Medical thought leaders in critical care aim to advance precision medicine using biomarker-based approaches

- *Innovative biomarkers open new avenues for precision medicine approaches in treating acute and critical diseases that need differentiation of the underlying pathophysiology.*
- *Physicians from Europe, Canada, and the USA explore the role of* biomarkers in *the leap from a "one-fits-all"-treatment to a personalized approach based on the patient's characteristics.*
- *International medical leaders discuss ways to successfully implement biomarkers penKid, bio-ADM and DPP3 from research into routine clinical practice.*

Hennigsdorf, Germany, August 8, 2022 – The diagnostics company SphingoTec GmbH (SphingoTec), announces that, during the 4th Scientific Symposium held near Potsdam, Germany, international medical experts discussed the latest developments in diagnostic and therapeutic innovations for advancing precision medicine in critically ill patients. The approach encompasses organ-specific biomarkers working hand in hand with drug candidates and existing therapies to improve the management of diseases such as sepsis and septic shock, acute kidney injury, COVID-19, and cardiogenic shock. The successful transition of the biomarkers from research to clinical routine is an important step that was addressed by current routine users.

Biomarkers from research to clinical practice

Acute kidney injury (AKI) affects 1 in 3 ICU patients. Since the therapeutical options are limited, the focus lies in managing the symptoms and avoiding the progression of AKI. However, current diagnostics are too late and insensitive, thus resulting in a limited intervention window.

Prof. Peter Pickkers, Head of research in Intensive Care Medicine at Radboud University Nijmegen Medical Centre, explained "In AKI we need to bring the diagnostic clock before the current clinical clock to avoid further organ dysfunction. Proenkephalin A 119 - 159 (penKid) is a kidney function biomarker with more swift kinetics that strongly correlates with the actual glomerular filtration rate (GFR). It allows to detect a change in kidney function more than 24 hours earlier compared to the current diagnostic standard creatinine. We have confirmed these findings by developing a formula for estimating the GFR using penKid. After measuring penKid against complex and invasive reference diagnostics and comparing it to existing formulas for kidney function, we have seen a superior performance of the new penKid model."

Notably, the biomarker penKid shows good kinetics in both adults and children (1,3). It is earlier than the current standard of care, and its property of not being influenced by muscle mass, inflammation and common comorbidities allows for monitoring the patient's condition, especially in critical care (2, 3). Scientists and routine users of penKid highlighted the potential to predict AKI development and recovery, as well as the need for renal replacement therapy (RRT) (3), which are unique features for a kidney biomarker (4, 5).

Prof. Gernot Marx, Clinic Director of the University Hospital RWTH Aachen, comments: "We have made the first steps in translating scientific research into clinical practice. Measuring penKid in the morning routine required a change of our procedure and the alignment of all teams. Once established, we have

seen immediate benefits in our daily practice that range from better risk stratification to early identification of worsening and improvement of renal function. The potential of this biomarker has not yet been fully exploited, therefore we are currently focused on better understanding the benefits for patients under RRT."

Precision medicine relies on biomarkers for a targeted approach

Not only diagnosing but also treating patients correctly can be a major challenge, especially if the underlying mechanisms of a disease vary and require different therapies. This is the case, for example, with sepsis, a disease that encompasses a very heterogeneous group of patients, making the discovery of new therapies very challenging. The biomarkers bioactive adrenomedullin (bio-ADM) and dipeptidyl peptidase 3 (DPP3) distinguish between two independent etiologies of septic shock (6). This facilitates the identification of separate homogenous groups of shock patients with the respective pathological mechanisms.

Prof. Alexandre Mebazaa, Head of the Department of Anesthesia and Critical Care Medicine at Lariboisière, Paris stated "The biomarkers bio-ADM and DPP3 are biologically active. This means they can be both, biomarkers that point at different pathophysiologies of sepsis, but also biotargets for new drug candidates that modulate their activity, allowing specific treatment of respective disease mechanisms."

Bio-ADM identifies patients with endothelial dysfunction causing vascular leakage, which escalates into shock and organ dysfunction. The medical experts discussed the latest findings on Adrecizumab, a new promising clinical late-stage drug candidate developed by Adrenomed AG, that targets endothelial barrier dysfunction (7, 8).

A separate disease mechanism, leading to hemodynamic instability and shock in sepsis, is the depletion of angiotensin II. DPP3, a biomarker that causes this depletion has been proposed to identify patients who may not be able to develop a positive treatment effect due to the different pathophysiology, thus excluding them from the respective clinical trials. Apart from the use of DPP3 as an enrichment tool for clinical trials, the modulation of DPP3 activity by the antibody Procizumab, a new drug candidate developed by 4TEEN4 Pharmaceuticals, has been discussed (9). Beyond sepsis and septic shock, the identified pathophysiologies could be of relevance in other distinct major mortality drivers such as COVID-19 (10) and cardiogenic shock (11).

