlining the cytology and defensive functions of plant tannin idioblasts; comparing them to specialized epithelial and myeloid cells in human barrier organs and detoxification hubs; and highlighting conserved molecular modules, including ATP-binding cassette (ABC) transporters, Phase II conjugation enzymes (UGTs and GSTs), KEAP1-NRF2-ARE signaling, and calcium-dependent secretory pathways [2- 4, 13- 16]. We further discuss how dietary plant polyphenols engage human defense systems via AhR, NRF2, hormetic stress responses, and microbiome-derived postbiotics (e.g., urolithin A), with potential implications for healthspan [17-18,21-24]. Finally, we outline idioblast-inspired therapeutic perspectives including biomimetic drug-delivery systems and precision nutraceutical strategies.***

Keywords: idioblasts; goblet cells; Paneth cells; tannins; polyphenols; ABC transporters; NRF2; AhR; hormesis; xenohormesis; longevity

Simple Summary

Plants protect long-lived organs using idioblasts- specialized cells that stockpile potent defensive molecules such as tannins in large vacuoles. Humans do not use the term "idioblast" in histology, but we repeatedly employ a similar design: discrete, morphologically distinctive cells that concentrate high-potency secretory or detoxifying functions at barrier surfaces and vascular gateways. Examples include goblet cells (mucus), Paneth cells (antimicrobial peptides), periportal hepatocytes (front-line detoxification), bronchiolar club cells (airway detox and repair), and tissue-resident macrophages (compartmentalized clearance and microbial killing) [5- 12]. Many plant polyphenols- often concentrated in idioblast-rich tissues- act as hormetic and xenohormetic signals that engage conserved human defense modules (Phase II- III enzymes, NRF2/ARE, and AhR), shape microbiome metabolism (e.g., urolithin production), and may support healthspan [13- 18, 22- 24].

Figures and Schemes

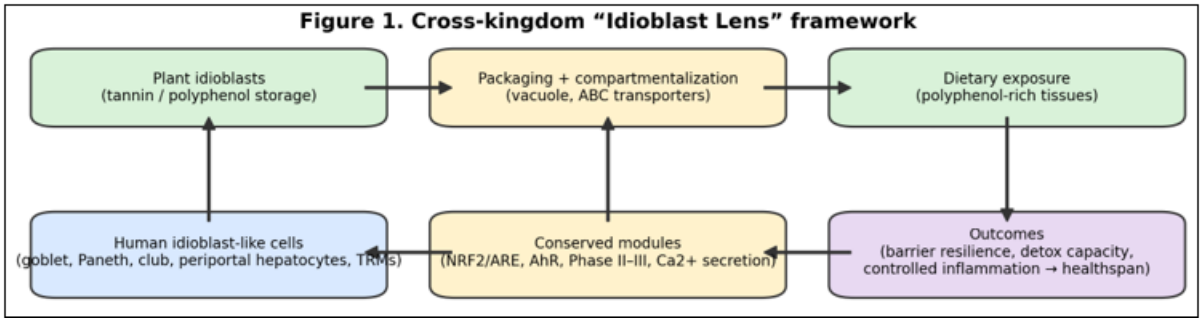


Figure 1: Cross-kingdom "idioblast lens" framework linking plant defensive packaging to human barrier/detox programs and healthspan outcomes.

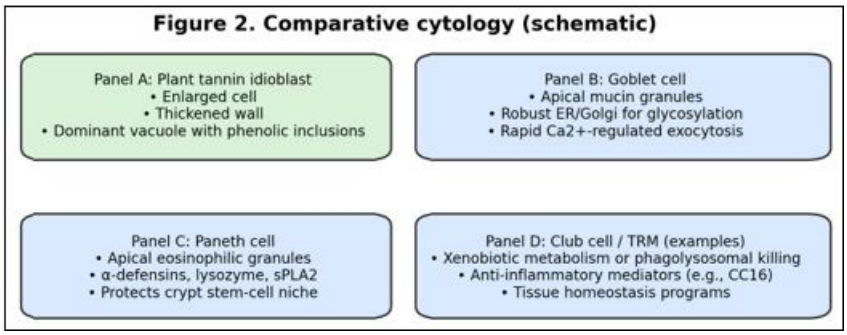


Figure 2: Comparative cytology panels (schematic): plant tannin idioblast, goblet cell, Paneth cell, and representative airway/immune idioblast-like cells.

