# Emerging Therapeutic Frontiers in Cardiology: What Does the Future Hold?

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AN ENLIGHTENING session, entitled 'Emerging therapeutic frontiers in cardiology: what does the future hold?', delivered at the European Society of Cardiology (ESC) 2025 Congress, held in Madrid, Spain, brought together leading specialists to explore transformative advances in cardiovascular health and future directions in patient care.

## MULTI-OMICS IN CARDIOVASCULAR HEALTH

Konstantinos Stellos, Heidelberg University, Germany, opened the session by highlighting the significant potential of multi-omic approaches in cardiovascular research. He emphasised that large-scale, high-resolution data are essential for personalised management strategies, given that: "Cardiovascular diseases, or circulatory diseases, are not diseases that are caused just by one risk factor or by one gene." Many ageing-related cardiovascular diseases are shaped by primary, antagonistic, and integrative hallmarks of ageing, including loss of proteostasis, cellular senescence, and gut dysbiosis.[1] Stellos described the heterogeneity of cardiovascular health, and how it affects diverse cell types and organs as well as cardiac cells.

Multi-omics allows clinicians and researchers to unravel this complexity across transcriptomics, proteomics, radiomics, and microbiomics. Each contribute their own unique insights into diseases at a molecular and cellular level, supporting the discovery of novel cell types, biomarkers, and pathways.

Using atherosclerosis as an example, Stellos illustrated how single-cell multi-omics has allowed precise subtyping of contributing immune and vascular cells. As described, the transformation of cardiovascular health through multi-omics-based approaches can be categorised into four sections: therapeutic target identification, drug discovery, biomarker discovery, and drug mechanisms and repurposing.

Stellos cited several recently published success stories, including a study in which PCSK9 was shown as a prime example of a molecular target discovered through genetic analysis, leading to the development of PCSK9 inhibitors that substantially reduce cardiovascular risk.[2] Similarly, genomic variants of lipoprotein(a) have reinforced its value as a therapeutic target due to its strong association with adverse cardiovascular outcomes.[3] A third example highlighted angiopoietin-like 3 inhibition, which reduces triglycerides, low-density lipoprotein cholesterol, and apolipoprotein B.[4]

Leading on from this, Stellos outlined the role of multi-omics in biomarker discovery. These biomarkers, together with large longitudinal data collection, can subsequently be measured for sophisticated patient stratification and risk assessment. In 2024, a study based on this concept identified multiple genes associated with atherosclerotic ischaemic cardiovascular disease,[5,6] and Stellos spotlighted IL-6 as one of the most promising targets from this list.

Beyond this, he explained the role of multi-omics in contributing to the understanding of drug mechanisms, efficacy, safety, and subsequently their repurposing for cardiovascular health. He noted that glucagon-like peptide-1 receptor agonists, sodium-glucose co-transporter 2 (SGLT2) inhibitors, and colchicine are now more extensively known and understood from a combination of transcriptomics, metabolomics, and proteomics approaches.

However, Stellos also noted the challenges associated with multi-omics and their assessment. He cautioned that in order to accurately assess data, knowledge of the collection methods, technologies applied, depth of sequencing, and how missing values are approached is required.[7]

He concluded by emphasising how spatiotemporal multi-omics can transform cardiovascular medicine through enabling earlier diagnosis, sharper risk stratification, and more targeted therapies.[8]

## METABOLIC REPROGRAMMING FOR CARDIOVASCULAR HEALTH

Continuing the session, Yibin Wang, Duke University, Durham, North Carolina, USA, provided insight into the origins and biological significance of metabolism. He related metabolism to ageing, before diving into more detail regarding the role of branched chain amino acids in life span extension. Valine, leucine, and isoleucine are all essential, branched-chain amino acids (BCAA) that play key roles in metabolic homeostasis. Wang explained their contributions to insulin resistance, cardiovascular disease, and obesity, and described how mitochondrial catabolism of BCAAs, mediated by specific enzymes, is closely tied to reactive oxygen species generation and protein nitrosylation. Multi-omics approaches have proven BCAA catabolic defects to be a key driver of a failing heart, which, Wang explained, can be exploited as a therapeutic target for cardiometabolic disease.[9]

