Environment and kidney damage: which role for micro- and nanoplastics?

Gavino Faa

gavinofaa@gmail.com

Microplastics and Nanoplastics

Microplastics (MPs)	• Smaller than 5 mm (Thompson RC. Science 2004)
Nanoplastics (NPs)	• Smaller than 1 micrometer
Micronanoplastics	• Long degradation time • Ubiquitous in the food chain • Detected in human stool (Schwabl P. 2019) • Siddiqui SA. Sci Total Environ 2023, 892, 164531

Micronanoplastics and kidney

- 1. MNP overexposure can induce nephrotoxicity in experimental animals
- 2. Toxic effects on kidney cells
- A. lysosomal dysfunction
- B. oxidative stress
- C. mitochondrial damage
- D. DNA damage
- E. Cell necrosis
- F. Apoptosis

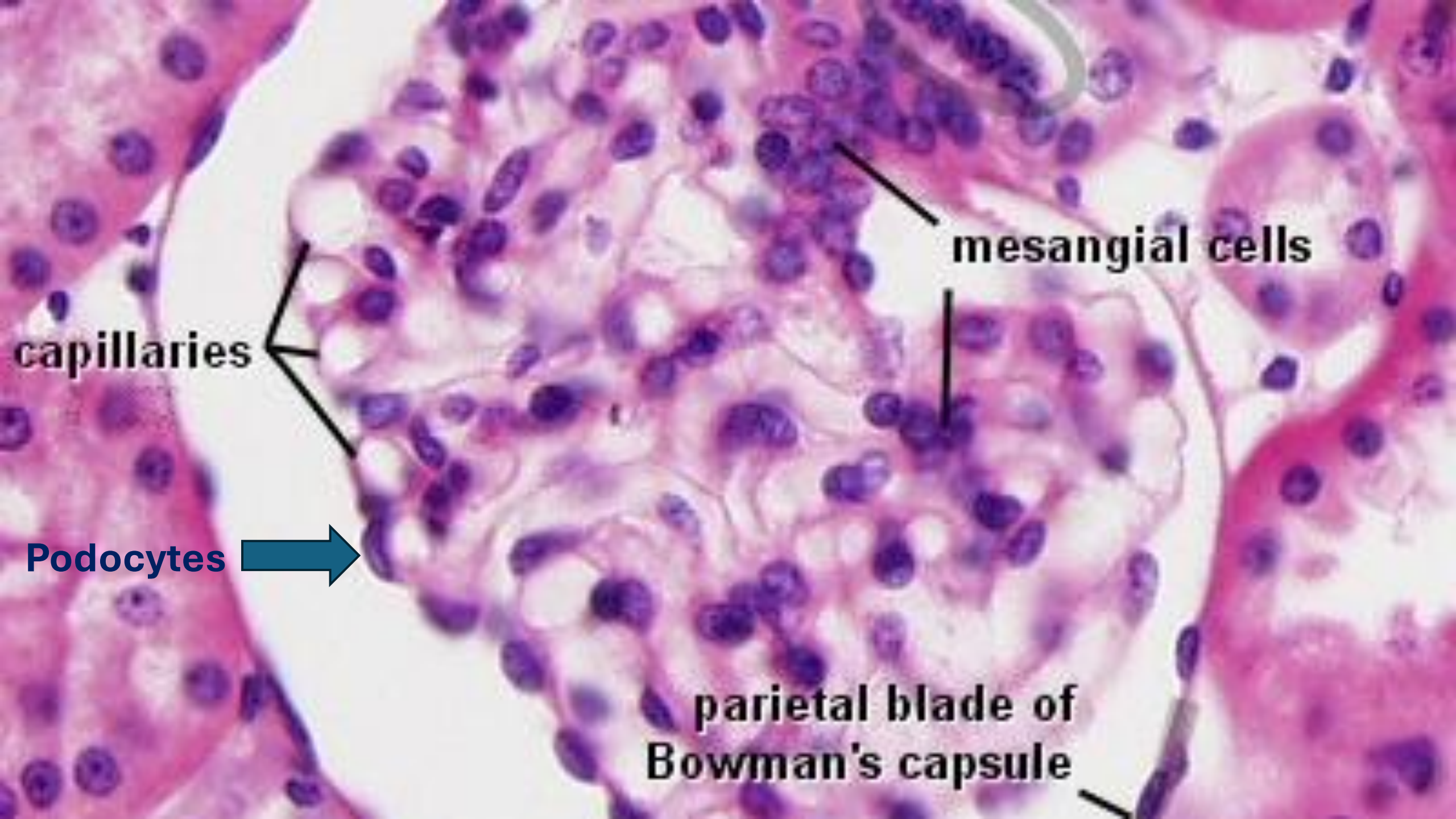
- Jiang N. The detrimental exposure to MNPs on kidney function. Front Med (Lausanne) 2025,12,1620733

Main targets of MNP-related nephrotoxicity

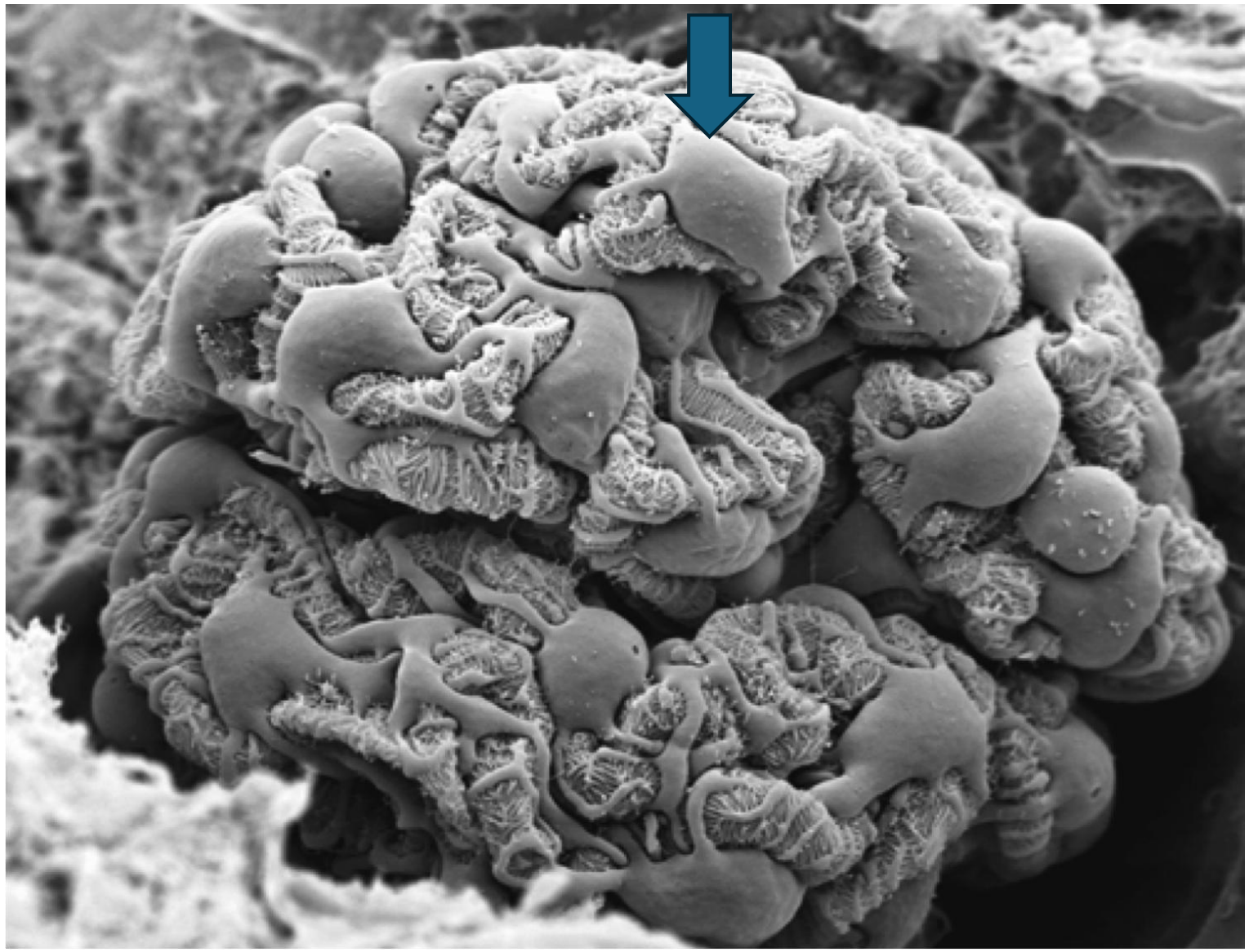
- 1. **Podocytes**
  - The renal cells that cannot regenerate
  - Podocyte damage cannot be recovered
  - May trigger a chronic insufficiency of the filtration barrier

- 2. **Proximal tubular cells**
  - The most complex specialized cells of the human kidney
  - Involved in reabsorption and secretion
  - In mice, Polystirene NPs induce apoptosis

