## Nano-omics

Nano-omics is an emerging interdisciplinary field that combines nanotechnology with omics sciences (like genomics, transcriptomics, proteomics, metabolomics, etc.) to study biological systems at ultrasmall scales, often down to single molecules or single cells.

It enables high-resolution, high-sensitivity, and real-time analysis of biomolecules, providing deeper insights into complex biological processes.

□ Key Concepts "Nano" refers to the nanoscale (1-100 nanometers), where unique physical and chemical properties emerge.

"Omics" refers to large-scale data-driven studies of biological molecules — like genes (genomics), RNA (transcriptomics), proteins (proteomics), and metabolites (metabolomics).

Nano-omics brings these together to analyze biological samples with nanodevices or nanomaterials for maximum precision.

© Common Nano-omics Technologies Nanopore sequencing

DNA, RNA, or proteins pass through a nanoscale pore.

Changes in current are measured to determine molecular identity and sequence.

Nanoparticle-based biosensors

Gold nanoparticles, quantum dots, or carbon nanotubes used to detect specific molecules via fluorescence or electrochemical signals.

Atomic force microscopy (AFM)

Used to probe molecular structures or detect interactions at the single-molecule level.

Lab-on-a-chip and microfluidic nanosystems

Integrate nano-devices for omics analysis on extremely small sample volumes (single-cell analysis possible).

Applications of Nano-omics Early disease diagnosis (e.g., cancer, neurodegenerative disorders)

Precision medicine

Single-cell analysis

Liquid biopsy development

Drug discovery and targeted delivery

Liu et al. introduce the Nano-omics integrative workflow that links systemic (plasma) and localised (tumour tissue) protein changes associated with GB progression. Mass spectrometry analysis of the

nanoparticle biomolecule corona in GL261-bearing mice at different stages of GB revealed plasma protein alterations, even at low tumour burden, with over 30% overlap between GB-specific plasma and tumour tissue proteomes. Analysis of matched plasma and surgically resected tumour samples from high-grade glioma patients demonstrates the clinical applicability of the Nano-omics pipeline. Cross-species correlation identified 48 potential glioblastoma biomarker candidates involved in actin cytoskeleton organisation, focal adhesion, platelet activation, leukocyte migration, amino acid biosynthesis, carbon metabolism, and phagosome pathways. The Nano-omics approach holds promise for the discovery of early detection and disease monitoring biomarkers of central nervous system conditions, paving the way for subsequent clinical validation <sup>1)</sup>

Liu et al. present an innovative Nano-omics integrative proteomics pipeline that links systemic (plasma) and localized (tumour tissue) protein changes associated with glioblastoma (GB) progression. The authors perform **mass spectrometry** analysis of the **biomolecule corona** formed on nanoparticles injected into **GL261-bearing mice**, uncovering alterations in plasma proteins even in the early stages of tumour development. Notably, over 30% of the **proteomic signatures** overlap between plasma and tumour tissue in these murine models.

The authors extend their findings to a clinical context by analysing **matched plasma and surgically resected tumour samples** from patients with high-grade glioma. This cross-species approach results in the identification of **48 potential GB biomarker candidates**, linked to key biological pathways including actin cytoskeleton organisation, focal adhesion, platelet activation, leukocyte migration, amino acidbiosynthesis, carbon metabolism, and phagosome pathways.

This study is a **translational proteomics** investigation, with elements of **comparative analysis** and **biomarker discovery** across species. It cleverly leverages the **nanoparticle protein corona** phenomenon as a biological readout of disease states, thereby extending the potential of liquid biopsy in brain tumours—a notoriously difficult domain for early detection.

The study's strengths lie in its cross-species validation, the integration of multi-tissue omics, and the real-world applicability demonstrated through patient samples. Importantly, the study bridges the gap between preclinical findings and clinical biomarker development, something many high-impact papers fail to achieve.

However, several **limitations** must be considered:

- The **GL261 mouse model** is widely used but does not fully replicate the genetic and microenvironmental heterogeneity of human GB.
- The **sample size** for the clinical arm is not specified in the abstract and may limit statistical power.
- While the proteomic overlap is promising, **functional validation** of these 48 biomarker candidates remains to be done.
- The specificity of these markers to GB versus other brain or systemic inflammatory diseases is not assessed.

Overall, Liu et al.'s study represents a **proof-of-concept** investigation and should be followed by larger **clinical validation studies**. The Nano-omics pipeline is a promising tool that might contribute to future glioblastoma diagnosis and biomarker development for central nervous system disorders.

This is a **translational, exploratory proteomics study** that combines **preclinical experimental models** with **human clinical samples** to identify potential biomarkers for glioblastoma. It is a non-

randomized hypothesis-generating study in nature.

1)

Liu X, Abmanhal-Masarweh H, Iwanowytsch O, Okwelogu E, Arashvand K, Karabatsou K, Ivo D'Urso P, Roncaroli F, Kostarelos K, Kisby T, Hadjidemetriou M. Plasma-to-tumour tissue integrated proteomics using nano-omics for biomarker discovery in glioblastoma. Nat Commun. 2025 Apr 10;16(1):3412. doi: 10.1038/s41467-025-58252-0. PMID: 40210624.

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Last update: 2025/04/11 06:52

