2025 Human RNome Project Consortium Meeting

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Overview

RNA biology has entered a new era with the recognition that RNA molecules carry a rich repertoire of chemical modifications that regulate their processing, localisation, translation and stability [1]. More than 180 modifications have been identified across organisms, with at least 50 distinct chemical marks identified in humans, yet their precise roles and distribution across tissues remain incompletely understood [2,3]. The Human RNome Project (HRP) is a global effort to reveal the complete landscape of human RNA biology. The 2025 Human RNome Project Consortium Meeting, held from August 4-8, at Goethe University Frankfurt, Germany, brought together a global, multidisciplinary community of researchers in RNA biology, epitranscriptomics and RNome. The five-day meeting featured interactive morning breakout discussions and hands-on mass spectrometry laboratory sessions, followed by afternoon plenary lectures from leading experts, fostering a comprehensive exploration of the current field. As a cornerstone event for the HRP, the meeting aimed to evaluate the current landscape of RNA modification research through both scientific discussions and hands-on experimentation. Throughout the breakout sessions, participants consistently emphasised technical innovation, novel computational approaches and collaborative strategies vital for advancing RNA modification research. Key topics included modification-specific and direct RNA sequencing (such as nanopore-based technologies), quantitative mass spectrometry, data analysis pipelines and functional annotation of RNA modifications. HRP aims to deliver a complete atlas of RNA molecules and their modifications in human cells, analogous in ambition to the Human Genome Project but with added complexity arising from the dynamic nature of the transcriptome and its chemical marks.

To ensure these themes were addressed in depth, the meeting was structured around a series of focused breakout sessions that provided space for targeted discussion and community input. Across five days, 10 sessions were facilitated by experts at different career stages, with designated note takers capturing key points to inform future HRP planning. The table below summarises the session topics and facilitators.

Breakout session schedule:

Date	Session 1	Session 2
04/08/2025	Modification-specific sequencing (chemical or antibody-based)	Nanopore Sequencing
05/08/2025	How to comprehensively detect and quantify all mods in RNA?	What are the biological implications, and how to advance those studies?
06/08/2025	Modomics, SciModom - intro and what are the capacities, what more is needed	Data Meets Lab: Bridging Experimentation and Analysis
07/08/2025	Future Vision: The Human RNome in 2030	What are the next steps?
08/08/2025	Develop collaborative projects	

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4th August 2025
Session 1: Modification-specific sequencing (chemical or antibody-based)
Chaired by Gudrun Stengel and Ameya Sinha

Key points and questions raised in discussions:

- A table of all the modification-specific methods.
- Discussion on the limitations of all current methods in capturing the full picture of the RNome.
- What are the most promising new modification-specific sequencing techniques on the horizon?
- How can we move towards more quantitative and high-throughput methods?
- What is the role of modification-specific sequencing in a world with direct RNA sequencing?

Summary:

This session examined advances and challenges in methods designed to detect individual RNA modifications with high specificity. Participants discussed pulldown strategies, naturally or chemically induced reverse transcription signatures and newly developed multiplexed approaches. Recent technologies such as eTAM-Seq were highlighted for their compatibility with low RNA input, while pulldown-based methods, including EpiPlex and m6A-Seq2, were recognised for enabling multiplexing or reducing assay noise through upstream barcoding. While antibody-based methods can introduce false positives and chemical conversion strategies may suffer from false negatives, both were considered valuable for complementary applications. A recurring theme was the urgent need for community-wide benchmarking. Participants proposed testing a single modification, such as m6A, across multiple laboratories and platforms to define a “gold standard.” Standards should include both spike-ins and synthetic RNAs, complemented by stable cellular references. Discussions emphasised that while conversion methods can offer single-base resolution and absolute stoichiometry, they are typically limited to one modification at a time, making parallel application of multiple protocols impractical for most laboratories. The group also reflected on the biological complexity underlying RNA modifications. Rare modifications in mRNAs may originate as by-products of tRNA editing, and enzymes often have secondary functions beyond their canonical roles. Participants warned against assuming homology equates to function across species, underscoring the need for careful annotation and validation. A strong consensus emerged that standards and shared datasets must be prioritised to overcome current variability and allow methods to be quantitatively compared. The session concluded that modification-specific sequencing will remain essential to complement direct RNA sequencing, providing chemical precision and validation capacity while helping to define the biological ground truth.