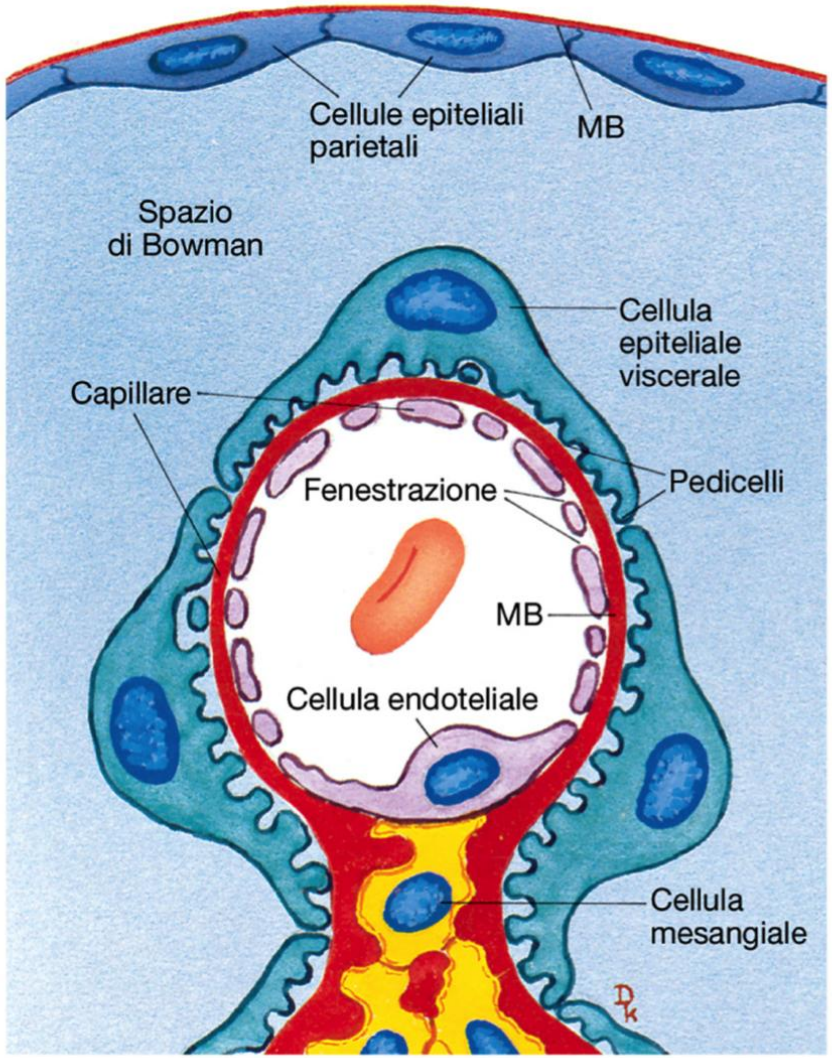
- Faa G. Micronanoplastics and kidney disease. Clinical Nephrology 2026, in press
- Jiang N. Front Med (Lausanne) 2025, 12, 1620733.


mesangial cells
capillaries
Podocytes
parietal blade of
Bowman's capsule

Scanning electron microscopy showing podocytes in a glomerulus



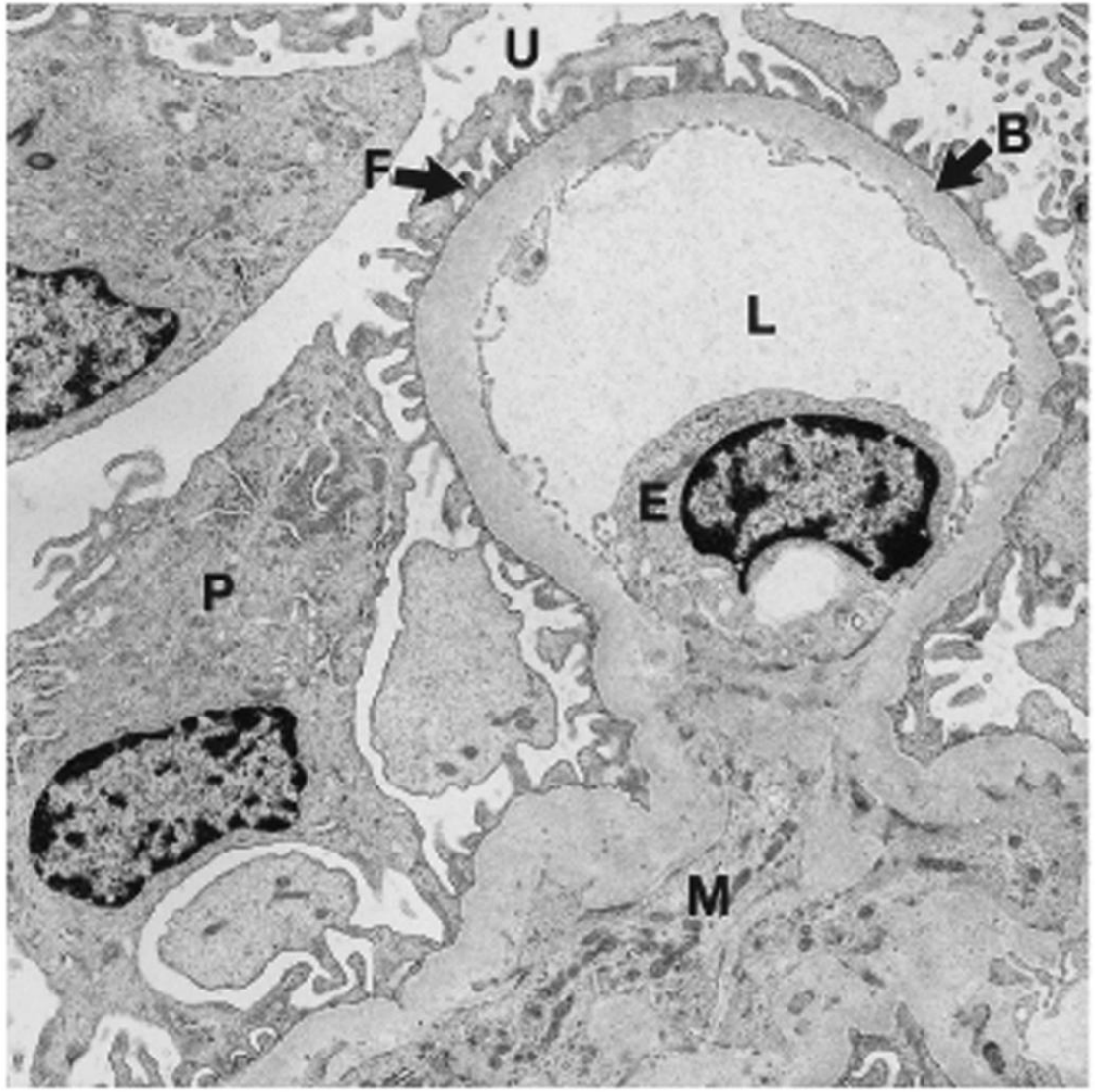
Schematic representation of podocytes in the glomerulus



Rubin, Patologia

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Podocytes are
Essential for
Maintaining
The integrity
Of the glomerular
Filtration barrier



Rubin, Patologia

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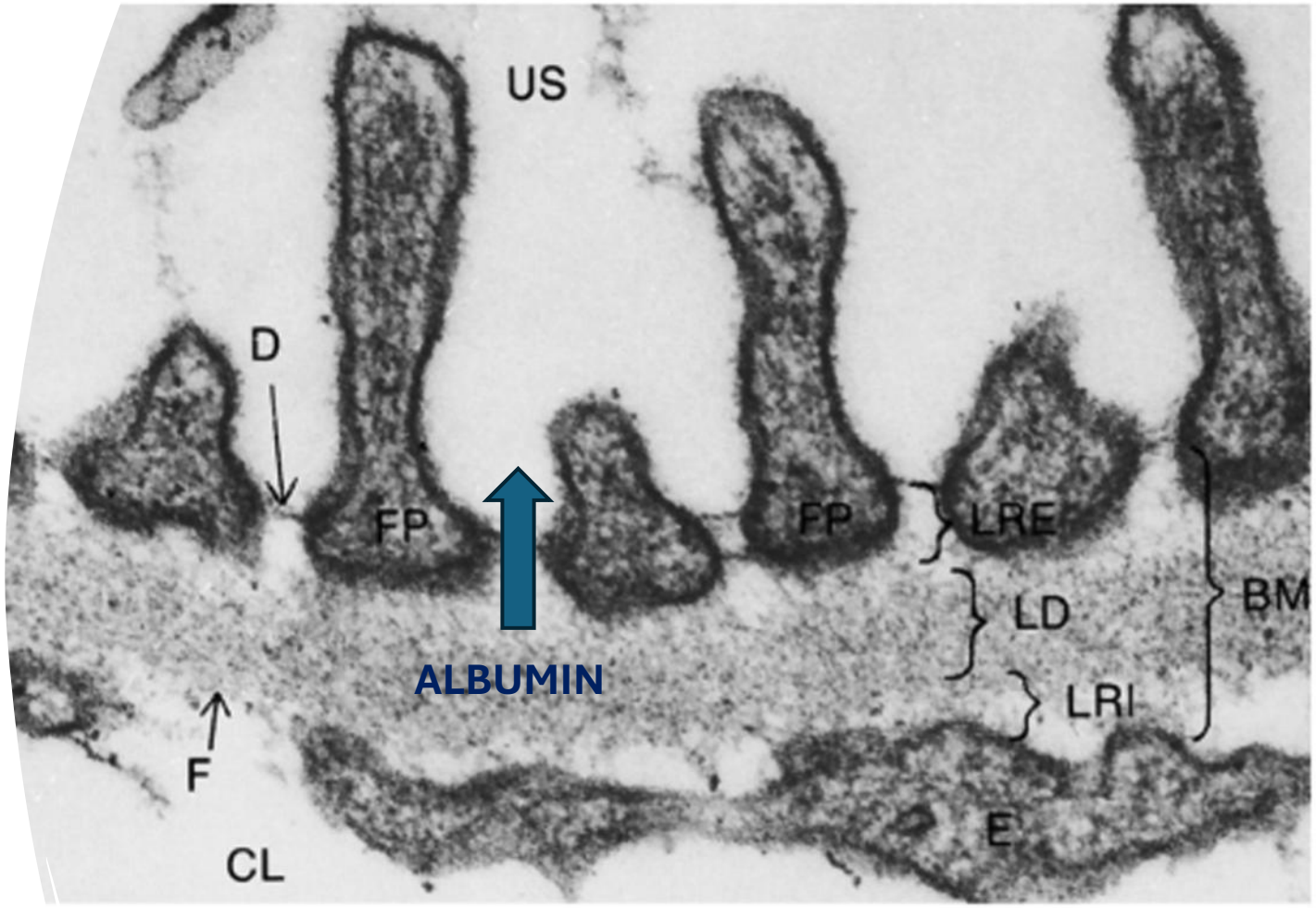
MNPs can damage
Podocytes
Disruptimg their
Structure and
function

Transmission Electron Microscopy: podocytes in the glomerulus

- **The filtration barrier in human kidney**

Marco Lombardi, Franco Bergesio
Micro- and nanoplastics and the kidney: Human evidences.
GCND 2026, 38, 3724.