Dr. Andreas Bergmann, the founder of the three companies SphingoTec, Adrenomed, and 4TEEN4, summarizes: "During the symposium, we have shared the same vision with prestigious representatives of the critical care community: bringing personalized medicine in critical care to the same level the colleagues in oncology have succeeded. At the core of this endeavor are biomarkers that guide clinical decision making and support the development of new therapies. Now SphingoTec's biomarkers are well positioned for the adoption in clinical routine, laying a strong basis for "precision medicine"."

References:

1. Hartman et al, Proenkephalin as a New Biomarker for Pediatric Acute Kidney Injury – Reference Values and Performance in Children Under One Year of Age, Clin Chem Lab Med, 2020; doi: 10.1515/cclm-2020-0381.
2. Kim et al. Proenkephalin Predicts Organ Failure, Renal Replacement Therapy, and Mortality in Patients with Sepsis. Ann Lab Med. 2020;40(6):466-73
3. Caironi P, Latini R, Struck J, Hartmann O, Bergmann A, Bellato V, Ferraris S, Tognoni G, Pesenti A, Gattinoni L, Masson S; ALBIOS Study Investigators. Circulating Proenkephalin, Acute Kidney Injury, and Its Improvement in Patients with Severe Sepsis or Shock. Clin Chem. 2018 Sep;64(9):1361-1369.
4. Khorashadi M, Beunders R, Pickkers P, Legrand M: Proenkephalin: A New Biomarker for Glomerular Filtration Rate and Acute Kidney Injury. Nephron 2020;144:655-661. Doi: 10.1159/000509352
5. Hollinger et al, Proenkephalin A 119-159 (Penkid) Is an Early Biomarker of Septic Acute Kidney Injury: The Kidney in Sepsis and Septic Shock (Kid-SSS) Study, Kidney Int Rep, 2018; doi: 10.1016/j.ekir.2018.08.006
6. van Lier (2020), Promotion of vascular integrity in sepsis through modulation of bioactive adrenomedullin and dipeptidyl peptidase 3, J. Intern. Med., DOI: doi.org/10.1111/joim.13220
7. Laterre PF, et al. Safety and tolerability of non-neutralizing adrenomedullin antibody adrecizumab (HAM8101) in septic shock patients: the AdrenOSS-2 phase 2a biomarker-guided trial. Intensive Care Med. 2021 Nov;47(11):1284-1294. Doi: 10.1007/s00134-021-06537-5.
8. Geven et al, Effects of the Humanized Anti-Adrenomedullin Antibody Adrecizumab (HAM8101) on Vascular Barrier Function and Survival in Rodent Models of Systemic Inflammation and Sepsis. Shock. 2018 Dec;50(6):648-654. Doi: 10.1097/SHK.0000000000001102.
9. Deniau et al, Circulating dipeptidyl peptidase 3 is a myocardial depressant factor: dipeptidyl peptidase 3 inhibition rapidly and sustainably improves haemodynamics. Eur J Heart Fail, 2020; 22: 290-299. Doi: 10.1002/ejhf.1601
10. Clinicaltrials.gov/ct2/show/NCT05156671
11. Takagi K, Blet A, Levy B, Deniau B, Azibani F, Feliot E, Bergmann A, Santos K, Hartmann O, Gayat E, Mebazaa A, Kimmoun A. Circulating dipeptidyl peptidase 3 and alteration in haemodynamics in cardiogenic shock: results from the OptimaCC trial. Eur J Heart Fail. 2020 Feb;22(2):279-286.

About SphingoTec

SphingoTec GmbH ("SphingoTec"; Hennigsdorf near Berlin, Germany) develops and markets innovative in vitro diagnostic (IVD) tests for novel and proprietary biomarkers for the diagnosis, prediction, and monitoring of critical medical conditions. SphingoTec's proprietary biomarker portfolio includes bioactive Adrenomedullin (bio-ADM), a biomarker for real-time assessment of endothelial function in conditions like sepsis, and Proenkephalin (penKid), a biomarker for real-time assessment of kidney function. Dipeptidyl Peptidase 3 (DPP3) is a biomarker for cardiac depression, in-licensed from 4TEEN4 Pharmaceuticals GmbH (www.4teen4.de). IVD tests for SphingoTec's biomarkers are made available as sphingotest® microtiter plate tests as well as point-of-care tests on the Nexus IB10 immunoassay platform by SphingoTec's subsidiary Nexus Dx Inc. (San Diego, CA, USA). The Nexus IB10 portfolio is complemented by established and commonly used biomarker tests for acute and critical care such as PCT, Troponin, NT-proBNP, D-Dimer, TSH and others.

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