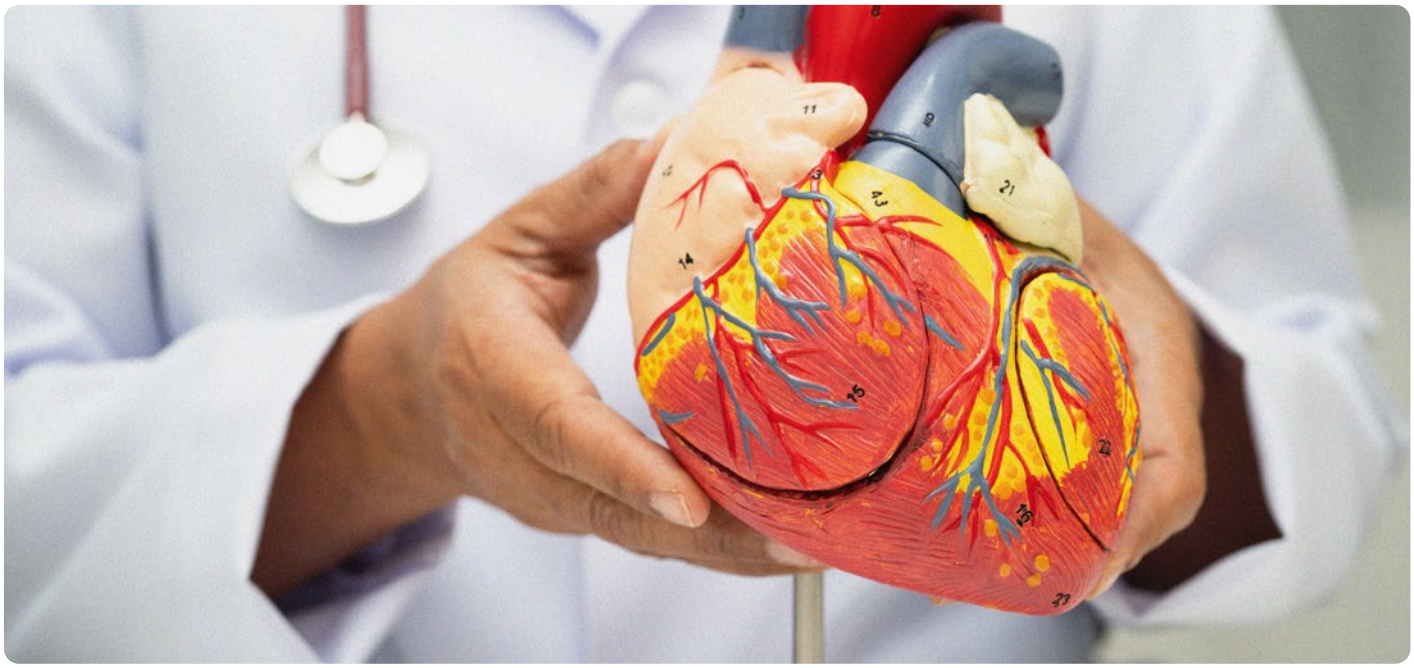
> **SGLT inhibitors have consistent benefits regardless of the ejection fraction, regardless of NT-proBNP, regardless of heart failure duration or characteristics**

## SODIUM-GLUCOSE CO-TRANSPORTER INHIBITORS FOR CARDIOVASCULAR HEALTH

Following on from Wang, Subodh Verma, University of Toronto, Canada, introduced the topic of SGLT inhibitors, whose evidence for use in heart failure has rapidly transformed and multiplied.[10] He highlighted that "SGLT inhibitors have consistent benefits regardless of the ejection fraction, regardless of NT-proBNP, regardless of heart failure duration or characteristics." These benefits include improved quality of life, renal efficacy and safety, and rapid onset of said benefits. Despite differences in hypertrophic responses, SGLT inhibitors are highly versatile and largely agnostic to the aetiology of heart failure.[11]