Exposure to MNPs > Albuminuria



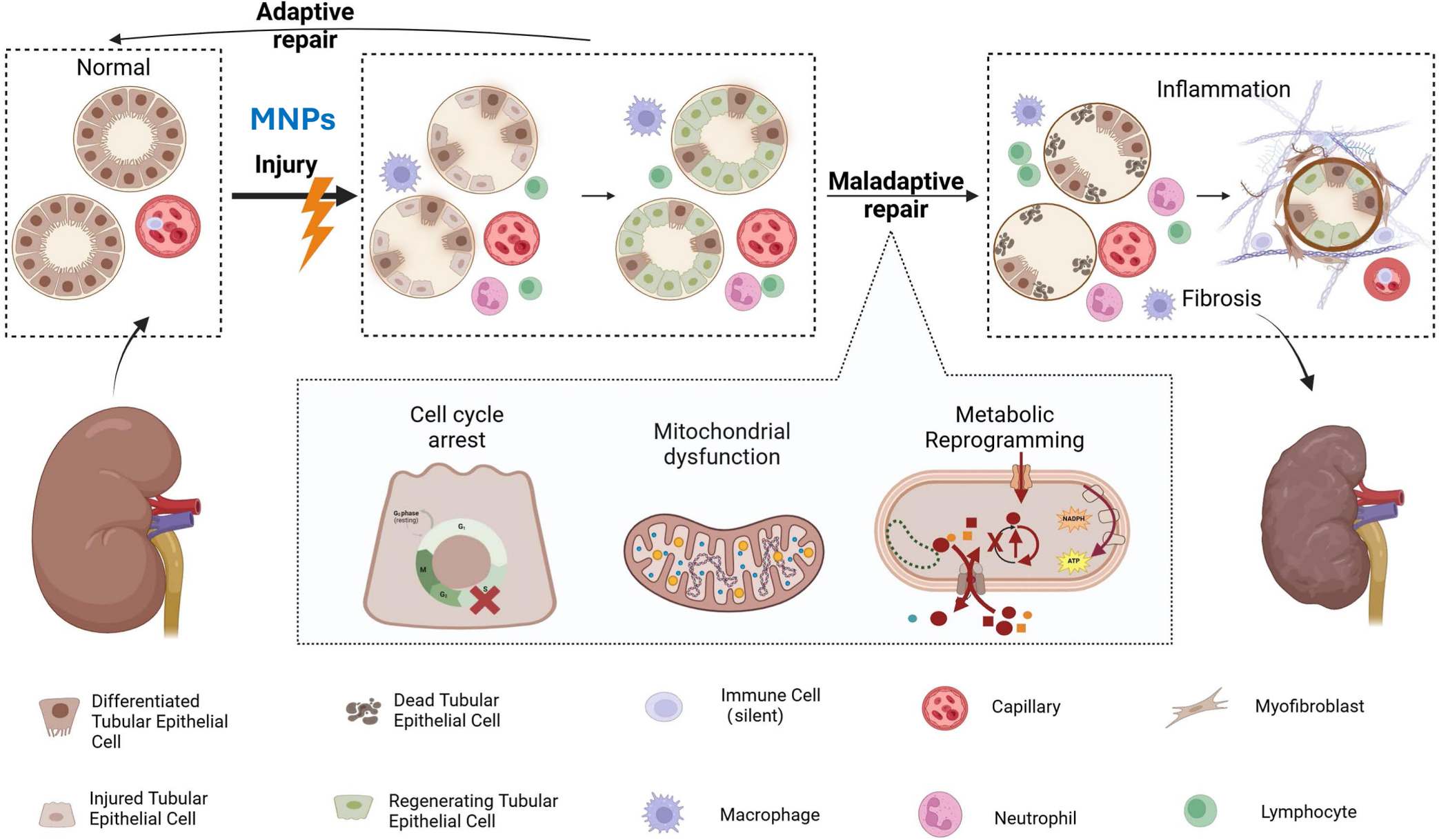
Rubin, Patologia

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MNP-induced podocyte damage

Exposure to MNPs and their contaminants
-bisphenols
-phtalates
-PFAS

1. damage of the glomerular filtration barrier
2. leakage of macromolecules into the urine
3. Proteinuria
4. Impaired kidney function
5. Renal failure

