



TFAM-TFB2M INTERACTION ASSAY FOR ASSESSMENT OF ORGAN DYSFUNCTION IN SEPSIS

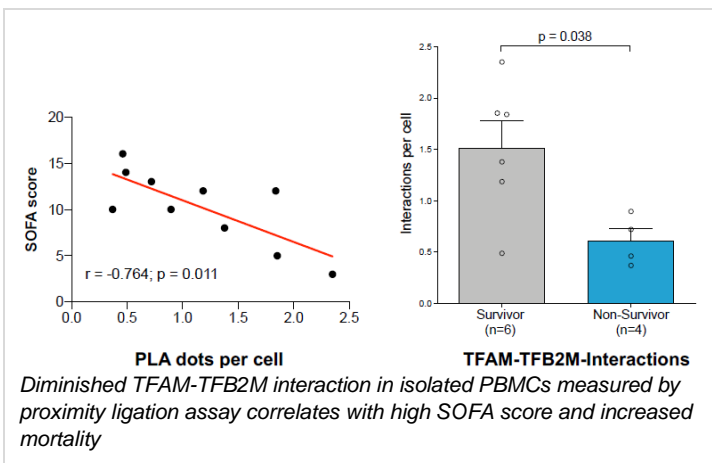
TFAM, TFB2M, proximity ligation assay, PLA, proxHCR, sepsis, mitochondrial dysfunction, biomarker

INVENTION NOVELTY

Scientists at University Hospitals of the Ruhr-University of Bochum (UK RUB) developed an innovative assay to evaluate the state of mitochondrial dysfunction in sepsis patients. Although the link between mitochondrial dysfunction and organ dysfunction in life-threatening conditions as sepsis has been recognized, mitochondrial dysfunction is highly variable and cannot be used as a general predictive tool for organ dysfunction progression. While it is known that sepsis patients show elevated cellular expression of mitochondrial expression factor A (TFAM), TFAM levels do not directly correlate with mitochondrial functionality. The novel assay considers the current finding that although extramitochondrial expression of TFAM in sepsis patients is clearly elevated, intramitochondrial TFAM levels are strongly diminished. Consistently, the level of intramitochondrial TFAM-TF2B interaction as measured by proximity ligation assay is indicative of mitochondrial functionality and negatively correlates with the SOFA score.

VALUE PROPOSITION

To date, the diagnosis of organ dysfunction relies on time-consuming *in vivo* measurements such as the SOFA score. However, sepsis or other organ dysfunctions are life-threatening conditions that need to be rapidly diagnosed, preferably by point-of-care devices that can be operated by non-professionals, as well. A fast and reliable biomarker assay for sepsis diagnosis that is indicative of the degree of severity of sepsis will help to improve the currently rather unspecific treatment of sepsis patients.



TECHNOLOGY DESCRIPTION

Mitochondrial interaction of TFAM with mitochondrial transcription factor 2B (TF2B) is measured by Proximity Ligation Assay (PLA) in peripheral blood mononuclear cells (PBMCs) isolated from whole blood. Cells are consecutively incubated with primary antibodies against TFAM and TF2B, proximity probes, and splint and backbone oligonucleotides. Ligated oligonucleotides are amplified using rolling circle amplification and visualized with a detection oligonucleotide to quantify PLA dots with single cell resolution in a Cell Profiler pipeline. Low dot number correlates with high SOFA score and increased mortality.

COMMERCIAL OPPORTUNITY

The technology is available for licensing or further collaborative development.

DEVELOPMENT STATUS

Clinical validation.

PATENT SITUATION

PCT application PCT/EP2021/082385 with priority of 2020 is pending.

FURTHER READING

Rahmel et al. (2020) Mitochondrial dysfunction in sepsis is associated with diminished intramitochondrial TFAM despite its increased cellular expression. *Sci Rep.* 2020 Dec 3;10(1):21029. doi: 10.1038/s41598-020-78195-4.