Methodologies discussed in breakout session one:

Method	Mod	Class	Chemistry
m6A MeRIP [4]	m6A	Pull down	Antibody
m6A-seq2 [5]	m6A		Sample barcoding and pooling
EndoVIPER-seq [6]	I		EndoV
m6A-CLIP/eClip [7,8]	m6A	Pull down and crosslinking	Antibody
EpiPlex [9]	m6A, I	Pull down and barcoding	Small protein scaffold
ICE-seq [10]	I	Chemical conversion	Cyanoethylation of inosines/cDNA truncation
CMC-seq [11]	Ψ		CMC modification and cDNA truncation
Bisulfite-seq [12]	m5C		Bisulfite conversion of all unmethylated C
GLORI [13]	m6A		Glyoxal/nitrite deamination of all unmethylated A
BID-seq [14]	Ψ		Selective chemical labelling of Ψ by bisulfite to induce nucleotide deletion signature
PRAISE [15]	Ψ		
CAM-seq [16]	m6A		N-Nitrosation of all unmethylated A
SAC-seq [17]	m6A	Enzymatic conversion	MjDim1, a dimethyl transferase and allylic-SAM
eTAM-seq[18]	m6A		Deamination of unmethylated A by TadA8.20
Matzer Seq[19]	m6A	Ribonuclease cleavage	Differential cleavage

Session 2: Nanopore sequencing
Chaired by Angela Gallo and Mattia Pelizzola

Key points and questions raised in discussions:

- How can we increase sensitivity to detect low-stoichiometry modifications?
- RNA standards – benchmarking
- What is the current accuracy of base calling for standard and modified bases on nanopore platforms?
- Discussion of throughput, multiplexing, and cost considerations for large-scale projects.
- What are the key hardware and software improvements needed to make nanopore sequencing a comprehensive tool for RNome profiling?
- What is the potential for single-cell direct RNA sequencing with nanopore?

Summary:

The nanopore sequencing session provided a broad overview of ONT's role in RNA modification detection. It was apparent that m6A, m5C, and pseudouridine (Ψ) were the most popular modifications studied by participants using this technology. Participants highlighted the inherent bias of ONT's poly(A)-dependent sequencing and the need for expanded protocols that accommodate non-polyadenylated RNAs. Participants examined the implications of 3′-initiated sequencing for transcript coverage, noting that incomplete representation of 5′ ends limits the resolution of isoforms and positional mapping of modifications. Computational tools for modification detection are advancing rapidly, but concerns remain around reproducibility, resource demands, and the need for consensus-based approaches. Benchmarking was identified as a priority, with calls for harmonised protocols and cross-laboratory validation. There was consensus that direct RNA sequencing with ONT will play a key role in detecting RNA modifications due to its ability to identify RNA modifications within sequence context, which is more challenging with mass spectrometry. Finally, the session concluded with reflections on ONT device throughput and cost, acknowledging that while platforms like PromethION offer high read volumes, multiplexing and signal-to-noise constraints continue to affect sensitivity; therefore, developments are still required for this approach.

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5th August 2025
Session 1: How to comprehensively detect and quantify all mods in RNA?
Chaired by Sandra Kienast and Martin Hengesbach

Key points and questions raised in discussions:

- Does it mean identifying every known modification on every RNA molecule in a sample?
- Does it include the discovery of entirely new, unknown modifications?
- How important is single-molecule vs. bulk quantification?
- What are the biggest blind spots in our current technological arsenal? Are there specific classes of modifications (e.g., isomeric, highly complex) that we consistently miss?
- Is the primary bottleneck in detection (finding the mod) or quantification (measuring its stoichiometry)?
- Imagining the Future: What does the ideal, "one-and-done" technology for comprehensive RNome analysis look like? What are the fundamental physics or chemistry breakthroughs needed to get there?
- What is one collaborative project the people in this room could start to move this forward? (e.g., A bake-off of different platforms on a standard sample, developing a data standard for integrated RNome
- data)

Summary:

The complete detection and quantification of RNA modifications session addressed the multifaceted challenges associated with achieving comprehensive detection and quantification of RNA modifications. Discussions centered on the need for methodological stringency, biological relevance, and the development of standardised frameworks to guide experimental design and data interpretation. Participants emphasised the importance of rigorous data collection and the need to consider RNA abundance when interpreting the significance of RNA modifications. For example, a framework was proposed where the biological relevance of RNA modifications is tied to a measurable phenotype. The group advocated for the development of a decision tree to guide researchers through modification-specific analytical pathways, recognising that a universal protocol may not yet be feasible at this time with the available technologies. Statistical interpretation of stoichiometry and fold changes remains complex, and this can be influenced by data type, enrichment status, and background noise, all of which need to be considered during analysis. The limitations of current technologies were acknowledged, and the need for orthogonal approaches, such as mass spectrometry, was emphasised, to ensure the modifications observed can be cross-validated. This reinforces the need for benchmarking efforts, a theme that emerged across multiple sessions, where proposals for a standardised resource combining synthetic and biological RNAs are required to establish ground truths. Participants also called for a deeper understanding of false negatives and the contextual factors that affect modification detection.

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Session 2: What are the biological implications, and how to advance those studies?
Chaired by Dan Ohtan Wang and Michael Jantsch

Key points and questions raised in discussions:

- A Whirlwind Tour of Function: A brief, high-level review of the most compelling examples of RNA modification functions
- What are the major cellular pathways and processes where the epitranscriptome is emerging as a key regulatory layer (e.g., stress response, innate immunity, neurodevelopment)?
- What are the biggest "known unknowns"? Which abundant and conserved modifications have the most enigmatic functions?
- What are the experimental tools and strategies needed to prove the function of a given modification?
- How do we foster a collaborative, rather than competitive, environment to tackle the functional RNome? How can we avoid a "one lab, one modification" scenario?
- What are the essential shared resources needed to accelerate progress? (e.g., a centralised database of modification functions, a repository of validated antibodies and editor plasmids, standardised
- experimental protocols).
- What would a "Functional RNome Committee in our Consortium" look like? What would be its top three priorities for the next five years?

Summary:
This session explored the biological roles and consequences of RNA modifications across diverse cellular contexts. Participants emphasised that while technological advances now enable increasingly precise mapping of modified nucleotides, the functional interpretation of these marks remains a major challenge. Discussion highlighted that RNA modifications often operate in a combinatorial and context-dependent manner, complicating efforts to assign single modifications to discrete phenotypes. Rare modifications in mRNAs may, in fact, represent collateral activity of tRNA- or rRNA-modifying enzymes, making attribution difficult. Similarly, homologous enzymes across species can evolve new functions, underscoring the risks of assuming conservation equates to functional equivalence. Participants stressed that annotation of modification writers, readers, and erasers is still incomplete, and that proteomic and mass spectrometry approaches may help to fill these gaps. Another theme concerned the biological “noise” inherent in modification maps. Because modifications can be opportunistic or stochastic, researchers cautioned against overinterpreting small quantitative differences without robust standards and orthogonal validation. Spike-ins and reference RNAs were recommended to distinguish true biological signals from technical or cell culture artefacts. The group agreed that developing a human tissue- and cell-type atlas of modifications, starting with m6A, would provide an invaluable framework for connecting chemical marks to gene regulation, cellular physiology, and disease. The session concluded that the key biological implications of RNA modifications will only be revealed through careful integration of multiple orthogonal methods, rigorous benchmarking across laboratories, and systematic mapping efforts spanning tissues and developmental states.

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6th August 2025
Session 1: Modomics, SciModom - intro and what are the capacities, what more is needed
Chaired by Janusz Bujnicki and Christoph Dieterich

Key points and questions raised in discussions:

- Brief intro of Modomics, SciModom
- Why are both types of databases-an encyclopedia and a quantitative atlas-essential for the success of the Human RNome Project? How do they serve different research questions?
- What is the most useful feature you've found in either database? What is a research question you were able to answer using Modomics or SciModom that you couldn't have answered otherwise?
- How can we create better more seamless links between Modomics and SciModom?
- What new data types should be prioritised for inclusion?
- How can we make the process of data submission easier and more rewarding for researchers?
- What is needed to ensure long-term funding, maintenance, and curation of these vital community resources?