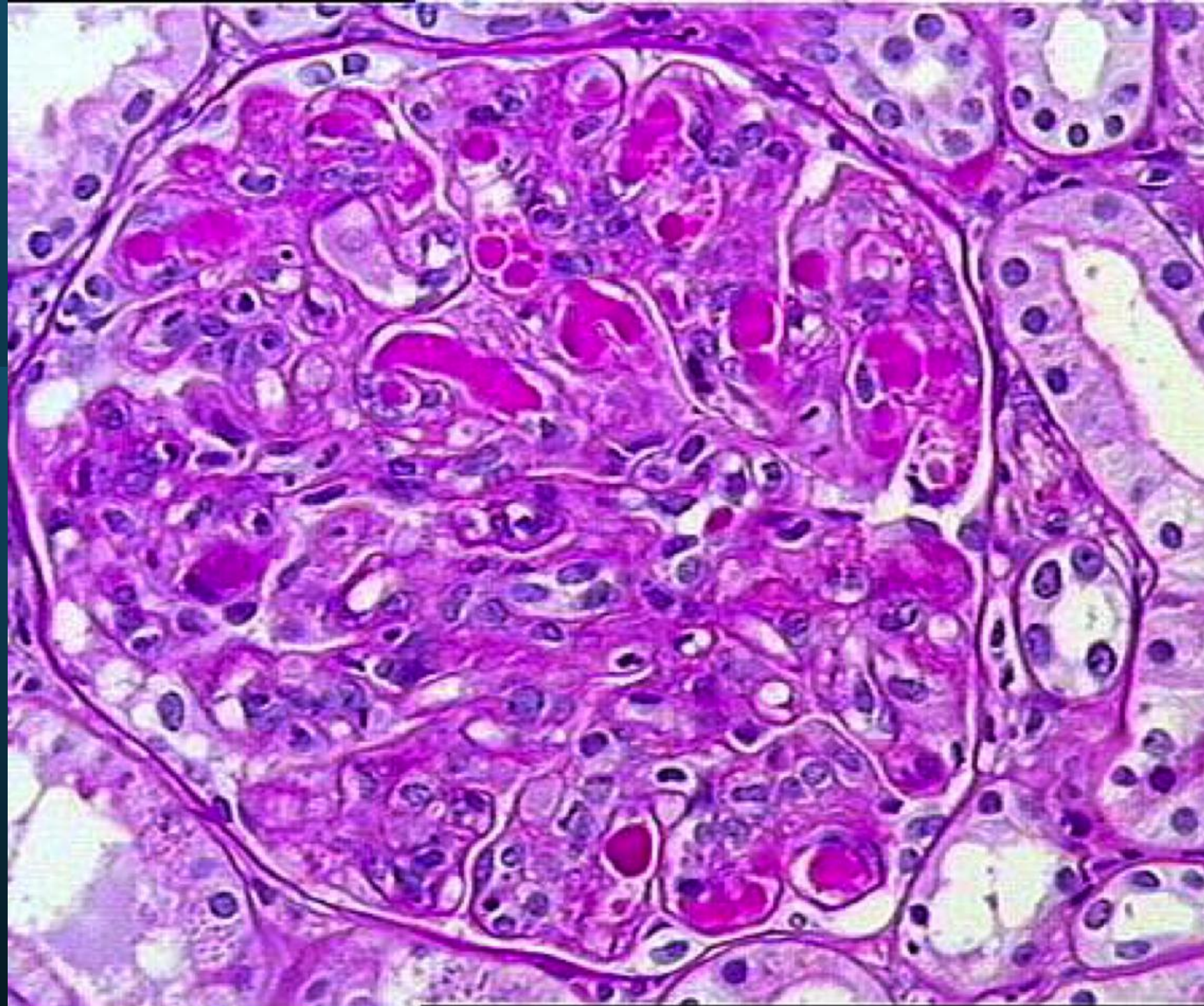


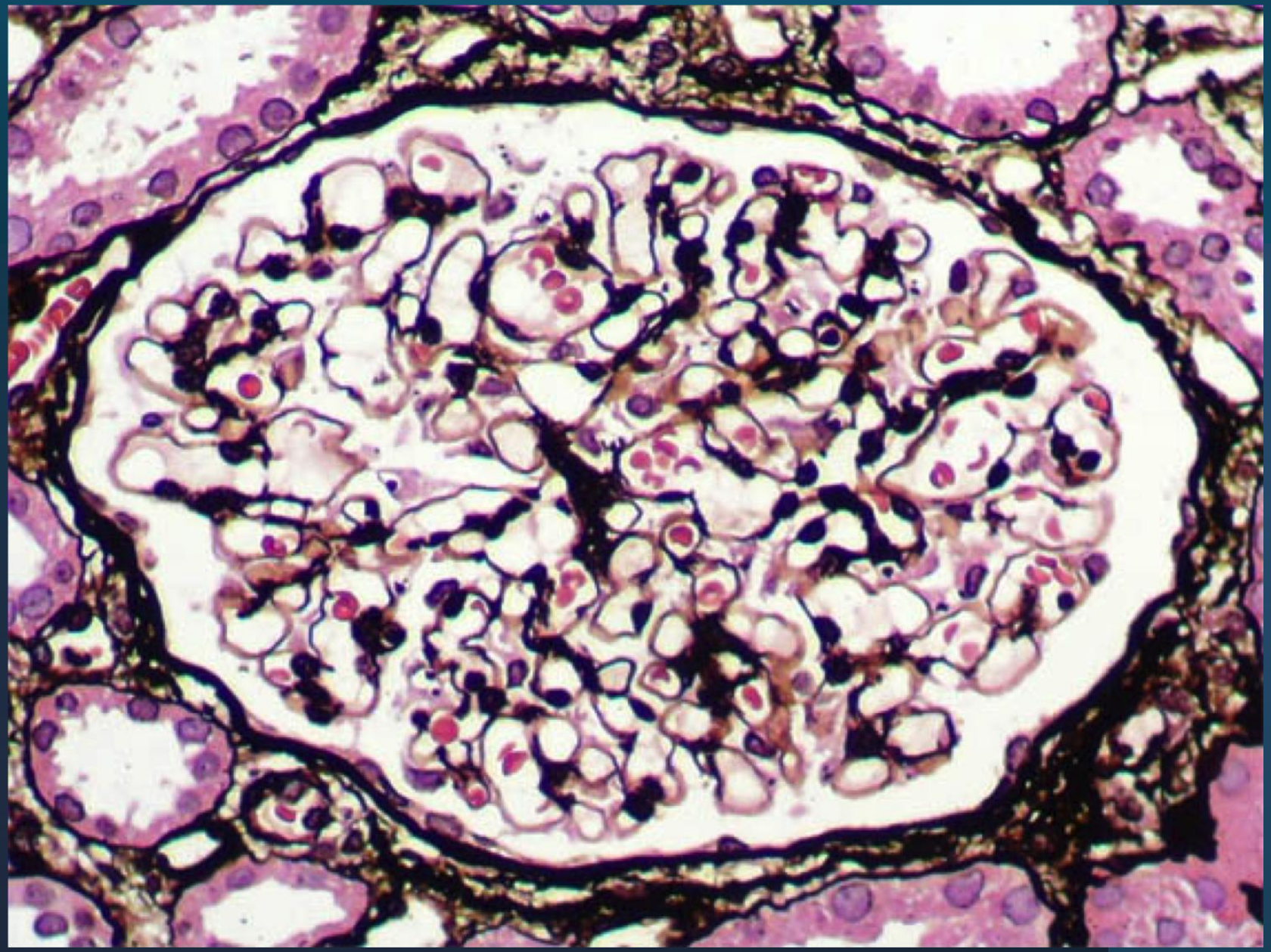
Putative MNP-related pathological changes in proximal tubular cells

