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Progress toward Implementing Multiomic Approaches in Atherosclerotic Cardiovascular Disease: Update from the 4th AtheroNET Meeting in Sarajevo (Bosnia and Herzegovina)

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ABSTRACT

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The COST Action CA21153 "Network for Implementing Multiomic Approaches in Atherosclerotic Cardiovascular Disease Prevention and Research" (AtheroNET; https://atheronet.eu) was launched in October 2022 with the mission to accelerate the application of multiomics in atherosclerosis research and to foster collaboration among experts from diverse disciplines. Born from the pressing need to advance atherosclerosis management and overcome existing challenges, AtheroNET creates a collaborative arena where innovation thrives through dialogue. The initiative was spearheaded by Prof. Miron Sopić (Faculty of Pharmacy, University of Belgrade), the primary proposer of the Action. The Action is led by Chair Prof. Paolo Magni (Università degli Studi di Milano) and Vice-Chair Prof. Yvan Devaux (Luxembourg Institute of Health), with strategic support from a dedicated leadership team:

- **Grant Holder Scientific Representative:** Dr. Ines Potočnjak.
- **Science Communication Coordinator:** Prof. Georgios Karagigas.
- **Grant Awarding Coordinator:** Dr. Susana Novella.
- **WG1** - Pathophysiological mechanisms: applying multiomics to uncover novel pathogenic players and processes; Leader: Prof. Dimitris Kardassis.
- **WG2** - Personalized clinical models: translating omics insights into improved management of ASCVD; Leader: Prof. Alberico Catapano.
- **WG3** - Standardization and harmonization: developing SOPs and guidelines to enhance reproducibility across omics research; Leader: Dr. Marie Mardal.
- **WG4** - Data integration and ML/AI: optimizing algorithms for integrating complex multiomic datasets; Leader: Dr. Aleksandra Gruca.
- **WG5** - Dissemination and communication: sharing advances with scientists, clinicians, patients, and the public; Leader: Prof. Georgios Karagigas.

Since its inception, AtheroNET has grown to 475 members from across Europe, embracing COST's core values of inclusiveness and excellence across geography, gender, and career stage. A significant proportion of members come from Inclusive Target Countries (n=282), with strong representation of women (n=277) and early-career researchers (n=223).

The 4th MC/WG Meeting – Sarajevo, Bosnia and Herzegovina

On 14-16 May 2025, AtheroNET COST Action held its fourth in-person Management Committee and Working Group meeting in Sarajevo

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(Bosnia and Herzegovina), hosted by Kanita Karaduzović-Hadžiabdić at the International University of Sarajevo. The event gathered over 80 participants, including 44 MC members from across the EU (**Figure 1**). Hybrid participation ensured broad access, and 16 young researchers and investigators (YRIs) were selected to showcase their work through oral and poster presentations, four of which are published along with this report.

The scientific programme of the 4th AtheroNET MC/WG meeting was crafted to reflect the breadth and depth of multiomics research in atherosclerosis, guiding participants on a journey from fundamental biological mechanisms to clinical translation. Presentations and discussions explored how molecular insights into inflammation, vascular biology, metabolic regulation, and tissue-specific changes can be uncovered and integrated using advanced omic technologies. Throughout the meeting, emphasis was placed on linking these discoveries to tangible improvements in patient care – from refining diagnostic markers and identifying novel therapeutic targets, to building predictive models that can guide personalized prevention strategies. A key feature of the programme was its focus on integration of disciplines, datasets, and perspectives. Rather than viewing biology, clinical science, and computational methods as separate domains, the meeting highlighted how their convergence is essential to unlocking the full potential of multiomics. Discussions repeatedly returned to the importance of harmonizing experimental approaches, ensuring reproducibility, and making effective use of artificial intelligence for data interpretation. This cross-cutting theme fostered a sense that the field is moving beyond isolated discoveries toward cohesive frameworks that can be adopted broadly and applied in real-world clinical settings.

A highlight of the programme was the keynote lecture delivered by Prof. Børge G. Nordestgaard, current President of the European Atherosclerosis Society (EAS). His presentation offered a comprehensive and thought-provoking perspective on residual lipid risk in atherosclerotic cardiovascular disease, stressing the critical importance of early and effective lipid-lowering strategies while pointing toward emerging therapeutic opportunities targeting triglyceride-rich remnant particles. The lecture not only synthesized the latest evidence but also set these insights in the context of global prevention strategies. Importantly, it reflected the close alignment between AtheroNET and the EAS in their shared mission to improve cardiovascular outcomes through research excellence, knowledge dissemination, and fostering the next generation of experts.