Summary:

The foundational discussion established MODOMICS and Sci-ModoM as complementary, yet functionally distinct infrastructures vital to the epitranscriptomics community and large-scale initiatives like the Human RNome Project. MODOMICS was defined as a qualitative “encyclopedia” built on rigorous expert manual curation, offering verified knowledge on RNA modifications, including their chemical structures, associated enzymes (writers, erasers, readers), and genomic locations. While time-consuming, this human-driven process ensures high data integrity, supports the management of retractions, and allows for nuanced decision-making on new data. In contrast, Sci-ModoM serves as a quantitative “atlas,” designed to standardise and disseminate high-throughput sequencing data at single-nucleotide resolution, formatted into a computable, human-readable bedM format. This enables researchers to query by publication, gene locus, or genomic region. Looking ahead, the session emphasised expanding the databases’ scope by incorporating Mass Spectrometry (MS) quantification, miRNA datasets, synthetic or unusual modifications, fluorescent analogues, and cross-species comparative data. Visualisation improvements, such as integration with the UCSC Genome Browser and the addition of confidence scores for modification sites, were highlighted as essential user-focused features. A critical technical bottleneck was identified in the lack of a centralised repository for nanopore fast5 files, whose size exceeds the limits of current archives like the SRA, posing serious threats to reproducibility and data sharing. The most pressing concern throughout was long-term sustainability. The session underscored the urgent need for stable, structural funding not only for infrastructure but also for dedicated positions, arguing against simple distribution of funds. A proposed solution was a fee-based model wherein consortium members financially support the databases to ensure fair data usage. Ultimately, participants called for substantial support from major agencies like the DFG or the HRP consortium, advocating a shift from short-term project grants to permanent, community-anchored infrastructure capable of evolving alongside the field’s demands.

Session 2: Data Meets Lab: Bridging Experimentation and Analysis
Chaired by Rebekah Penrice-Randal and Rami Bechara

Key points and questions raised in discussions:

- The State of the Union: typical data lifecycle: Hypothesis -> Experimental Design -> Sample Prep -> Sequencing/Measurement -> Data QC -> Analysis -> Interpretation -> New Hypothesis.
- From the Experimentalist's View: What information do you wish you had from bioinformaticians before starting an experiment? What are the biggest frustrations when you receive results back?
- From the Analyst's View: What is the most common reason an analysis fails or yields ambiguous results? What is the single most important piece of information or metadata you wish you had with every
- What datasets do you receive? (e.g., detailed sample prep notes, passage number, reagent lot numbers).
- What does a truly collaborative experimental design process look like? What questions should be asked at the very beginning?
- What would the perfect, seamless workflow from sample to insight look like in 5-10 years?
- What is one concrete practice that everyone in this room can commit to implementing in their own lab to improve the data-lab bridge starting next week?

Summary:

The data repository session addressed the infrastructural and collaborative challenges of managing mass spectrometry data and raw ONT reads in RNA modification research, as no suitable repository or database currently exists. A survey conducted during the meeting revealed persistent friction between wet lab and computational teams, often due to inconsistent sample labelling, incomplete metadata, and ambiguous terminology. These issues contribute to reproducibility problems and miscommunication. Participants stressed the importance of early-stage planning, mutual training, and transparent documentation. Suggested actions included establishing regular cross-disciplinary meetings, creating shared communication platforms, and developing a common glossary to reduce ambiguity. Clear assignment of responsibilities for protocols, workflows, and metadata was recommended, alongside the designation of method-specific leads to support standardisation. Pilot experiments were encouraged to validate study designs, and early agreement on goals, controls, and outputs was deemed essential. Benchmarking, discussed again, resulted in the concept of an “RNome in a bottle”. By combining the analysis of synthetic oligonucleotides and biologically derived RNAs across multiple protocols and multiple labs, we will be able to establish ground truths for modification detection. This would support reproducibility and enable cross-platform comparisons. Participants also raised concerns about RNA quality metrics, questioning whether standard measures such as the RNA Integrity Number (RIN) are sufficient for assessing modification stability and detection fidelity. Collection of this metadata across labs during this characterisation stage is essential for us to be able to understand how these variables contribute to detection and quantification. Data storage emerged as a major concern, as there is no centralised database or repository for RNA modification data. Current cloud-based solutions prove costly and are inadequate for long-term needs. The group proposed estimating total storage requirements through 2030 and identifying institutional or consortium-based repositories, favouring cold storage for large datasets such as LC-MS and ONT RNA reads. Computational tools and pipelines should be hosted on a shared GitHub organisation to allow for appropriate use of version control and to ensure reproducibility during the analysis component of these studies. Long-term planning should involve mapping out experimental and computational roadmaps, aligning timelines and capabilities, and defining clear criteria for reproducibility and success in RNA modification research.