Normal proximal tubular cells

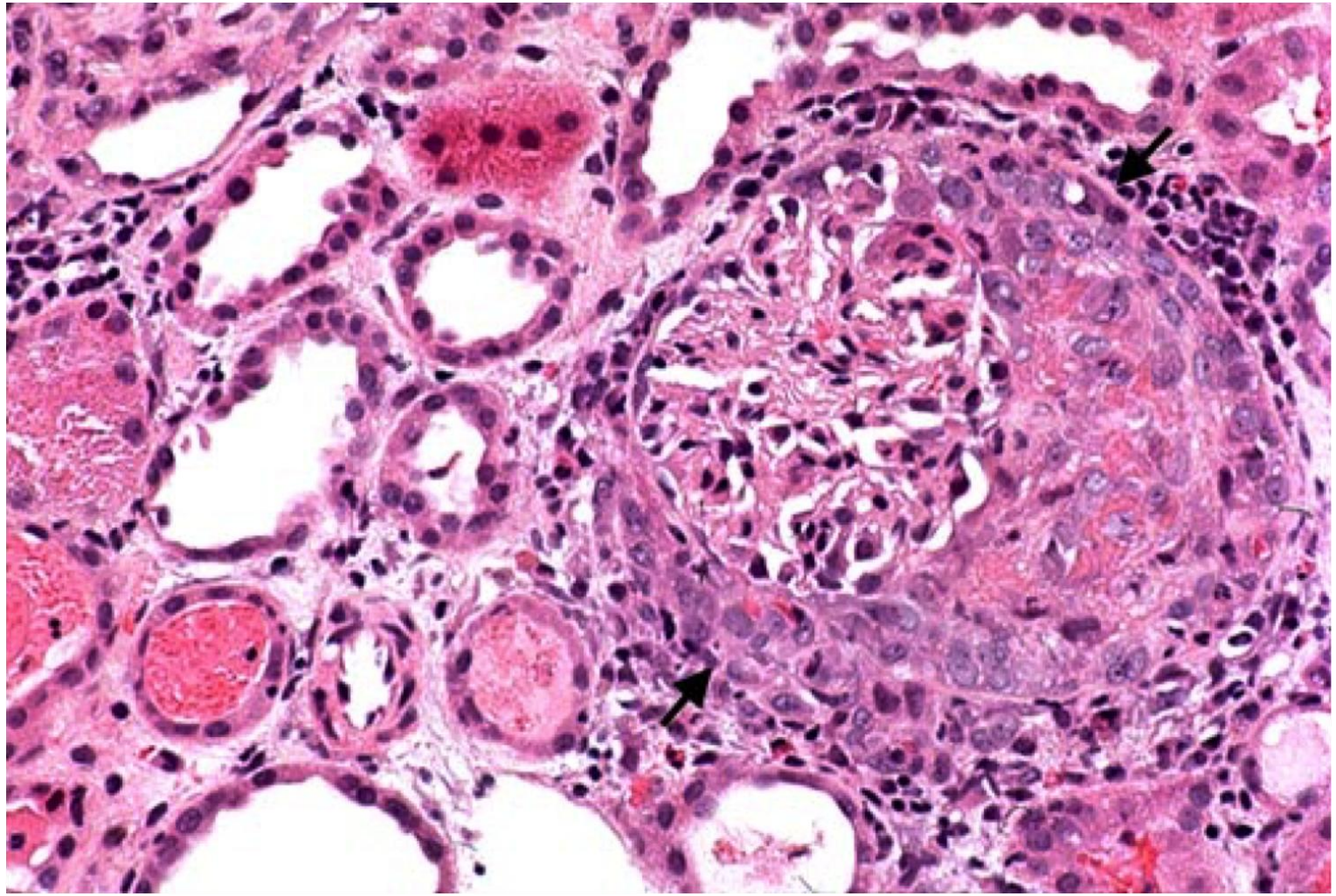
Microthrombosis

Podocyte loss





Damaged proximal tubular cells

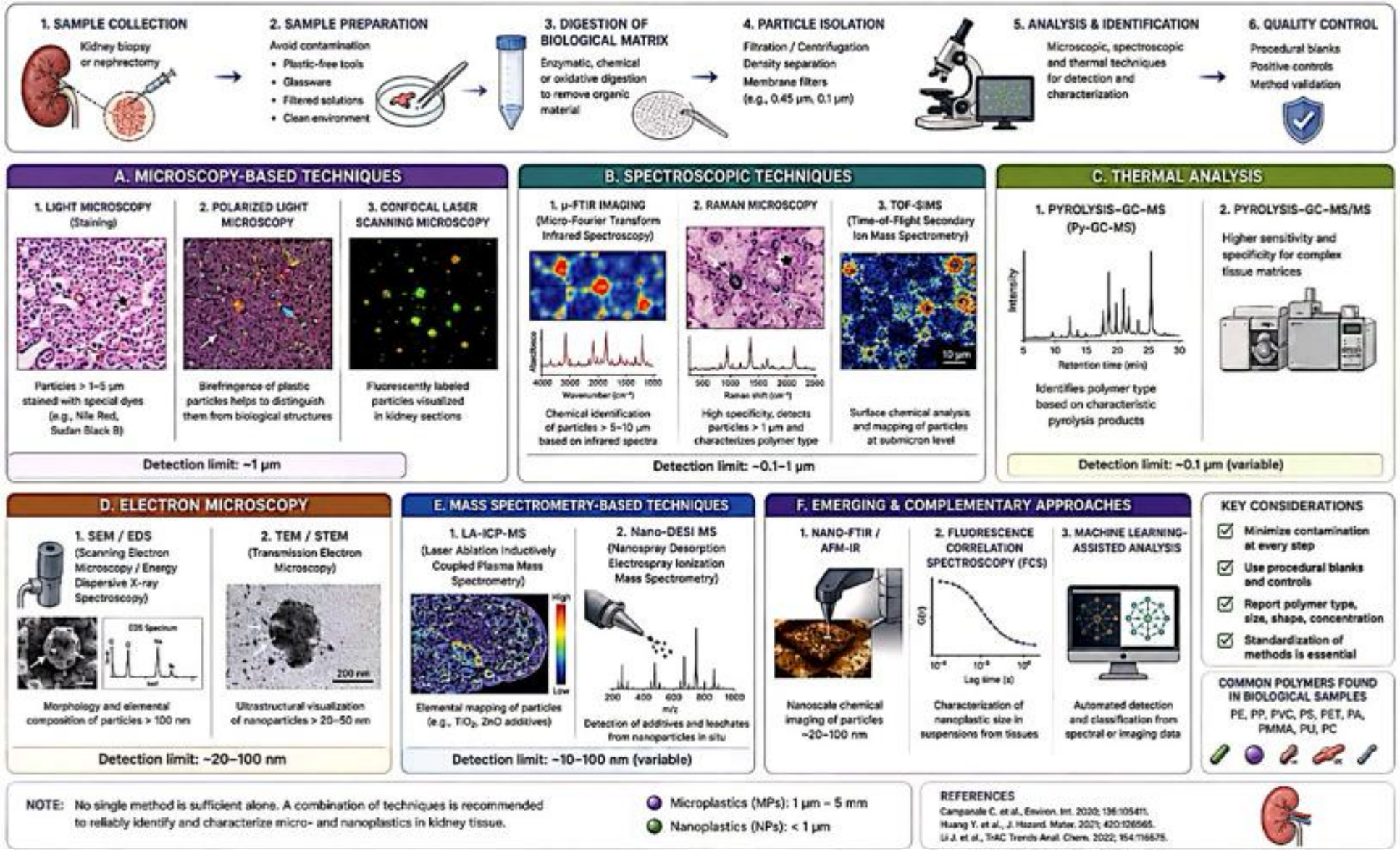


Polarized Light Microscopy

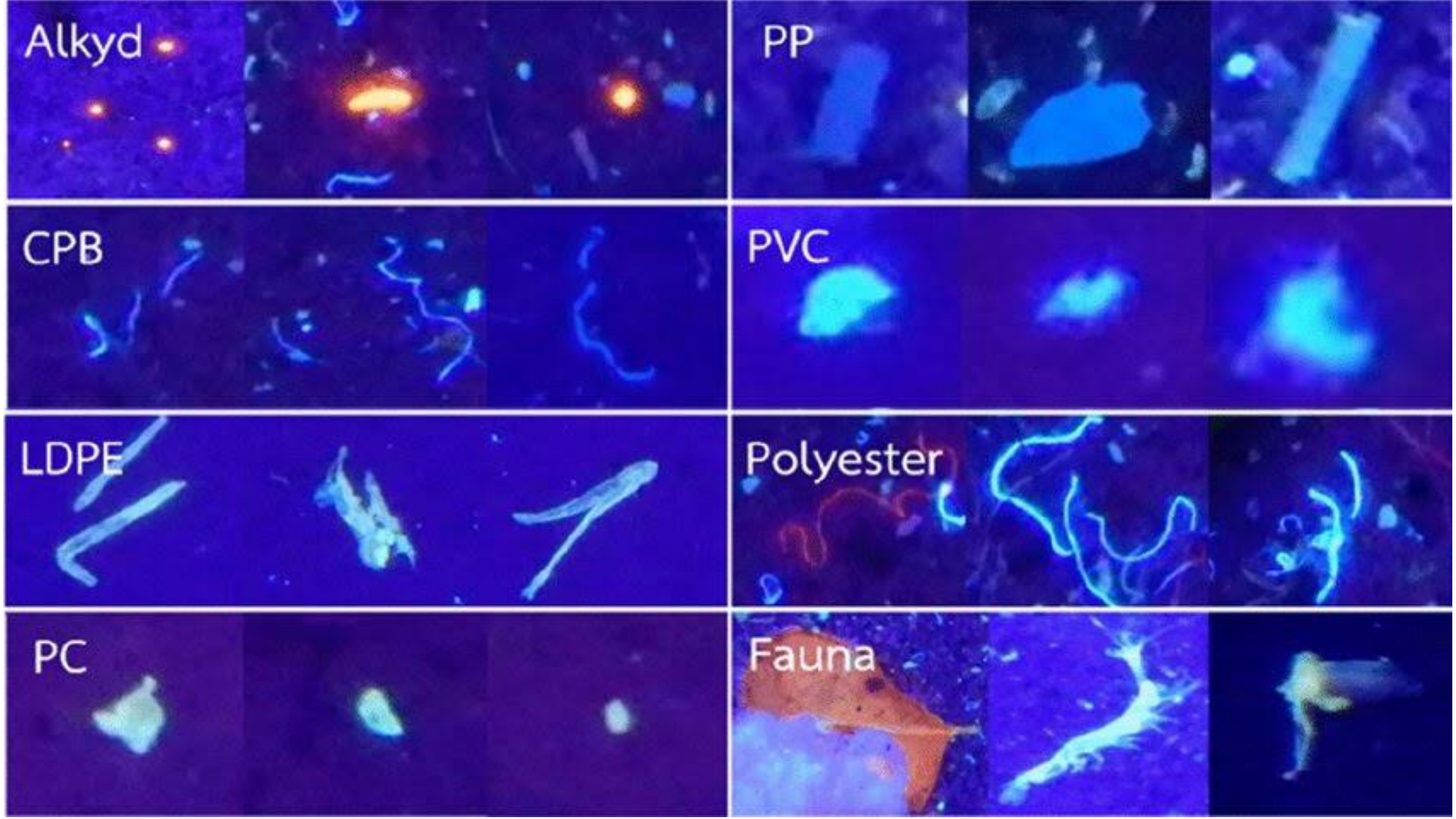
The Simplest And Most Valuable Method?

METHODS FOR EVIDENCING MICRO-NANO PLASTICS IN KIDNEY TISSUE

From sample collection to particle identification and quantification



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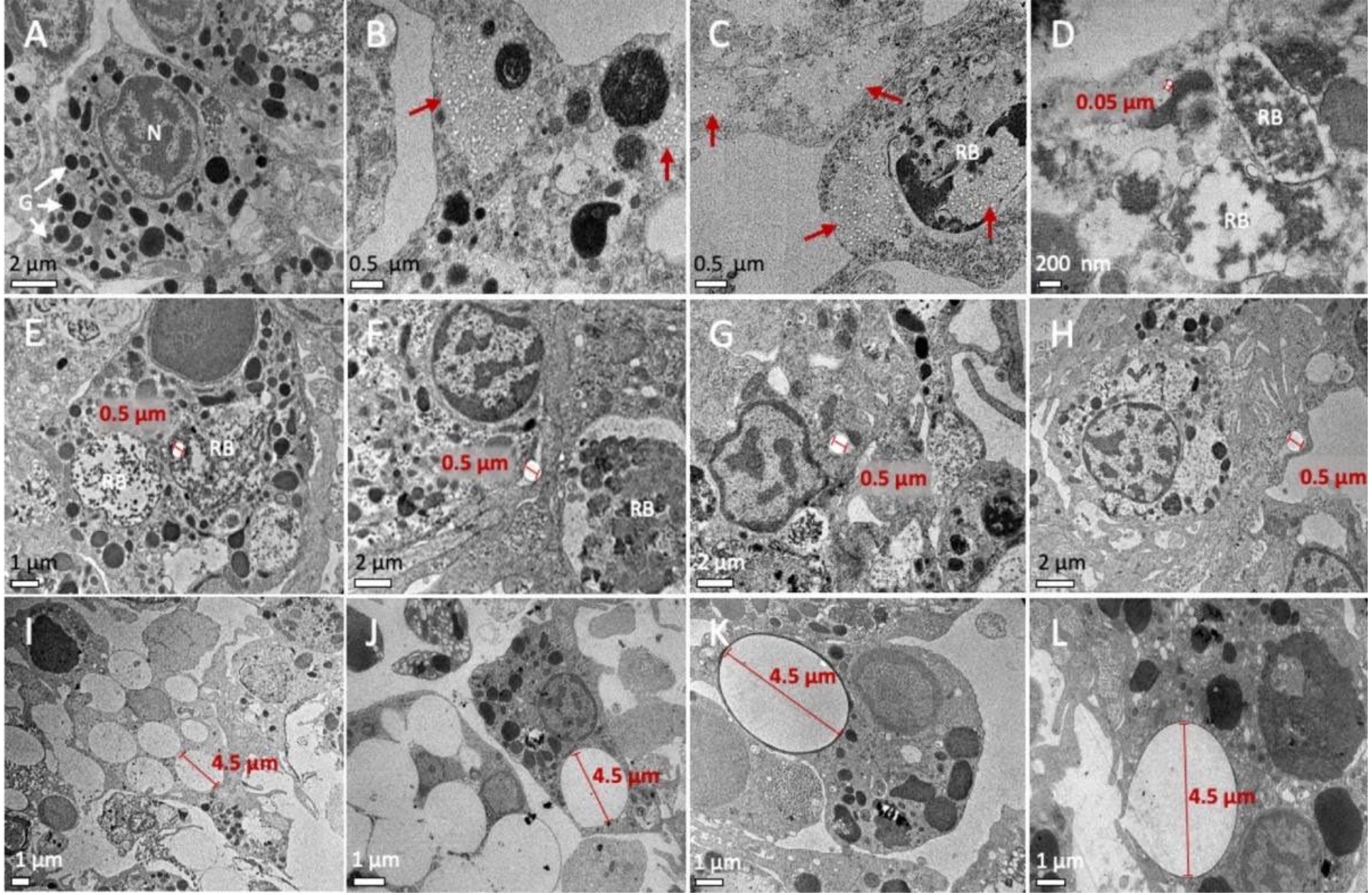