Roundtable sessions are a central feature of AtheroNET meetings, specifically designed to foster collaborative, open discussions that drive progress toward the Action's set deliverables. They provide a platform for targeted, multidisciplinary dialogue on topics that require integration of perspectives across basic, clinical, and computational research. Unlike formal presentations, these discussions encourage open exchange, critical questioning, and the identification of concrete, actionable steps. They also serve as incubators for collaborative projects, enabling participants to align methodologies, share resources, and explore emerging concepts in real time.

WG1 Roundtable – Perivascular Adipose Tissue and the Exposome in Atherosclerosis

This Roundtable was chaired by Dimitris Kardassis, Tijana Mitić, and Nuria Amigo. The discussion, led by Sònia Benítez González and Francesc Jiménez Altayó, explored how perivascular adipose tissue may function as an active modulator of vascular biology, influencing inflammation, vascular tone, and plaque development. This perspective challenges the traditional view of adipose tissue as a passive structural component. The conversation then broadened to the concept of the "exposome" – encompassing factors such as smoking, menopause, air pollution, and vascular ageing – and considered how multiomic approaches and machine learning could be leveraged to disentangle their complex, interrelated effects.

WG2 Roundtable – ApoB-Containing Lipoproteins in CVD: Integrating Omics

Led by Luis Masana and Liv Tybjærg Nordestgaard, this roundtable examined how multiomic strategies can refine our understanding of ApoB-containing lipoproteins in the pathogenesis of cardiovascular disease, also in light of the recent research and clinical interest in circulating lipoprotein (a) measurement and pharmacological management and the opportunity of lipidomics approaches in this area. Discussion was centered on how to uncover mechanisms underlying residual cardiovascular risk, with participants weighing the opportunities such integration offers against the methodological and interpretive challenges it poses.

WG3 Roundtable – Reproducibility in microRNA Biomarker Research

Chaired by Miron Sopić and David De Gonzalo Calvo, this session addressed the critical challenge of reproducibility in biomarker studies, with microRNA-based diagnostics serving as a focal example. AtheroNET is currently preparing its first large-scale inter-laboratory "ring trial," aimed at standardising pre-analytical, analytical, and post-analytical protocols for circulating microRNA analysis. The roundtable provided an opportunity to examine each step of the workflow in detail, drawing on the diverse experiences of participating laboratories. Discussions focused on identifying sources of variability, aligning

Figure 1 | Participants to 4th AtheroNET Meeting in Sarajevo (Bosnia and Herzegovina).

best practices, and working toward a consensus protocol that will be uniformly applied during the ring trial. This harmonised approach is expected to enhance the reliability, comparability, and translational value of microRNA biomarker research across the network.

WG4 Roundtable – ML/AI Pipelines for Multiomic Integration in ASCVD Prevention

Moderated by Artemis Hatzigeorgiou and Aleksandra Gruca, this roundtable considered the design of machine learning and AI pipelines for integrating multiomic data into personalised prevention models for atherosclerotic cardiovascular disease. Discussions highlighted the need for harmonised data structures, rigorous validation frameworks, and transparent algorithms to ensure clinical interpretability. The exchange exemplified AtheroNET's interdisciplinary ethos, drawing equally from computational sciences and clinical cardiology to chart a path toward implementation.

Recognising that its diverse and multidisciplinary membership offers fertile ground for high-impact collaboration, AtheroNET established a dedicated Grant Application Committee (Eric Biessen, Miron Sopić, Johannes Schmit, David De Gonzalo Calvo, Noemi Rotllan, and David Kreil). The committee's role is to actively monitor upcoming funding calls, identify opportunities aligned with AtheroNET's scientific priorities, and catalyse the formation of competitive EU-level consortia. This proactive approach has already borne fruit, resulting in the submission of two MSCA Doctoral Network proposals, five MSCA Postdoctoral Fellowship applications, one EpiPERMed proposal, and two Pathfinder calls. The Sarajevo meeting provided a valuable platform to advance this strategic agenda. A dedicated roundtable led by Erik Biessen and Miron Sopić brought together senior investigators and early-career researchers to exchange ideas on how to position AtheroNET's expertise within the evolving European funding landscape. Discussions centred on identifying high-priority research themes, mapping potential partnerships across disciplines and countries, and aligning proposals with the thematic priorities of upcoming Horizon Europe calls. Particular attention was given to opportunities in late 2025 and 2026, with the aim of maintaining momentum and ensuring AtheroNET remains at the forefront of multiomics-driven cardiovascular research at the EU level. This session not only strengthened the network's collective readiness to respond to competitive calls but also reinforced the culture of collaborative grant development as a core pillar of the Action's long-term impact.