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7th August 2025
Session 1: Future Vision: The Human RNome in 2030
Chaired by Fred Tyson and Vivian Cheung

Key points and questions raised in discussions:

- It's 2030. We're looking at the cover of a major journal celebrating the success of the HRP. What's the headline? What's the main image?" This exercise rapidly surfaces the group's highest aspirations.
- What can we DO? (Technology & Capability): In 2030, what is the one technological capability that has fundamentally changed the game for RNome research?
- What do we KNOW? (Scientific Knowledge) In 2030, what is the single most important piece of fundamental biological knowledge we will have gained thanks to the HRP?
- What have we CHANGED? (Clinical & Societal Impact) In 2030, what is the most significant real-world impact the HRP has had on a specific human disease?
- What is the single most important "Grand Challenge" project the HRP community needs to launch in the next 18 months to meet the above goals?

Summary:
This forward-looking session invited participants to imagine the state of RNome science in the year 2030. Discussions were structured around three guiding questions: what will we be able to do technologically, what will we know scientifically, and what will we have changed clinically and societally? From a technological perspective, the community envisioned single-molecule methods capable of identifying all isoforms and associated modifications at base-level resolution, with precision and error rates approaching those of DNA sequencing. Improved nanopore chemistries, novel ligases, and more sensitive mass spectrometry platforms were highlighted as areas for innovation. A critical milestone will be the establishment of robust community standards, including benchmarking of synthetic and biological RNA references across laboratories, enabling comparability and reproducibility. In terms of scientific knowledge, participants anticipated that by 2030, the field would have achieved comprehensive maps of modification distributions across tissues and cell types, including their spatial localisation and co-occurrence patterns. Importantly, the group emphasised the need to link modifications causally to RNA metabolism, translation, and protein abundance, with particular focus on the extent of crosstalk between different marks. Fundamental questions include whether modifications are heritable, how they vary across populations, and how they contribute to cell fate decisions. The clinical and societal vision is centred on the potential of RNA modifications as biomarkers and therapeutic targets. Participants highlighted applications in cancer, metabolic disorders, rare “RNA modopathies,” and antimicrobial resistance, as well as translational opportunities in agriculture and biotechnology. The group emphasised that whether modifications are causal drivers of disease, manipulating them may enable therapeutic reprogramming of cells. A grand challenge proposed for the next 18 months was a systematic functional screen of all RNA modification enzymes, combining epitranscriptomic profiling with transcriptomic, genomic, and metabolic readouts. Such a resource would establish the foundation for understanding modification biology at scale. The session concluded with broad agreement that realising the vision of the Human RNome Project requires coordinated infrastructure, transparent data sharing, and an international commitment to standards and benchmarking.

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Session 2: What are the next steps?
Chaired by Silvo Conticello and Peter Dedon

Key points and questions raised in discussions:

- To make that 2030 vision a reality, what must we prioritise now? This section is about defining our immediate marching orders.
- What specific, action-oriented working groups need to be formed or commissioned by the people in this room?
- "Before We Meet Again" List: What are the top 3-5 concrete action items this group must accomplish before the next HRP workshop?
- Session leader summarises the key next steps, the newly formed working groups, and the shared commitment to turning the 2030 vision into a tangible research plan.

Summary:
The foundational workshop for the HRP culminated in a clear action plan, centring on a first collaborative project to map RNA modifications. The consortium agreed to use a common stock of total RNA from ENCODE GM12878 B-cells as a standardised reference sample. For this project to succeed, key resources and infrastructure must be established. An urgent priority is securing a central, funded data repository for both raw and processed data, with RMDB suggested as a potential solution. Furthermore, the consortium plans to develop a shared resource on the HRP website for standardised protocols, kit recommendations, and sources for reagents. The need for dedicated project management to oversee this complex logistics and infrastructure was also clearly identified.