Micronanoplastics at Polaryzed light microscopy

Nanoplastics

Nanoplastics

Microplastics



Transmission Electro Microscopy of Micro-nanoplastics

The cocktail effect in the Plasticene

- MNPs act as a chemical sponges
- MNPs absorb multiple endocrine disrupting chemicals (EDCs) on their surface
- MNPs can absorb copper ions
- Synergistic interaction between MNPs, metals and EDCs originates the
- **The Cocktail effect**

- Rangel-Buitrago N. The Plasticene. Mar Pollut Bull 2022, 185, 114358
- Lastretti M, Fanos V. Phtalates and bisphenols as endocrine disruptor chemicals. 2026

environments

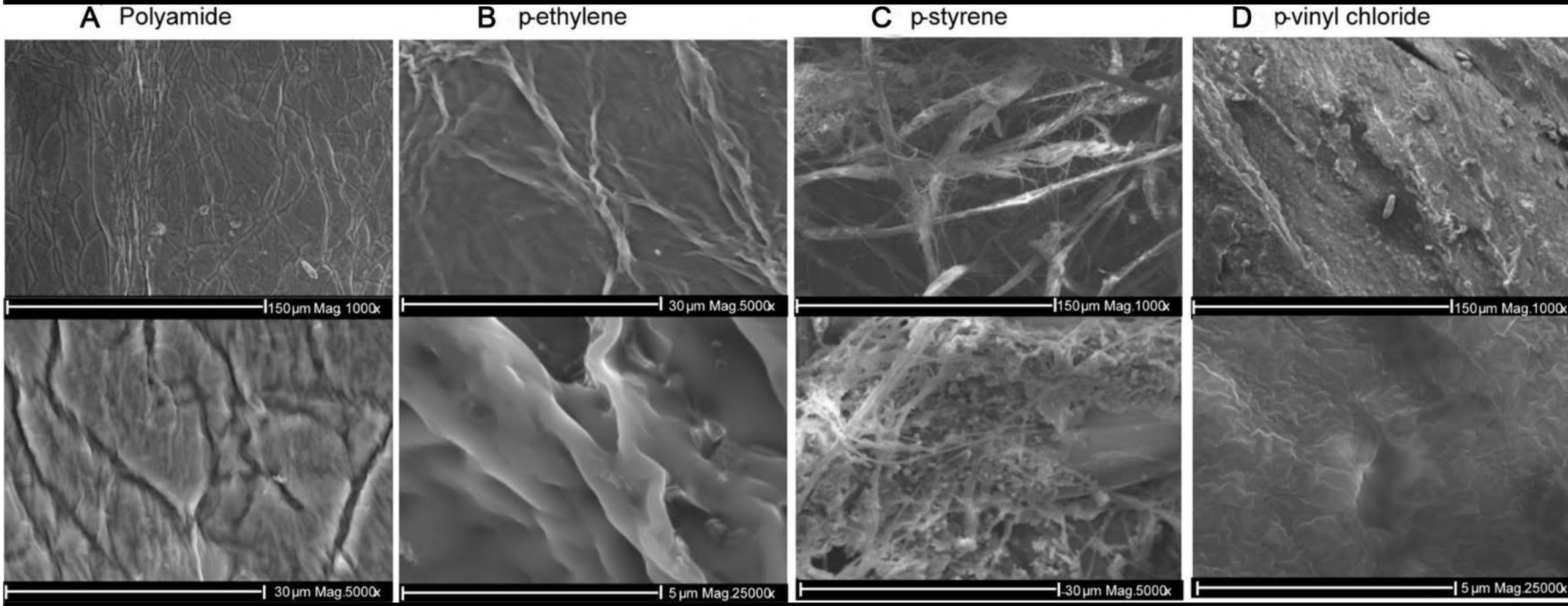
MDPI

Review

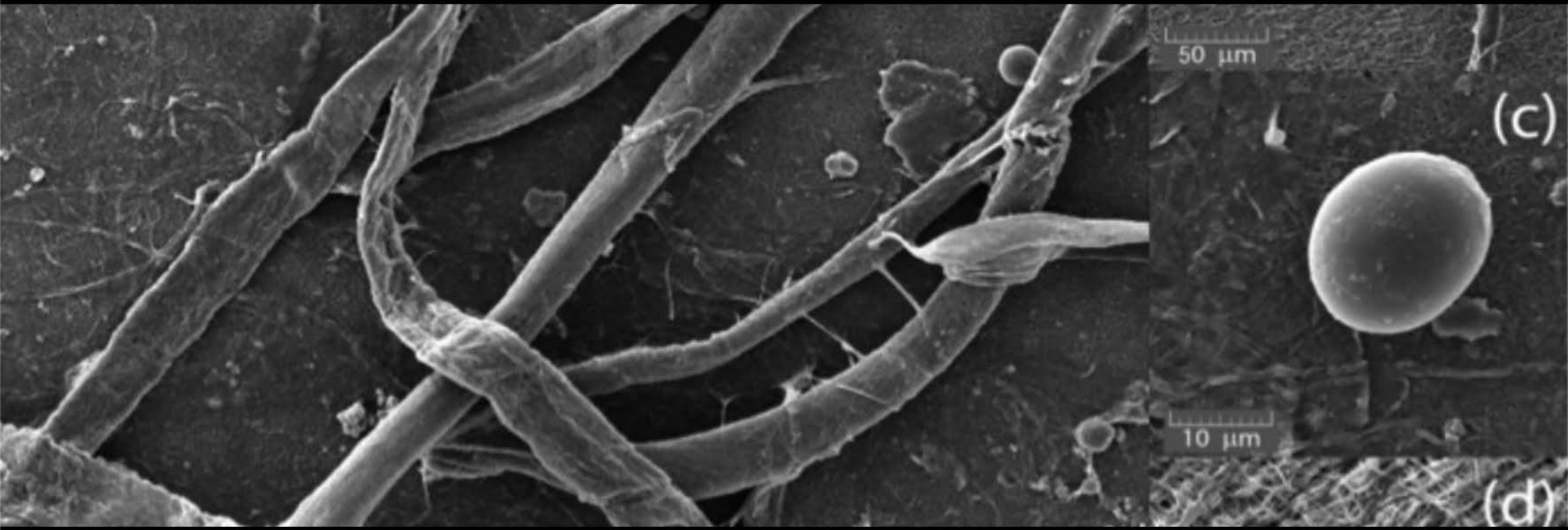
Phthalates and Bisphenols as Endocrine-Disrupting Chemicals: Possible Determinants of Mood Disorders

Mara Lastretti [1,*], Andrea Faa [2], Monica Piras [2], Angelica Dessì [3], Pasquale Paribello [4], Marco Piludu [5], Germano Orrù [6], Mirko Manchia [4,7], Gavino Faa [2,8] and Vassilios Fanos [3]

Scanning Electron Microscopy of Microplastics



Scanning electron microscopy of microplastics



MNPs exposure and nephrogenesis

Microplastics exposure disrupts nephrogenesis in human kidney organoids

1. impair cell membrane integrity
2. disturb mitochondrial homeostasis
3. alter nuclear morphology
4. decrease cell proliferation and organoid growth
5. increase renal cell apoptosis
6. alter nephron patterning through disruption of Notch signaling

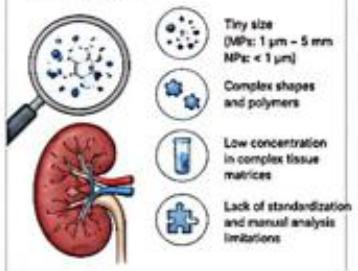
Zhou B. Environmental Pollution 2024, 360, 124645.

THE ROLE OF AI IN MICRO-NANO PLASTICS PATHOLOGY

Artificial Intelligence for detecting, quantifying and understanding the impact of micro- and nanoplastics in human tissues

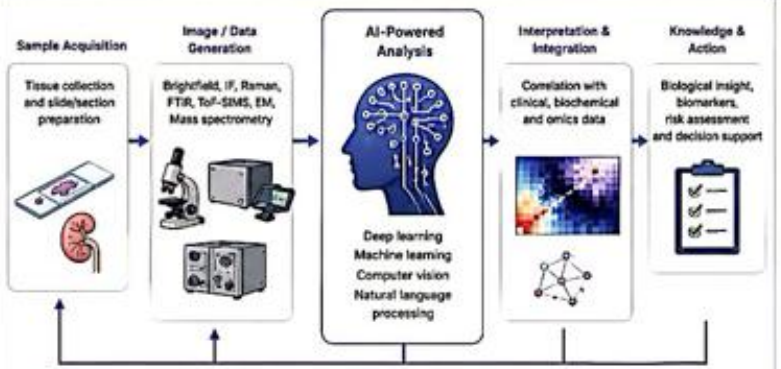
1. THE CHALLENGE

Micro- and nanoplastics (MNPs) are ubiquitous and can accumulate in human tissues, contributing to inflammation, oxidative stress and organ dysfunction.



- Tiny size (MPs: 1 µm – 5 mm NPs: < 1 µm)
- Complex shapes and polymers
- Low concentration in complex tissue matrices
- Lack of standardization and manual analysis limitations

2. WHERE AI ADDS VALUE: THE PATHOLOGY WORKFLOW



3. AI APPLICATIONS IN MICRO-NANO PLASTICS PATHOLOGY



Automated Detection & Localization
Deep learning models detect and localize MPs/NPs in histology and microscopy images with high accuracy.