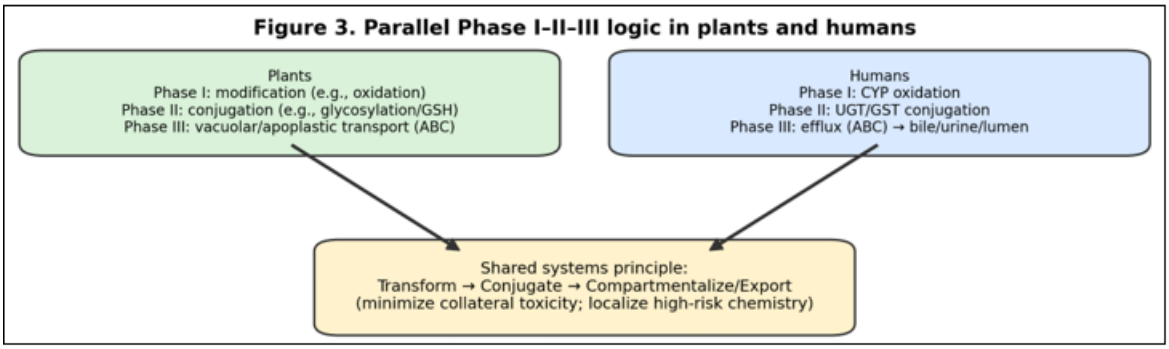


Figure 3: Parallel Phase I-II-III logic in plants and humans: transformation, conjugation, and compartmentalization/export of reactive small molecules.

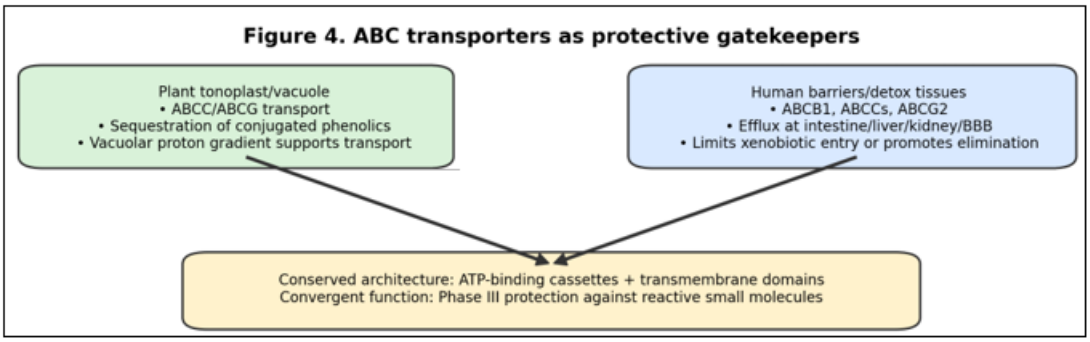


Figure 4: ABC transporters as protective gatekeepers: vacuolar sequestration in plants versus efflux at human barriers and detoxification organs.

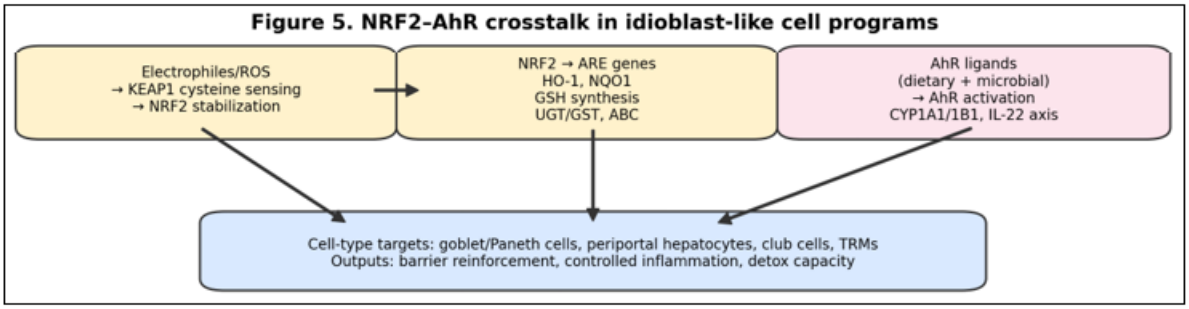


Figure 5. NRF2-AhR crosstalk in idioblast-like cell programs with downstream cytoprotective and barrier-repair outputs