Proposed actions and deadlines for benchmarking collaboration:

Action Item	**Lead/Status**
Shipping GM12878 RNA	15th Oct 2025
Wet-lab experiments completed	15th Jan 2026
Data uploaded to a common repository	1st February 2026
Joint data mining and analysis	February-June 2026
Report results and compare methods at the next HRP workshop	Aug-Sep 2026

Parallel to the scientific work, a major focus will be on community engagement and communication. Plans are underway to maintain momentum through regular community gatherings, the first of which is suggested for January 2026 or sooner. The group will explore communication platforms for ongoing discussion and may record talks for a YouTube channel to increase exposure. A key initiative is the formation of subgroups, particularly for Early Career Researchers (ECRs), which will include activities like a monthly journal club. To effectively organise these efforts, a Google Form will be circulated to survey members' skills and resources, creating a valuable skill matrix for the entire consortium. Two critical writing projects were initiated to document and promote the consortium's efforts. First, there is a strong drive to publish a report on this foundational workshop to formalise the project and attract broad attention. ECRs have volunteered to lead the writing, with a target draft deadline of November 1st, though the challenge remains to find a journal that accepts meeting reports. Second, and crucial for funding, is the creation of a compelling Impact Statement. All members are encouraged to contribute points with citations to a shared Google Doc, which will be synthesised by Majd Abdulghani into a final statement accessible to the public and funding agencies. The discussions also highlighted several open questions for future resolution. The very nature of the consortium, whether it is a project, a society, or something else, needs further definition. Funding models, including the possibility of paid membership, and formal legal frameworks for international data sharing and privacy, will need to be addressed as the project evolves beyond its initial unofficial status.

Additional actions determined by workshop participants with proposed leads and deadlines:

Action Item	Lead/Status	Deadline/Note
Shipping GM12878 RNA	Vivian Cheung, Peter Dedon and Mark Helm	15th Oct 2025
Data repository	Volunteers needed	Urgent
Create skill matrix	Session facilitators	ASAP
HRP website	Volunteers needed	Ongoing
Community zoom	Volunteers needed	Jan 2026
ECR subgroup	Rami Bechara, Rebekah Penrice-Randal and Bennett Henzeler	Oct 2025
Workshop report	Rami Bechara, Rebekah Penrice-Randal and Bennett Henzeler	Nov 2025
Impact statement	Majd Abdulghani	

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8th August 2025
Session 1 and 2: Develop collaborative projects
Chaired by Ana Raquel Soares and Majd Abdulghani

Key points and questions raised in discussions:

- The session leader asks everyone to silently write down 1-3 key research questions or project ideas on sticky notes that they believe are high-priority and require collaboration.
- The session leader gives a quick 2-minute summary of the main project clusters that have emerged on the board (e.g., "Technology Benchmarking," "m6A in cancer," "Building a Centralised Analysis Pipeline").
- Now, stand up and go to the project cluster that you are most passionate about contributing to. The goal is to form small, organic teams of 3-6 people around these core ideas.
- From ideas to action: Team Breakout & Canvas Completion (50 mins):
- Each newly formed team works through Project Canvas together.

Project Canvas Questions:

- Project Title: Give your project a clear, memorable name.
- The Core Question: In one sentence, what is the central scientific question this project will answer?
- The Approach: What are the top 3-5 key methods, technologies, or model systems you will use?
- The "Who" (The Team): Who is on this initial team, and what key expertise does each person/lab bring to the table? (e.g., Lab A: Nanopore expertise, Lab B: Mass Spec, Lab C: Computational modelling, Lab D: Clinical samples).
- The Deliverables: What are the tangible outcomes of this project? (e.g., A benchmarked dataset, a new open-source tool, a joint grant proposal, a high-impact publication).
- The First Step: What is the single, concrete action you will take within the next month to get this project started? (e.g., "Schedule a kickoff Zoom call," "Draft a shared document outlining the experimental plan," "Lab A will share their sample prep protocol with Lab B").
- Each team designates a spokesperson to give a 2-minute "pitch" to the entire room, summarising their completed Project Canvas. The focus is on the core question, the team, and the first step. Allow people to switch groups if needed.

Summary:

The final breakout session successfully fostered dynamic interaction among consortium members to identify shared scientific interests and catalyse the design of actionable collaborative projects. Through a structured exercise, participants proposed ideas that coalesced into three thematic clusters: technology-driven, functional/mapping-focused, and disease-oriented. Participants self-selected into groups based on these themes and spent 90 minutes developing detailed project concepts, outlining research questions, approaches, required expertise, and funding strategies. The session successfully generated three distinct yet highly complementary project proposals, demonstrating a strong collective drive to advance the goals of the RNome initiative through targeted collaboration.