Particle Characterization & Classification
AI classifies particles by size, shape, color, polymer type (integrating hyperspectral, Raman, FTIR, ToF-SIMS data).



Quantification
Automated counting and size distribution analysis for objective and reproducible quantification across large datasets.



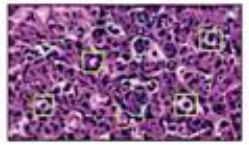
Tissue Impact Assessment
AI models evaluate co-localization with cells and structures, and predict pathological effects (e.g., inflammation, fibrosis, oxidative stress).

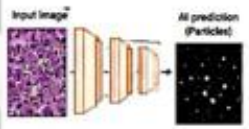


Data Integration & Prediction
Multi-omics and clinical data integration to identify biomarkers, exposure signatures and predict disease risk or progression.

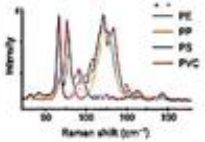
4. AI TECHNIQUES AND EXAMPLES

Deep Learning for Image Analysis
CNNs identify MPs/NPs in histology and fluorescence images





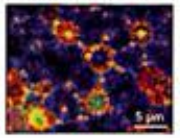
Hyperspectral & Raman Data Analysis
AI unmixes spectra and identifies polymer signatures



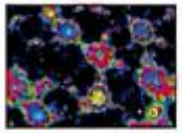
AI classification

PE | PP | PS | PVC | Others

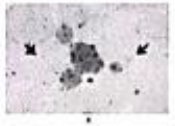
ToF-SIMS / FTIR Spectral Imaging
Machine learning classifies chemical maps at submicron level



AI segmentation



Electron Microscopy AI Enhancement
AI improves particle detection in EM images (denoising, segmentation)



AI enhanced detection



Natural Language Processing (NLP)
AI extracts knowledge from scientific literature

microplastics
inflammation
oxidative stress
fibrosis
toxicity
exposure

NLP example:
"What are the reported effects of microplastics on the kidney?"

AI-generated summary with key findings and references

5. BENEFITS OF AI IN MICRO-NANO PLASTICS PATHOLOGY

- High-throughput analysis of large datasets
- Increased sensitivity and accuracy
- Objective and reproducible results
- Discovery of new patterns and biomarkers
- Faster translation to risk assessment and clinical decision support

6. CHALLENGES AND FUTURE DIRECTIONS

- Limited and heterogeneous annotated datasets
- Standardization of sample preparation and data
- Model generalizability and external validation
- Integration with multi-center and longitudinal studies
- Explainable AI for transparent and trustworthy results

Future Vision
AI-driven digital pathology platforms for a deeper understanding of micro-nano plastics exposure and its impact on human health.



AI is transforming micro-nano plastics pathology by enabling precise detection, advanced characterization, and meaningful interpretation of complex data, ultimately supporting better understanding, prevention and management of plastic-associated diseases.

KEY TAKE-HOME MESSAGE

The synergy of advanced analytical techniques and AI will be essential to unravel the hidden impact of micro- and nanoplastics on human health.

Abbreviations: MP = Microplastic; NP = Nanoplastic; CNN = Convolutional Neural Network; IF = Immunofluorescence; FTIR = Fourier Transform Infrared Spectroscopy; ToF-SIMS = Time-of-Flight Secondary Ion Mass Spectrometry; EM = Electron Microscopy.

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Benefits of the application of AI models to MNP-related renal patholgoy

1. Analysis of large multimodal datasets, including laboratory, radiological and clinical data

2. Increased sensitivity and accuracy in the detection and characterization of MNPs in liquids and tissues

3. Identification of subtle lesions induced by MNPs in kidney biopsy histological images

4. Faster translation to risk assessment and critical decision support from histological images of kidney biopsies

Conclusions

Although a causal link between MNP exposure and kidney damage has not been definitely demonstrated in humans,

the irony lies in the semantic shift

While «plasticity» once symbolized the kidney's ability for change and adapt to the environmental changes,

now «plastic» threatens that very adaptability,

making nephrotoxicity a rising concern.

Ragusa A, Fanos V. JPNIM 2025, 14, e140206.

MICROPLASTICS AND NANOPLASTICS IN HUMAN PATHOLOGY

From environmental exposure to cellular injury and human disease

1 ORIGINS AND HUMAN EXPOSURE

ORIGINS

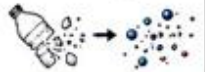
PRIMARY MICROPLASTICS

- Microbeads in personal care products
- Plastic pellets (nurdles)
- Industrial abrasives
- Synthetic fibers



SECONDARY MICRO/NANOPLASTICS

Fragmentation of larger plastic items by weathering, UV, mechanical forces and biodegradation



EXPOSURE PATHWAYS



Food	Drinking Water	Air	Textiles	Consumer Products
Seafood, salt, sugar, honey, beer, etc.	Tap water, bottled water	Indoor & outdoor air, dust	Synthetic fibers release	Cosmetics, packaging, etc.

HUMAN EXPOSURE

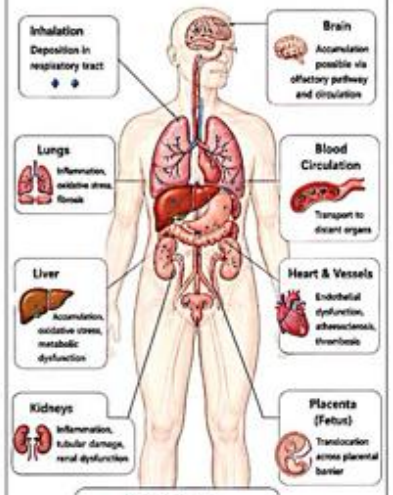
INGESTION (Oral route) → ← INHALATION (Respiratory route)



KEY POINTS

- Ubiquitous presence in the environment
- Humans are exposed daily through multiple routes
- Nanoplastics (<1 µm) can translocate across biological barriers

2 HUMAN BIODISTRIBUTION AND PATHOLOGY



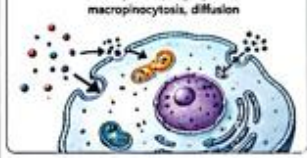
KEY POINTS

- Micro/nanoplastics detected in human tissues: lung, placenta, liver, spleen, kidney, brain, blood, etc.
- Ability to cross biological barriers (gut, lung, placenta, BBB)
- Potential for bioaccumulation and long-term effects

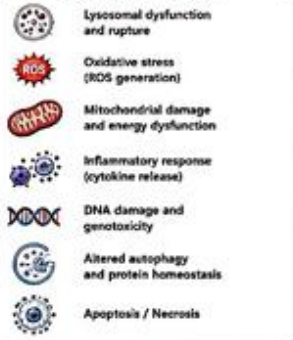
3 CELLULAR PATHOLOGY

CELLULAR UPTAKE

Endocytosis, phagocytosis, macropinocytosis, diffusion



INTRACELLULAR EFFECTS



- Lysosomal dysfunction and rupture
- Oxidative stress (ROS generation)
- Mitochondrial damage and energy dysfunction
- Inflammatory response (cytokine release)
- DNA damage and genotoxicity
- Altered autophagy and protein homeostasis
- Apoptosis / Necrosis

KEY POINTS

- Particle size, shape, polymer type and surface chemistry influence toxicity
- Nanoplastics (<1 µm) show higher cellular uptake and reactivity
- Mixture with additives and adsorbed pollutants increases harm

4 DIAGNOSIS: DETECTION OF NANOPLASTICS IN TISSUES AND CELLS

1. TISSUE / CELL SAMPLING
Biopsy, autopsy, surgical specimens, cell cultures



2. CONTAMINATION CONTROL
Clean environment, cotton lab coats, metal tools, blank controls, HEPA filtration



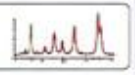
3. SAMPLE PREPARATION
Enzymatic/chemical digestion to remove organic matter
Density separation



4. MICROSCOPY SCREENING
Light microscopy, fluorescence microscopy (size, shape, localization)



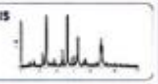
5. SPECTROSCOPIC IDENTIFICATION
µ-FTIR / Raman microscopy (chemical fingerprint of particles)



6. ELECTRON MICROSCOPY AND ELEMENTAL ANALYSIS
SEM / TEM with EDS (Nanoplastics <100 nm visualization & composition)



7. THERMAL / CHEMICAL ANALYSIS
Pyrolysis–GC/MS (Polymer identification and quantification)



NANOPLASTIC DETECTION GAP

- Particles <100 nm are below the detection limit of many methods
- Lack of standardized protocols and reference materials
- Risk of contamination and false positives
- Need for method validation and interlaboratory harmonization



KEY POINTS

- Multi-analytical approach is essential for reliable identification
- Localization within tissues/cells is crucial to assess relevance
- Current methods are still evolving, especially for nanoplastics

MAJOR CHALLENGES

- ⚠ Ubiquity and contamination
- ⚠ Complex matrices and low concentrations
- ⚠ Heterogeneity of methods and results
- ⚠ Uncertain long-term health effects

FROM ENVIRONMENTAL EXPOSURE TO PRECISION PATHOLOGY



Can we reliably detect, localize and quantify microplastics and nanoplastics within human tissues and individual cells?