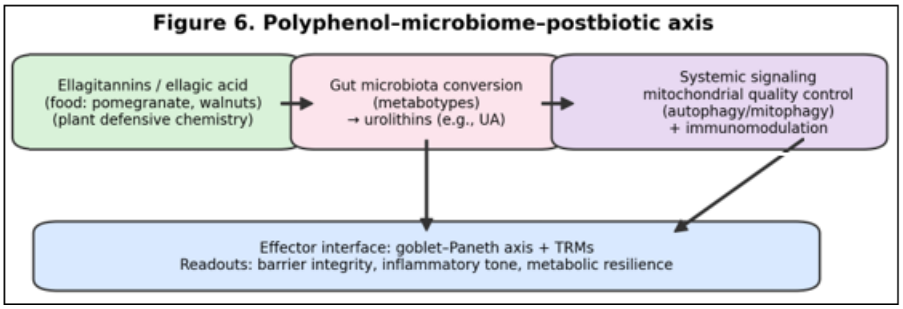


Figure 6: Polyphenol-microbiome-postbiotic axis: ellagitannins/ellagic acid conversion to urolithins and downstream mitochondrial/immune effects.

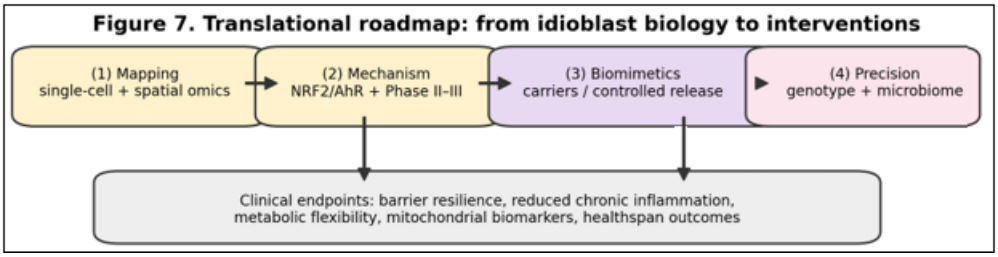
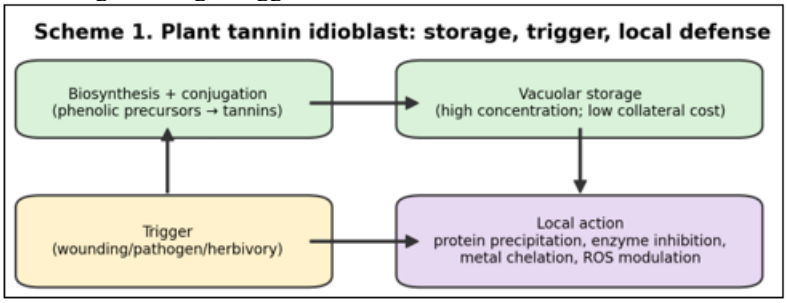
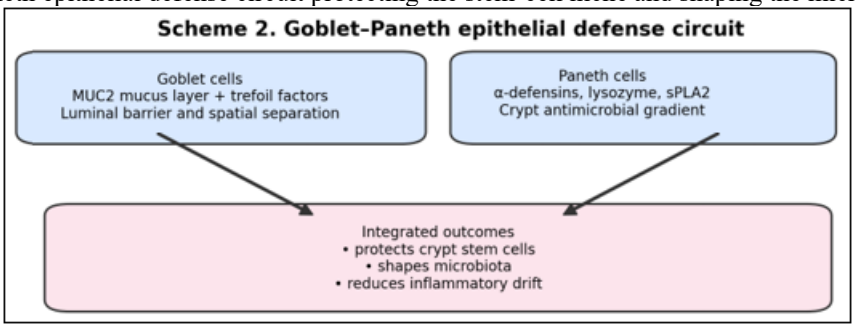


Figure 7: Translational roadmap: mapping, mechanism, biomimetic delivery, and precision xenohormesis approaches toward clinical endpoints.

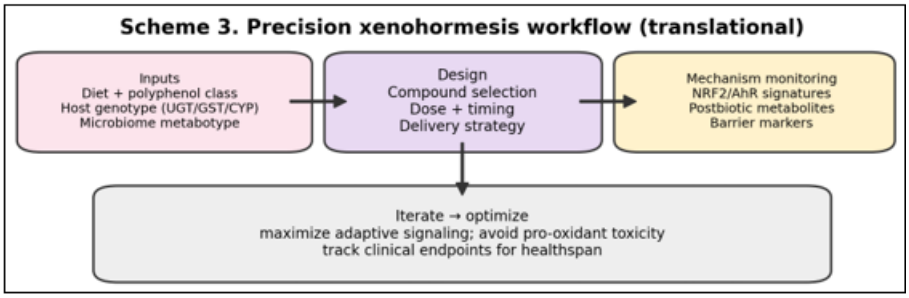
Scheme 1: Plant tannin idioblast logic: storage, triggers, and local defensive action.