The first group, focused on Technology, proposed a project titled "From Molecule to Modification: Integrating Detection Platforms for Comprehensive RNA Profiling." Its core goal is to develop a standardised, benchmarked system for detecting any RNA modification across any species or RNA type using multiple analytical platforms. The approach is structured into four work packages: synthesising tailored standards and RNA preparations (WP1), benchmarking existing technologies like Illumina and Nanopore sequencing and LC/MS (WP2), developing methods for cross-platform harmonisation (WP3), and building a robust computational pipeline for integrated data analysis (WP4). The team brings together expertise in sequencing, mass spectrometry, oligonucleotide synthesis, and bioinformatics. They aim to secure funding through Horizon Europe, leveraging a consortium of European research groups.

The second group, centred on Mapping and Function, conceived "The Functional RNome Atlas" project. Its ambitious core goal is to create a complete, dynamic map of the modified transcriptome across time, from cell to organ to organism. The approach will combine NGS-based detection in key cell lines (e.g., iPSCs, fibroblasts, GM12878 B-cells) to study development, ageing, and immune response, followed by studies in engineered mouse models and human tissues from biobanks. The team includes experts in molecular biology, 'omics technologies, bioinformatics, and animal models. Their strategy is to apply for Horizon Europe grand challenges grants, and their first steps involve lobbying and cataloguing available resources within each principal investigator's lab.

The third group, addressing Disease, designed the "RNA Epitranscriptomic Landscape in Immune Regulation (ReLi)" project. This initiative seeks to answer how RNA modifications shape immunological responses in cancer and autoimmunity, using glioblastoma and Sjögren's disease as representative models. The project is split into two work packages: WP1 will map the baseline epitranscriptomic landscape in patient-derived tissuoids and organoids using ONT sequencing, spatial transcriptomics, and proteomics. WP2 will functionally validate key findings from WP1 through knockdown experiments, site-directed mutagenesis, and immune cell response assays. The consortium combines expertise in immunology, cancer biology, and bioinformatics and will also pursue joint funding through a Horizon Europe grant application.

Summary of collaborative projects formed in the workshop:

Project Focus	Project Title	Core Question	Models/Technologies	Funding
Technology	From Molecule to Modification	How to develop a standardized, benchmarked system for detecting any RNA modification across platforms?	Synthetic standards, Illumina, ONT, LC/MS, Computational Pipelines	Horizon Europe (Consortium of European groups)
Mapping & Function	The Functional RNome Atlas	To create a complete dynamic and functional map of the modified transcriptome across time and biological scales.	Cell lines (iPSCs, fibroblasts, B-cells), Mouse models, Human tissues	
Disease (Immunology)	RNA Epitranscriptomic Landscape in Immune Regulation (ReLi)	How do RNA modifications shape immunological responses in cancer and autoimmunity?	Glioblastoma & Sjögren's tissuoids/organoids, ONT, Spatial Transcriptomics, Flow Cytometry	

Take home message

A consistent message across sessions was that no single technology or lab can capture the full scope of RNA modifications. Instead, success will require benchmarking across platforms, standardised reference samples, and interoperable computational pipelines. Proposals such as the “RNome in a bottle” and the use of common RNA stocks reflect a strong community drive toward shared standards and reproducibility. Biological interpretation of modifications remains a major challenge. Discussions highlighted the complexity of modification patterns, the limitations of current detection tools, and the need for orthogonal validation. Functional mapping efforts, including tissue- and cell-type specific atlases, were seen as essential next steps, alongside improved annotation of writer, reader, and eraser enzymes. Sessions proposed concrete solutions, such as collaborative checklists and regular cross-functional meetings. The workshop concluded with the formation of three flagship collaborative projects focusing on technology benchmarking, functional mapping, and disease applications, demonstrating strong momentum for action. Looking ahead to 2030, participants envision a research environment where modifications are mapped with single-molecule precision, linked to biological outcomes, and translated into clinical insights. Realising this vision will require immediate progress on infrastructure, benchmarking, and funding. But the tone of the meeting was optimistic and unified: the Human RNome Project is no longer just an idea, it is a growing, global movement poised to unlock a new dimension of RNA biology.

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