DPP3 predicts organ failure and in-hospital mortality in post-operative patients

- *Dipeptidyl Peptidase 3 (DPP3) has been shown to be a biomarker for refractory shock and a cardiac depression factor*
- *DPP3 is released upon tissue death during major surgical procedures, such as open and endovascular thoracoabdominal aortic (TAAA) surgery*
- *New findings indicate that elevated post-operative DPP3 levels show remarkable predictive accuracy for the development of organ failure and in-hospital after TAAA surgery*
- *Monitoring DPP3 blood levels allows for early risk stratification of patients after surgery and is a desirable tool to guide adequate treatment initiation*

Hennigsdorf/ Berlin, Germany, March 25, 2021 - 4TEEN4 Pharmaceuticals GmbH ("4TEEN4") announced that DPP3 can support risk stratification of postoperative patients and is a strong predictor of organ failure in those patients (1). Patients undergoing invasive surgical procedures such as open or endovascular TAAA surgery often develop postoperative complications that lead to organ dysfunction. DPP3 is a biomarker for hemodynamic instability and endo-organ hypoperfusion which has been proven to timely predict the risk of short-term organ dysfunction in various clinical settings (3,4,5).

The research team lead by Dr. Alexander Gombert has demonstrated that elevated blood levels of DPP3 measured postoperatively are strong predictors of organ failure in patients undergoing open or endovascular TAAA repair. An invasive and major surgical procedure, TAAA repair often leads to severe complications in the first 48h after surgery (2). This raises the need to identify biomarkers that can support decision making in this time window in order to initiate early treatment strategies. The current data shows that DPP3 blood levels change dynamically according to patient status, leading to better risk stratification of postoperative patients within 12 and 48h after the surgical intervention.

DPP3 is an enzyme at the core of a newly discovered disease mechanism responsible for hemodynamic instability and short-term organ failure. Although intracellular DPP3 is involved in normal cellular processes, upon massive cell death, DPP3 is released into the bloodstream where it inactivates Angiotensin II, a hormone important for hemodynamic balance and heart function. This inactivation leads to hemodynamic instability which ultimately results in short-term organ dysfunction in conditions such as cardiogenic shock (3,4), burns (5) and major surgeries (1). Clinical data has shown that rapidly decreasing blood levels of DPP3 are strong predictors of improved outcomes. (3,4,5,6) Furthermore, DPP3-blocking antibody Procizumab shows promising results in preclinical models.

Dr. Andreas Bergmann, founder and CEO of 4TEEN4 mentioned: "The effects of DPP3 release in the bloodstream poses, in many medical conditions, significant challenges and it's still a blind spot in the clinical practice. The current data confirms once again the role DPP3 plays in early identifying the risk for organ failure, paving the way for future precision treatment strategies in major cardiovascular surgical procedures."

References:

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(2) Gombert et al (2019). Outcomes After One Stage Versus Two Stage Open Repair of Type II Thoraco-abdominal Aortic Aneurysms. Eur J Vasc Endovasc Surg. DOI : https://doi.org/10.1016/j.jvs.2019.03.014

(3) Deniau et al (2019) Circulating dipeptidyl peptidase 3 is a myocardial depressant factor: dipeptidyl peptidase 3 inhibition rapidly and sustainably improves haemodynamics. Eur J Heart Fail., DOI: 10.1002/ejhf.1601

(4) Takagi et al (2019) Circulating dipeptidyl peptidase 3 and alteration in haemodynamics in cardiogenic shock: results from the OptimaCC trial. Eur J Heart Fail. 2020;22:279-86.

(5) Dépret (2020) Circulating dipeptidyl peptidase-3 at admission is associated with circulatory failure, acute kidney injury and death in severely ill burn patients, Critical Care, DOI: 10.1186/s13054-020-02888-5

(6) Magliocca A, Omland T, Latini R. Dipeptidyl peptidase 3, a biomarker in cardiogenic shock and hopefully much more. Eur J Heart Fail. 2020;22:300-2.

About 4TEEN4
At 4TEEN4 we are dedicated to improve critically ill patient lives who suffer from hemodynamic instability, end-organ hypoperfusion and multiple organ failure with our first-in-class humanized monoclonal antibody" Procizumab" targeting human dipeptidyl peptidase 3 (DPP3).
4TEEN4 licensed its novel biomarker DPP3 for diagnostic purposes in critical care conditions.
4TEEN4 Pharmaceuticals GmbH ("4TEEN4") was established in 2013 in Hennigsdorf near Berlin, Germany, by Dr. Andreas Bergmann, CEO of 4TEEN4, as part of his Medicine4Future Initiative.
For further information please visit www.4teen4.de

About DPP3
Dipeptidyl peptidase 3 an active enzyme which, when released into the blood, inactivates angiotensin II, and Enkephalin, hormones that are important for the hemodynamic balance as well as cardiac and renal function. This inactivation leads to hemodynamic instability and consequently to cardiac depression. The DPP3 release is a newly identified disease mechanism explaining short-term organ failure in critically ill patients. Early identification of DPP3 release may allow better patient stratification and earlier therapy escalation to improve outcomes.

About Procizumab
Procizumab is a humanized monoclonal antibody in preclinical development specifically binding circulating Dipeptidyl Peptidase 3 (DPP3). It will be a first-in-class drug that targets and modulates DPP3 as an essential regulator of cardiovascular function. Procizumab has an innovative mode of action, relevant in acute diseases.

Massive cell death and release of DPP3 into the bloodstream lead to degradation of its substrates, including angiotensin II and enkephalin, that are responsible for cardiac and renal function regulation. Procizumab inhibits the activity of DPP3, thereby reducing bioactive peptide degradation, stabilizing hemodynamics, cardiovascular function and potentially increasing survival chances e.g., in cardiogenic and septic shock. Preclinical studies of Procizumab in models of cardiovascular failure showed instant efficacy.

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