AtheroNET places a strong emphasis on nurturing the next generation of scientists who will carry forward progress in atherosclerosis research. This commitment is reflected in the significant number of Young Researchers and Innovators (YRIs) involved in the Action (223 members), as well as in a range of initiatives designed to empower them both scientifically and professionally. In collaboration with the MSCA Staff Exchange CardioSCOPE, AtheroNET has organised 15 webinars on diverse and highly relevant topics, providing YRIs with direct access to leading experts in the field. These sessions are intended to transfer cutting-edge knowledge, expose early-career researchers to different perspectives, and inspire new lines of inquiry. Building on this effort, the MSCA SE *CardioSCOPE* project and AtheroNET jointly organised a 2024 training school, *"Omics for Precision Medicine in ASCVD"*, held in Heraklion, Crete, and will co-organise another in September 2025 in Milan, *"Shaping Scientific Careers in Cardiovascular Research: Within and Beyond Academia"*. Complementing these training initiatives, and inspired by the success of similar activities in the COST Action CardioRNA, AtheroNET has established its own Journal Club – a monthly event led by Melody Chemaly, Ignazio Fernando Hall, and Christina Pagiatakis. The Journal Club invites first or lead authors of high-impact publications in atherosclerosis to present their work, explain the scientific concepts and ideas underpinning it, and share insights into the peer review and revision process. This initiative not only promotes scientific literacy but also offers a rare behind-the-scenes view of academic publishing for emerging researchers. To further support hands-on research experience and international collaboration, AtheroNET funded 18 Short-Term Scientific Missions (STSMs) and 5 ITC congress grants to YRIs in 2024-2025. These mobility grants enabled YRIs to work in leading laboratories across Europe, strengthening their technical skills, expanding their professional networks, and fostering cross-institutional collaborations. At the Sarajevo meeting, YRIs who had completed STSMs presented their findings in dedicated sessions, complemented by 10 poster presentations from other early-career members. The meeting was concluded with awards for the best presentations, given to Melody Chemaly (Karolinska Institute), Veronika Boichenko (University of Verona), and Mannekomba Roxane Diagbouga (University of Geneva), who will be invited to return to the next AtheroNET meeting to update the network on their continuing research progress.

Beyond its rich scientific content, the 4th AtheroNET meeting in Sarajevo was also a celebration of the social bonds and friendships that make this network so vibrant. AtheroNET gatherings are not only about exchanging data and discussing methodologies – they are also an opportunity to reconnect with old colleagues, welcome new members into the community, share personal experiences, and forge lasting international friendships. This time, participants enjoyed a memorable guided tour of Sarajevo, a city poised at the crossroads of East and West, where Ottoman, Austro-Hungarian, and modern influences blend seamlessly. Its multicultural heritage and unique character seemed to mirror the very essence of AtheroNET – a network built on diversity, inclusiveness, and the blending of perspectives for a common goal. The closing dinner gathered all participants into a joyful celebration, where conversation turned to laughter and to music and dance beneath the shared rhythm of science and friendship.

Looking Ahead

As AtheroNET enters its final year, the focus sharpens on delivering the Action's ambitious objectives. The rapid evolution of single-cell and spatial omics, coupled with the transformative potential of AI, positions the network to break new ground in atherosclerosis research. The coming months will be dedicated to completing a series of concrete milestones that will define the Action's legacy.

One of the flagship outputs, the Cardio2Share database, is in the process of being launched and populated. This resource will serve as a centralised repository for multiomic and clinical data, facilitating data sharing, integration, and re-use across the network and beyond. In parallel, guidelines for the preparation of blood-based samples for multiomic analysis are being finalised, aiming to standardise protocols and ensure reproducibility across laboratories. The miRNA ring trial – the first large-scale inter-laboratory effort within AtheroNET – is being implemented to harmonise pre-analytical, analytical, and post-analytical steps in biomarker research.

Alongside these technical and infrastructural deliverables, AtheroNET is actively catalysing the formation of new research consortia around targeted scientific questions. These initiatives are designed to probe the intricate mechanisms underlying atherosclerosis and to develop innovative tools for personalised prevention and treatment. By consolidating know-how, fostering collaboration, and addressing unmet needs, AtheroNET is shaping the future of multiomics in cardiovascular science – advancing from current best practice toward bold, new horizons.