Scheme 2: Goblet- Paneth epithelial defense circuit protecting the stem-cell niche and shaping the microbiota.



Scheme 3: Precision xenohormesis workflow integrating diet, host genetics, and microbiome metabotypes for rational intervention design.



1. Introduction

Idioblasts are a classic solution in plant anatomy for localizing high-potency defensive chemistry into discrete cells or small cell clusters embedded within otherwise homogeneous tissues (Figure 1) [2- 4]. Tannin-rich idioblasts occur in organs exposed to chronic stress and attack- leaf epidermis/mesophyll, bark, fruit skins- and can accumulate phenolic polymers at very high concentrations in vacuoles, creating protective "hotspots" with limited interference in primary metabolism [1- 4]. Transport into storage compartments relies on specialized trafficking and transporter systems, including ABC transporters [3,4].

Human histology does not use the term "idioblast", yet human tissues repeatedly employ an analogous design principle: discrete cell types that are morphologically and functionally distinct from their neighbors and that concentrate either (i) barrier polymers, (ii) antimicrobial effectors, (iii) xenobiotic metabolism and export, or (iv) compartmentalized phagocytic killing (Figure 2; Table 1) [5-12]. Examples include mucosal goblet cells and Paneth cells in the intestine [5-9], periportal hepatocytes shaped by liver zonation [12], bronchiolar club cells and their secreted proteins (e.g., CC16/SCGB1A1) [10,11], and tissue-resident macrophage populations such as Kupffer cells, alveolar macrophages, and microglia [12].

This review proposes an "idioblast lens" as an integrative framework linking plant defense biology to mucosal immunology, detoxification, microbiome metabolism, and healthspan science. We summarize (i) tannin idioblast cytology and compartmentalization in plants; (ii) candidate idioblast-like cells in humans; and (iii) conserved molecular modules—ABC transport, Phase II conjugation, KEAP1-NRF2-ARE stress control, AhR ligand sensing, and Ca2+-regulated secretion—that couple localized defense to organismal resilience (Figures 3-6; Tables 2-4) [2-4,13-18,21-24].

2. Plant Idioblasts as Focal Defensive Units

2.1 Definition, Cytology, and Distribution

Plant idioblasts are defined as individual cells or small cell groups that differ markedly from surrounding cells in size, wall structure, cytoplasmic organization, and stored metabolites [2-4]. Tannin idioblasts commonly exhibit enlarged cell size, thickened walls, and a dominant vacuole filled with phenolic inclusions. In oak systems, gall development provides a striking example of localized tissue remodeling accompanied by tannin deposition, consistent with a coordinated defense/stress program [1].

2.2 Chemical Composition: Tannins and Other Polyphenols

Tannins are polyphenolic compounds broadly classified as hydrolyzable tannins (e.g., ellagitannins) and condensed tannins (proanthocyanidins). They can precipitate proteins, inhibit microbial enzymes, chelate redox-active metals, and modulate oxidative stress, supporting broad-spectrum defense [2-4]. Packaging tannins within idioblast vacuoles enables plants to deploy high local concentrations while minimizing off-target effects on cellular housekeeping [2-4].

2.3 Transport and Compartmentalization: Vacuolar "Phase III"

Specialized metabolite accumulation depends on transport and self-tolerance mechanisms, including sequestration into organelles such as the vacuole [2,3]. ABC transporters support membrane transport of plant secondary metabolites and contribute to sequestration-based self-protection (Figure 4) [4]. This systems logic—chemical transformation, conjugation, and compartmentalization—resembles the conceptual Phase I-II-III architecture used to describe xenobiotic handling in animals (Figure 3) [2-4].

3. Human Idioblast-Like Cells: Comparative Anatomy and Cytology

3.1 Goblet Cells: Mucin-Secreting Barrier Idioblasts

Goblet cells are specialized epithelial cells characterized by an apical domain packed with mucin granules and a basally displaced nucleus [5,6]. They synthesize and secrete gel-forming mucins (notably MUC2 in the intestine), building mucus layers that provide a first-line defense and spatial separation between microbiota and epithelium (Scheme 2) [5,6]. Mucins show dynamic regulation across physiological and pathological conditions, linking mucus biology to disease mechanisms [13].