FUTURE DIRECTIONS

- Standardization of protocols
- Development of sensitive methods for <100 nm
- Toxicological and epidemiological studies
- Regulatory actions to reduce exposure

LEGEND: Microplastics (1 µm – 5 mm) Nanoplastics (<1 µm)

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MICROPLASTICS AND NANOPLASTICS AND KIDNEY DISEASE

From exposure to kidney injury: pathways, mechanisms and health impacts

MICROPLASTICS (MPs) > 1 µm
NANOPLASTICS (NPs) < 1 µm

1. SOURCES & EXPOSURE

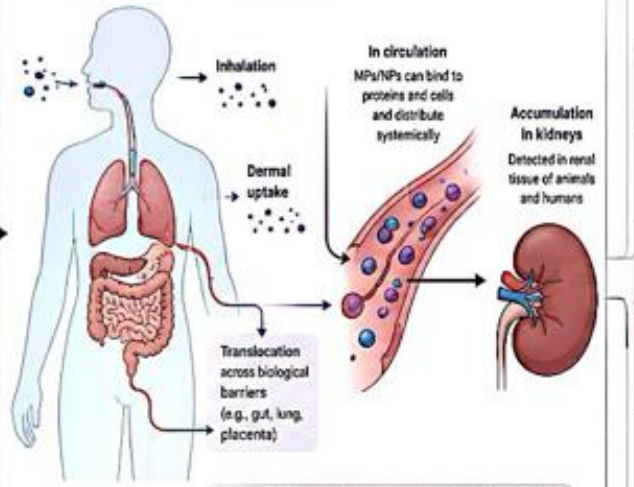
PLASTIC PRODUCTS BREAKDOWN
Bottles, bags, packaging, tires, textiles, etc.

ENVIRONMENTAL DISTRIBUTION
Air • Water • Soil • Food

HUMAN EXPOSURE ROUTES
Ingestion
Inhalation
Dermal contact

COMMON POLYMERS
PE, PP, PVC, PS, PET, PA, PMMA, PU
Additives: BPA, phthalates, PBDEs, heavy metals, etc.

2. ENTRY & BIOKINETICS



MICROPLASTICS (MPs) 1 µm – 5 mm
NANOPLASTICS (NPs) 1 nm – 1 µm

3. MECHANISMS OF KIDNEY INJURY

OXIDATIVE STRESS
↑ ROS production, antioxidant depletion, lipid peroxidation, DNA damage

INFLAMMATION
Activation of NF-κB, ↑ pro-inflammatory cytokines (IL-1β, IL-6, TNF-α)

CELLULAR TOXICITY
Mitochondrial dysfunction, apoptosis of podocytes & tubular cells

ENDOTHELIAL DYSFUNCTION
Impaired NO production, vascular inflammation, microvascular damage

ALTERED AUTOPHAGY & PROTEIN AGGREGATION
Disrupted cellular homeostasis

GLOMERULAR & TUBULAR DAMAGE
Podocyte injury, GBM disruption, tubular cell degeneration, interstitial fibrosis

4. KIDNEY DISEASE OUTCOMES

GLOMERULAR DISEASE
Proteinuria, hematuria, glomerulosclerosis

TUBULOINTERSTITIAL DISEASE
Tubular injury, interstitial fibrosis, reduced renal function

CHRONIC KIDNEY DISEASE (CKD)
Decline in eGFR, albuminuria, progression to end-stage kidney disease (ESKD)

KIDNEY FAILURE
Need for dialysis or transplantation

5. HEALTH IMPACTS (BEYOND KIDNEYS)

Cardiovascular disease
Neurotoxicity
Hepatotoxicity
Reproductive & developmental toxicity
Immune system dysregulation

6. FACTORS INFLUENCING TOXICITY

- Particle size, shape, concentration
- Polymer type & additives
- Surface charge & functional groups
- Co-exposure to pollutants (heavy metals, POPs)
- Duration of exposure
- Individual susceptibility (age, genetics, comorbidities)

7. PREVENTION & SOLUTIONS

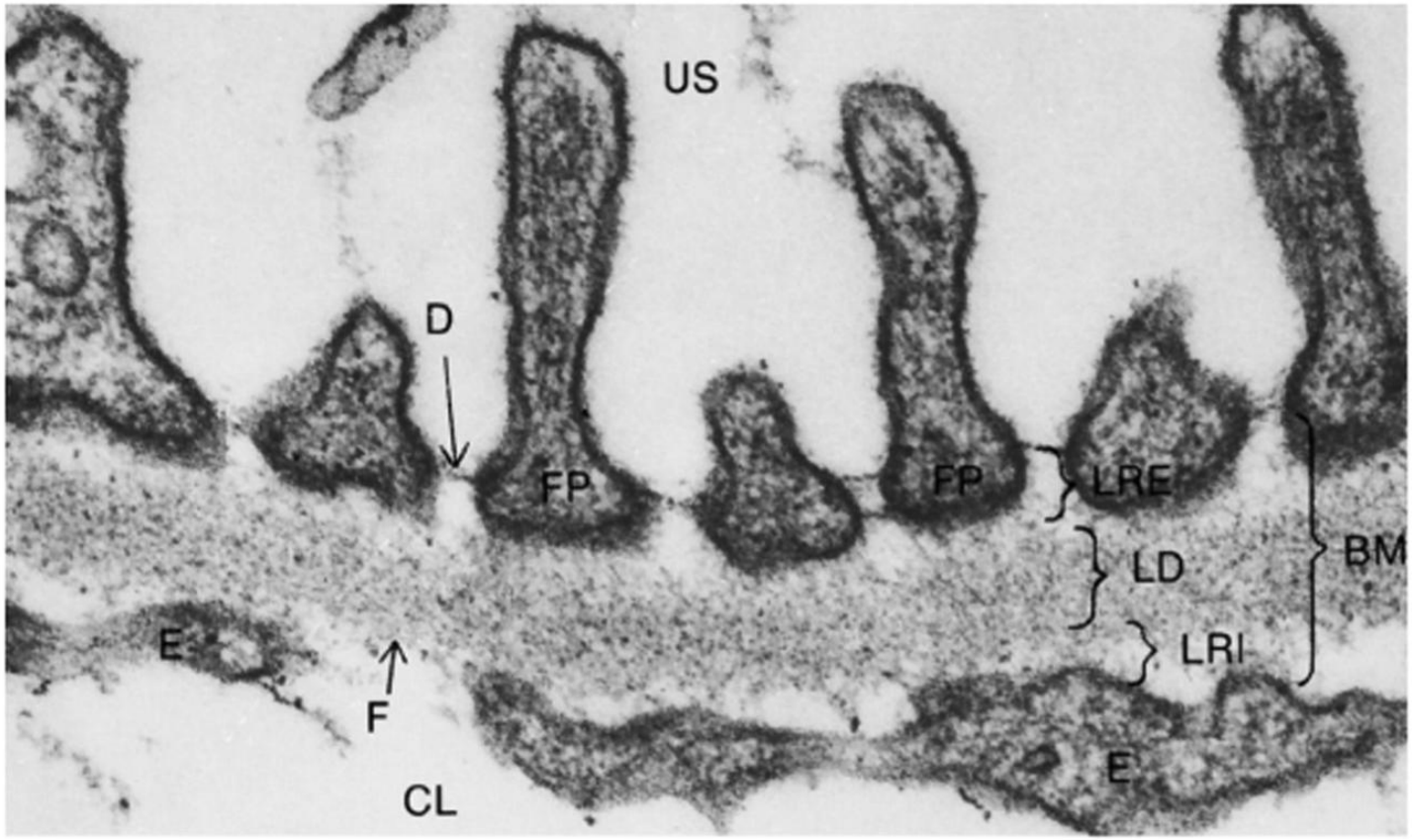
Reduce plastic use
Improve waste management & recycling
Advanced water treatment & filtration
Research & monitoring
Public awareness & policy interventions

Emerging evidence links micro/nanoplastics exposure to kidney injury through oxidative stress, inflammation, and cellular toxicity. More research is needed to understand long-term effects and to develop strategies to reduce exposure and protect kidney health.

KEY REFERENCES
Li et al., J Hazard Mater. 2019; 380:120887
Cai et al., Ecotoxicol Environ Saf. 2021; 208:111731
Ramesh et al., Environ Int. 2022; 159:107053
Wang et al., J Hazard Mater. 2023; 453:131362

(Illustrative schematic – not to scale)

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Rubin, Patologia

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- PS = polystyrene MP
- PVC = polyvvynilchloride
- PC = Polycarbonate
- LDPE = low-density polyethylene
- PP = polypropylene
- PE = polyethylene

AI methods applied to MNPs : advantages

1. high thoughput Large datasets
2. increased sensitivity
3. Increased accuracy in the detection and characterrization of the different MNPs
4. Ability to reach quantitative data on MNP-related kidney pollution
5. discovery of new patterns and biomarkersfrom kidney biopsies' images

Sierra I. Environmental Science and Pollution Research 2019, 27, 7409-7419.

AI-driven models: usefullness in MNP-related pathology

1, automated detection and classification of MNPs from

- High resolution spectral peaks
- Microscopic images
- Electron microscopic images

2. Identification of polymer type in milliseconds

3. Project of sophisticated in vivo studies able to simulate the effects of real-life exposure to MNPs

Sadique SA. Emerging Contaminants 2025, 11, 100545.

Gaps in our knowledge regarding MNPs detection, toxicity and exposure assessment

- 1. MNPs burden in the CNS and the insurgence of dementia
- 2. MNPs burden and proteinuria
- 3. MNPs renal burden and insurgence of chronic kidney disease
- 4. Fast and low-cost methods for the detection and classification of MNPs in liquids and tissues
- 5. Evidence of a direct causal link between MNP exposure and human pathology
- 6. Studies of patients over-exposed to MNPs, such as patients under dialysis
- 7. Detection of MNPs in kidney biopsies