Verma then described his predictions for developments in this space, highlighting erythropoietin and iron metabolism as one of the most significant. He noted that the SGLT class of inhibitor has a diuretic sparing benefit, demonstrated by the EMPEROR and EMPA-RESPONSE trials.[12,13] Speaking to physiologists in particular, Verma noted that the EMPULSE trial further demonstrated that empagliflozin reduces pulmonary artery pressure.[14]

Ventricular remodelling was presented as another promising area in the future of cardiovascular health. The EMPA-HEART and EMPA-HEART2 trials have shown SGLT2 inhibitors to reduce diastolic tension and passive myofilament stiffness, as well as increase erythropoietin production, a critical component of oxygen delivery.[15,16,17] Erythropoietin as a driver of cardiac outcome has been further supported by the ERPEROR programme. With this in mind, Verma reiterated the value of SGLT inhibitors as a therapy that improves myocardial performance regardless of heart failure aetiology.[18]



Moving on to discuss cardiac energetics and challenging the assumption of ketone oxidation being a driver of improved myocardial energy supply, Verma noted that the origins of additional ATP following SGLT inhibition were actually due to glucose oxidation, not ketone oxidation.[19] Beyond the immediate effects on the heart, he emphasised the profound bidirectional relationship between cardiac failure, haemodynamics, neurohormonal mechanisms, and inflammation.[20]

## INFLAMMATION AND IMMUNITY IN CARDIOVASCULAR DISEASE

The session concluded with Peter Libby, Harvard Medical School, Boston, Massachusetts, USA, who provided an overview of inflammation and immunity in cardiovascular disease, a rapidly expanding area of the field. He explored targeted anti-inflammatory therapy for cardiovascular disease, noting the CANTOS study, which demonstrated that blocking IL-1β, a pro-inflammatory cytokine, significantly reduces mortality.[21] Interestingly, a decrease in severity of arthritis, osteoarthritis, and gout was also observed. However, there was an increased susceptibility to infection, given the role of IL-1β in immune defence.[22]

Colchicine, a well-known anti-inflammatory drug, also showed cardiovascular benefits in the COLCOT and LoDoCo2 trials, as did anti-IL-6 in the RESCUE study.[23] Libby also referenced other potential anti-inflammatory therapies, including regulatory cytokine therapy, depleting antibodies, anti-cytokine neutralising antibodies, antibodies against oxidised low-density lipoprotein, and cytoskeleton targeting therapies.[24]

He then moved on to discuss the significance of the inflammasome complex, which activates IL-1β and subsequently induces IL-1 and IL-6. This in turn activates the hepatic acute phase and thrombosis formation.[25] Libby argued that IL-6, given its downstream position from IL-1β, may be a more favourable target in order to preserve innate defence and mitigate the risks associated with infection. The RESCUE trial supported this approach, displaying a significant reduction in C-reactive protein following inhibition of IL-6.[26]

Incretin mimetics were noted as a promising approach, having shown impressive cardiovascular benefits. The SELECT trial presented a similar CRP drop following semaglutide treatment.[27]

Libby concluded his session by describing the current position of inflammation in atherosclerosis research as a crucial inflection point providing a surge in research momentum across the field.

## CONCLUSION

The session highlighted a field undergoing rapid evolution on many levels. From the deep molecular insights provided by multi-omics approaches and the metabolic and haemodynamic benefits of SGLT inhibitors, to the promise of targeted anti-inflammatory therapies.

Each presentation highlighted pathways that are reshaping cardiovascular care. Together, these advances point toward a future in which earlier detection, precision-guided treatment, and integrated cardiometabolic and immunologic strategies become central to improving patient outcomes.

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