3.2 Paneth Cells: Crypt-Based Antimicrobial Idioblasts

Paneth cells reside at the base of small intestinal crypts and secrete high local concentrations of antimicrobial effectors, including alpha-defensins, lysozyme, and secretory phospholipase A2 [8,9]. Topographical distribution and quantification of human Paneth cell antimicrobial peptides across gastrointestinal tissues underscore a crypt-centered defensive program (Table 2) [8]. Paneth cell alpha-defensins are central components of enteric innate immunity and contribute substantially to secreted bactericidal peptide activity [9].

3.3 Periportal Hepatocytes: Detoxification Front-Line Cells

The liver exhibits spatial zonation along the porto-central axis, generating regionally specialized metabolic programs relevant to physiology and disease [12]. Periportal hepatocyte fields are positioned as early gateways for blood-borne substrates and xenobiotic handling. New technologies are refining the mapping of zonation and its regulatory logic, supporting mechanistic interpretation of detoxification and stress-response compartmentalization [12].

3.4 Club (Clara) Cells: Respiratory Detox and Immunomodulation

Club cells are non-ciliated bronchiolar epithelial cells involved in airway protection, xenobiotic metabolism, and repair programs [10]. Their secreted protein CC16/SCGB1A1 is linked to airway homeostasis and

inflammation modulation, and club-cell dysfunction has relevance to chronic lung disease (Table 2) [10,11].

4. Evolutionarily Conserved Molecular Modules

4.1 ABC Transporters and Barrier Protection

ABC transporters support plant secondary metabolite transport and self-protection [4]. In mammalian systems, ABC transporters mediate xenobiotic/drug efflux at barrier tissues and detoxification organs, contributing to protection and pharmacokinetic control. Notably, plant secondary metabolites can inhibit ABC transporters and reverse resistance phenotypes in cancer cells and microbes, illustrating cross-kingdom chemical interactions relevant to therapy (Figure 4) [19].

4.2 KEAP1-NRF2-ARE: Antioxidant and Cytoprotective Control

KEAP1 represses NRF2 under basal conditions; oxidative/electrophilic stress stabilizes NRF2, enabling nuclear activation of ARE-driven cytoprotective genes [14]. NRF2 regulates broad antioxidant and detoxification programs and is widely discussed as a healthspan-associated protective pathway (Figure 5) [15,16].

4.3 AhR Signaling: Nutritional and Microbial Ligands

Nutritional AhR ligands influence intestinal immunity and epithelial functions, including barrier integrity and innate immunity programs [17]. Polyphenols can modulate AhR-regulated immune function, and metabolic context is important for net biological outcomes [18]. Mechanistically focused reviews emphasize therapeutic potential of AhR modulation in gut immunity and inflammation (Figure 5) [20].

5. Functional Analogies: Defense, Detoxification, and Inflammation

5.1 Antimicrobial Defense Modules

Plant tannins can inhibit microbial growth through protein binding, enzyme inhibition, and metal chelation, while Paneth cell alpha-defensins provide broad-spectrum microbicidal activity in the intestinal lumen [9]. This represents convergent defensive logic: high local concentration of multi-target antimicrobials deployed by specialized cells (idioblasts; Paneth cells) (Scheme 2) [8,9].

5.2 Mucus-Antimicrobial Coupling

Mucus and mucins form the first defense line of the gastrointestinal tract and interact bidirectionally with the immune system [5]. Mucin biology is dynamic and context-dependent across disease states [13]. MUC2 mucin can regulate beta-defensin 2 expression and antimicrobial activity in inflammatory contexts, highlighting coupling between barrier polymers and antimicrobial programs [7].

6. Polyphenols as Molecular Bridges: Hormesis, Xenohormesis, and the Microbiome

6.1 Hormesis and Xenohormesis

Many phytochemicals act as hormetic agents: moderate exposures can induce adaptive stress-response pathways, including NRF2-linked cytoprotection, whereas excessive exposures may become pro-oxidant [23]. The xenohormesis concept proposes that animals evolved to sense stress-induced plant molecules as cues, triggering resilience programs that may support health and longevity (Scheme 3) [22].

6.2 Microbiome Conversion to Urolithins

Urolithins are gut microbial metabolites produced from ellagitannin- and ellagic-acid-containing foods. Isolation of urolithin-producing bacteria from human feces demonstrated microbial conversion capacity and provided a basis for understanding inter-individual variability in urolithin production [23]. Direct supplementation with urolithin A can overcome variability in microbial production and achieve consistent systemic exposure in healthy adults, enabling clinical translation of mitochondrial and functional endpoints (Figure 6) [24].

7. Idioblast-Inspired Therapeutic Perspectives

7.1 Biomimetic Compartmentalization and Delivery

Idioblasts illustrate how potent chemistry can be stored safely and released in a controlled manner (Scheme 1). This inspires biomimetic delivery systems designed to protect labile phytochemicals and enable triggered release at target tissues.

7.2 Precision Nutraceutical Strategies

Precision strategies can combine polyphenol class selection with host genotype (detox and transport capacity) and microbiome metabotype profiling to optimize adaptive signaling while minimizing adverse effects (Scheme 3). This framework aligns with hormesis/xenohormesis and relies on measurable pathway readouts (NRF2 targets, AhR signatures, postbiotic profiles) (Table 4) [15- 18,22- 24].

8. Conclusions and Outlook

Plant idioblasts and human idioblast-like cells converge on a shared architectural principle: localizing high-potency biochemistry into specialized cells positioned at environmental and vascular interfaces (Figures 1-2; Table 1) [2-12]. Polyphenols concentrated in plant defensive tissues can engage conserved human defense modules (KEAP1-NRF2-ARE and AhR signaling) and can be transformed by the microbiome into bioactive postbiotics such as urolithin A (Figures 5-6) [14-18,23,24]. Future research integrating spatial/single-cell mapping, systems pharmacology, and microbiome science should refine testable hypotheses

connecting idioblast-like cell function to organ resilience and healthspan outcomes (Figure 7).

Tables

Key comparative summaries are provided in Tables 1-4.

Table 1: Defining features of plant idioblasts versus human idioblast-like cells.

Feature	Plant tannin idioblasts	Human idioblast-like cells
Hallmark	Discrete cell(s) distinct from neighbors	Discrete specialized cells or zonated subfields distinct in function
Stored payload	Tannins/polyphenols/crystals	Mucins; defensins/lysozyme; detox enzymes; phagolysosomal effector machinery
Compartment	Vacuole/tonoplast	Secretory granules; ER/Golgi; canalicular export; phagolysosomes
Strategic placement	Epidermis, mesophyll near veins, bark, fruit skins, galls	Mucosa; portal axis; distal airways; tissue interfaces
Release/activation	Stress/wounding/pathogen cues	Ca2+-regulated exocytosis; PRR/cytokine cues; metabolic sensing
Primary function	Local chemical defense + stress buffering	Barrier integrity, antimicrobial defense, detoxification, immune homeostasis

Table 2: Candidate human idioblast-like cells: location, outputs, and healthspan relevance (conceptual).

Cell type	Location	Key outputs	Core role	Healthspan linkage (conceptual)
Goblet cell	Intestine/airway and other mucosa	Mucins (e.g., MUC2), trefoil factors	Barrier polymer shield	Limits microbe-epithelium contact; reduces inflammatory drift
Paneth cell	Small intestine crypt base	Alpha-defensins, lysozyme, sPLA2	Crypt antimicrobial defense	Protects stem-cell niche; shapes microbiota
Periportal hepatocyte field	Portal region of liver lobule	Zonated metabolic programs	Gateway handling of blood-borne substrates	Controls systemic toxin burden; supports redox balance
Club cell	Bronchioles	CC16/SCGB1A1, detox/repair mediators	Airway detox + repair	Protects distal lung; modulates chronic inflammation
Tissue-resident macrophages	Liver/lung/CNS, etc.	Phagocytosis, cytokines, homeostasis programs	Surveillance + clearance	Controls sterile inflammation and tissue remodeling

Table 3: Conserved or analogous molecular modules supporting “idioblast logic”.

Module	Plant context	Human context	Representative outputs
ABC transport	Secondary metabolite transport and sequestration [4]	Efflux at barriers/detox tissues; drug disposition	Reduced intracellular toxin load; controlled compartmentalization/export
Conjugation capacity	Self-tolerance and storage readiness [2,3]	UGT/GST conjugation; glutathione networks	Reduced electrophile toxicity; enhanced elimination
Stress transcriptional control	Redox/hormone stress networks	KEAP1-NRF2-ARE activation [14-16]	HO-1, NQO1, antioxidant and detox gene induction
Diet-microbiome sensing	Phenolics shape microbial ecology	AhR ligand sensing and immune tuning [17,18,20]	Barrier reinforcement; IL-22 axis; immune balance
Regulated secretion	Defense deployment on stress cues	Ca2+-regulated exocytosis in secretory cells	Rapid mucus/antimicrobial release

Table 4: Idioblast-inspired intervention concepts and measurable readouts (non-exhaustive).

Strategy	Target node	Example modality	Representative readouts
Biomimetic carriers	Barrier/detox interfaces	Triggered-release delivery (pH/redox/enzyme)	Target exposure; pathway activation signatures
Barrier reinforcement	Goblet-Paneth axis	Diet/postbiotic tuning; AhR/NRF2 engagement	Mucus properties; antimicrobial peptide profiles
Detox augmentation	Hepatic/intestine Phase II-III	Support conjugation/efflux balance	Conjugated metabolite panels; bile/urine excretion
Airway resilience	Club cells	Anti-inflammatory + repair support	CC16/SCGB1A1 levels; airway inflammation markers
Precision xenohormesis	Whole system	Genotype + metabotype-guided dosing	NRF2/AhR signatures; postbiotic outputs; clinical endpoints

Abbreviations

ABC, ATP-binding cassette; AhR, aryl hydrocarbon receptor; ARE, antioxidant response element; CC16/CCSP, club cell secretory protein (SCGB1A1); CYP, cytochrome P450; ER, endoplasmic reticulum; GST, glutathione S-transferase; HO-1, heme oxygenase 1; IBD, inflammatory bowel disease; KEAP1, Kelch-like ECH-associated protein 1; MUC, mucin; NRF2, nuclear factor erythroid 2-related factor 2; NQO1, NAD(P)H quinone dehydrogenase 1; ROS, reactive oxygen species; SCFA, short-chain fatty acid; UGT, UDP-glucuronosyltransferase; UA, urolithin A.

Competing interests

None declared.

Funding

Institute for Personalized Medicine (Tbilisi, Georgia) and Foconsci Chemical Industry, Department of Biotechnology (China). The funders had no role in study design, data collection/analysis, or the decision to publish.

Authors' contributions
All authors contributed to study design, patient management, data interpretation, and manuscript preparation. All authors approved the final manuscript.

Acknowledgements
We thank our experts and the clinical and laboratory teams for their dedication.

References

[1] Jankiewicz, L.S.; Guzicka, M.; Marasek-Ciolakowska, A. Anatomy and Ultrastructure of Galls Induced by Neuroterus quercusbaccarum (Hymenoptera: Cynipidae) on Oak Leaves (Quercus robur). Insects 2021, 12, 850. https://doi.org/10.3390/insects12100850.
[2] Shitan, N. Secondary Metabolites in Plants: Transport and Self-Tolerance Mechanisms. Biosci. Biotechnol. Biochem. 2016, 80, 1283-1293. https://doi.org/10.1080/09168451.2016.1151344.
[3] de Brito Francisco, R.; Martinoia, E. The Vacuolar Transportome of Plant Specialized Metabolites. Plant Cell Physiol. 2018, 59, 1326-1336. https://doi.org/10.1093/pcp/pcy039.
[4] Yazaki, K. ABC Transporters Involved in the Transport of Plant Secondary Metabolites. FEBS Lett. 2006, 580, 1183-1191. https://doi.org/10.1016/j.febslet.2005.12.009.
[5] Pelaseyed, T.; Bergstrom, J.H.; Gustafsson, J.K.; et al. The Mucus and Mucins of the Goblet Cells and Enterocytes Provide the First Defense Line of the Gastrointestinal Tract and Interact with the Immune System. Immunol. Rev. 2014, 260, 8-20. https://doi.org/10.1111/imr.12182.
[6] Kim, Y.S.; Ho, S.B. Intestinal Goblet Cells and Mucins in Health and Disease: Recent Insights and Progress. Curr. Gastroenterol. Rep. 2010, 12, 319-330. https://doi.org/10.1007/s11894-010-0131-2.
[7] Cobo, E.R.; Kissoon-Singh, V.; Moreau, F.; Chadee, K. Colonic MUC2 Mucin Regulates the Expression and Antimicrobial Activity of beta-Defensin 2. Mucosal Immunol. 2015, 8, 1360-1372. https://doi.org/10.1038/mi.2015.27.
[8] Wehkamp, J.; Chu, H.; Shen, B.; et al. Paneth Cell Antimicrobial Peptides: Topographical Distribution and Quantification in Human Gastrointestinal Tissues. FEBS Lett. 2006, 580, 5344-5350. https://doi.org/10.1016/j.febslet.2006.08.083.
[9] Ouellette, A.J. Paneth Cell alpha-Defensins in Enteric Innate Immunity. Curr. Opin. Gastroenterol. 2011, 27, 533-538. https://doi.org/10.1097/MOG.0b013e328347b7b5.
[10] Barnes, P.J. Club Cells, Their Secretory Protein, and COPD. Chest 2015, 147, 1447-1448. https://doi.org/10.1378/chest.14-3171.
[11] Laucho-Contreras, M.E.; Polverino, F.; Tesfaigzi, Y.; et al. A Protective Role for Club Cell Secretory Protein-16 (CC16) in the Development of COPD. Am. J. Respir. Crit. Care Med. 2015, 192, 1054-1063. https://doi.org/10.1164/rccm.201501-0171OC.
[12] Cunningham, R.P.; Porat-Shliom, N. Liver Zonation—Revisiting Old Questions with New Technologies. Front. Physiol. 2021, 12, 732929. https://doi.org/10.3389/fphys.2021.732929.
[13] Melhem, H.; Regan-Komito, D.; Niess, J.H. Mucins Dynamics in Physiological and Pathological Conditions. Int. J. Mol. Sci. 2021, 22, 13642. https://doi.org/10.3390/ijms222413642.
[14] Itoh, K.; Wakabayashi, N.; Katoh, Y.; et al. Keap1 Represses Nuclear Activation of Antioxidant Responsive Elements by Nrf2 through Binding to the Amino-Terminal Neh2 Domain. Genes Dev. 1999, 13, 76-86. https://doi.org/10.1101/gad.13.1.76.
[15] Ngo, V.; Duennwald, M.L. Nrf2 and Oxidative Stress: A General Overview of Mechanisms and Implications in Human Disease. Antioxidants 2022, 11, 2345. https://doi.org/10.3390/antiox11122345.
[16] Lewis, K.N.; Mele, J.; Hayes, J.D.; Buffenstein, R. Nrf2, a Guardian of Healthspan and Gatekeeper of Species Longevity. Integr. Comp. Biol. 2010, 50, 829-843. https://doi.org/10.1093/icb/icq034.
[17] Huang, F.C. Therapeutic Potential of Nutritional Aryl Hydrocarbon Receptor Ligands in Intestinal Immune Homeostasis. Biomedicines 2024, 12, 2912. https://doi.org/10.3390/biomedicines12122912.
[18] Tang, J.S.; Iyer, S.S.; et al. Practical Approach to Explore the Effects of Polyphenols on Aryl Hydrocarbon Receptor-Regulated Immune Function. Int. J. Mol. Sci. 2021, 22, 8212. https://doi.org/10.3390/ijms22158212.
[19] Chen, Y.; Wang, Y.; Fu, Y.; et al. Modulating AHR Function Offers Exciting Therapeutic Potential in Gut Immunity and Inflammation. Cell Biosci. 2023, 13, 85. https://doi.org/10.1186/s13578-023-01046-y.
[20] Wink, M. Secondary Metabolites from Plants Inhibiting ABC Transporters and Reversing Resistance of Cancer Cells and Microbes to Cytotoxic and Antimicrobial Agents. Front. Microbiol. 2012, 3, 130. https://doi.org/10.3389/fmicb.2012.00130.
[21] Martel, J.; Ojcius, D.M.; Ko, Y.F.; et al. Hormetic Effects of Phytochemicals on Health and Longevity. Trends Endocrinol. Metab. 2019, 30, 335-346. https://doi.org/10.1016/j.tem.2019.04.001.
[22] Baur, J.A.; Sinclair, D.A. What is Xenohormesis? Am. J. Pharmacol. Toxicol. 2008, 3, 152-159. https://doi.org/10.3844/ajptsp.2008.152.159.
[23] Selma, M.V.; Beltran, D.; Garcia-Villalba, R.; et al. Isolation of Human Intestinal Bacteria Capable of Producing the Bioactive Metabolite Isourolithin A from Ellagic Acid. Front. Microbiol. 2017, 8, 1521. https://doi.org/10.3389/fmicb.2017.01521.
[24] Singh, A.; D'Amico, D.; Andreux, P.A.; et al. Direct Supplementation with Urolithin A Overcomes Limitations of Dietary Exposure and Gut Microbiome Variability in Healthy Adults to Achieve Consistent Levels Across the Population. Eur. J. Clin. Nutr. 2022, 76, 297-308. https://doi.org/10.1038/s41430-021-00950-1.