Next generation sepsis diagnosis

Sprawozdania

Informacje na temat projektu

SMARTDIAGNOS

Identyfikator umowy o grant: 687697

Strona internetowa projektu

DOI
10.3030/687697

Projekt został zamknięty

Data podpisania przez KE
9 Grudnia 2015

Data rozpoczęcia
1 Lutego 2016

Data zakończenia
31 Stycznia 2020

Finansowanie w ramach
INDUSTRIAL LEADERSHIP - Leadership in enabling and industrial technologies - Information and Communication Technologies (ICT)

Koszt całkowity
€ 4 797 602,09

Wkład UE
€ 4 027 909,00

Koordynowany przez
DANMARKS TEKNISKE UNIVERSITET
Denmark

Periodic Reporting for period 3 - SMARTDIAGNOS (Next generation sepsis diagnosis)

Okres sprawozdawczy: 2019-02-01 do 2020-01-31

Podsumowanie kontekstu i ogólnych celów projektu

•What is the problem/issue being addressed?
Sepsis is a potentially fatal condition arising when the body’s response to an infection, damages its own tissues and organs. Sepsis is one of the biggest health issues in the EU and worldwide due to its high incidence, mortality, and economic cost. Globally approx. 27 million people experience sepsis

each year, and only around 18 million survive. This means that more people die of sepsis than of heart attack, HIV/ AIDS, lung, breast and prostate cancers. Early diagnosis is crucial, as every hour of delay in appropriate antimicrobial (AM) therapy increases mortality by 5-10%.
Sepsis diagnosis remains one of the greatest challenges in critical care. Current laboratory (LAB) methods for detection of the pathogens causing sepsis, including blood culture and different nucleic acid-based multiplex amplification technologies, are impaired by the significant time-delay of 1-2 days and/or low sensitivity of 30-50%. Hence there is an urgent need to develop new diagnostic tools that can provide more accurate and earlier pathogen detection, so that sepsis patients can be administered with rapid and correct AM treatment.

•What are the overall objectives?
The proposed SMARTDIAGNOS platform will advance sepsis diagnosis by simplifying clinical sample analysis methods and integrating the required numerous steps into streamlined point-of-care (POC) and LAB devices.

Prace wykonane od początku projektu do końca okresu sprawozdawczego oraz najważniejsze dotychczasowe rezultaty

In the first 18 months of the project we have: 1) defined user requirements based on literature; on end-user interviews; expert interviews, and review of existing commercial products; 2) designed and fabricated 3-dimensional structures for concentration of pathogens; 3) designed PCR-probes and microarray probes to detect 7 genera and 45 species of the most relevant sepsis-causing bacteria and 3 genera and 13 species of the most relevant sepsis-causing fungi, respectively, and 6 of the most relevant AM resistant (AMR) genes by SP-PCR; 4) designed and fabricated arrays of SAF microlenses which increases fluorescence sensitivity by 1-2 orders of magnitude; 5) a pilot study resulted in a list of 10 potential miRNAs that could be applied as sepsis biomarkers to stratify between patients having bacterial sepsis and patients having non- infectious SIRS. However these results need to be further validated.

Exploitation and dissemination: 2 patent applications, 2 scientific publications, 12 conference presentations and exhibitions, 1 award, 4 seminars, 2 workshops, 2 newspaper articles, 3 public & health-care articles, 3 press releases, and 2 public events.

In month 19-39 of the project the main focus has been on design and fabrication of prototype system for diagnoses of sepsis in hospital laboratory (LAB) setting as well as design and fabrication of prototype system for diagnoses of sepsis in hospital point-of-care (POC) setting. Both the LAB and the POC prototype system were completed successfully, and both system were demonstrated at the project review meeting in February 2019. A plane for performance evaluation of the two different prototype systems in clinical setting has been completed, and according to this plan, the two systems will be tested in the coming 8 months.
Exploitation and dissemination: 2 patent published, 8 scientific publications, 2 book chapters, 2 articles in trade periodicals, 14 oral conference presentations, 12 poster conference presentations, 2

conference exhibitions, 1 award, 14 seminars and workshops, 4 newspaper articles, 4 television presentation, 1 radio presentation, 3 public & health-care articles, 5 press releases, 10 web news, 2 Youtube, 1 webinar, 2 demo and evaluation, and 2 public events.

Innowacyjność oraz oczekiwany potencjalny wpływ (w tym dotychczasowe znaczenie społeczno-gospodarcze i szersze implikacje społeczne projektu)

Nowadays, routine clinical diagnosis of Sepsis is too slow. Sepsis patients are a very heterogeneous group and it is challenging to differentiate sepsis from non-infectious systemic inflammatory response syndrome (ni-SIRS) that has similar symptoms, but requires a different treatment. Using blood cultures (BC), the current gold standard, it typically takes 14-48 hrs to detect pathogens in the blood and even longer (typically 50-90 hrs) to identify the exact pathogen and their AM susceptibility for an optimal AM therapy. Furthermore, BC has only 30-50% diagnostic sensitivity as positive BC can be found for only approximately 30-50% of sepsis patients.

Several DNA based technologies are commercially available for identifying pathogens in positive BC or directly from whole blood (Table 1), but these methods suffer from either low diagnostic sensitivity, a limited panel of pathogens, test for no or only few AM resistance markers, or they are too laborious and slow to deliver results.

The new SMARTDIAGNOS diagnostic equipment will be orders of magnitude faster: Results from whole blood without the need of time-consuming BC or DNA purification steps. Confirmation of sepsis, pathogen and possible AM resistances in 1-3 hrs will allow immediate, targeted therapy. Furthermore, both common user cases will be implemented: The LAB system will be used at a clinical laboratory setting and the POC system will be at ICUs.

The new SMARTDIAGNOS diagnostic equipment will be more sensitive and more selective: Combining concentration of pathogens from large blood volumes (5-10 ml) and highly sensitive read-out technology (SAF and TDI) will improve the limit of detection (LOD) by 1-3 orders of magnitude and double the diagnostic sensitivity to 95%.

TABLE - see uploaded summary under images

The new SMARTDIAGNOS diagnostic equipment will be more specific: Innovative amplification technologies (direct PCR, nested solid phase PCR, SAF array).

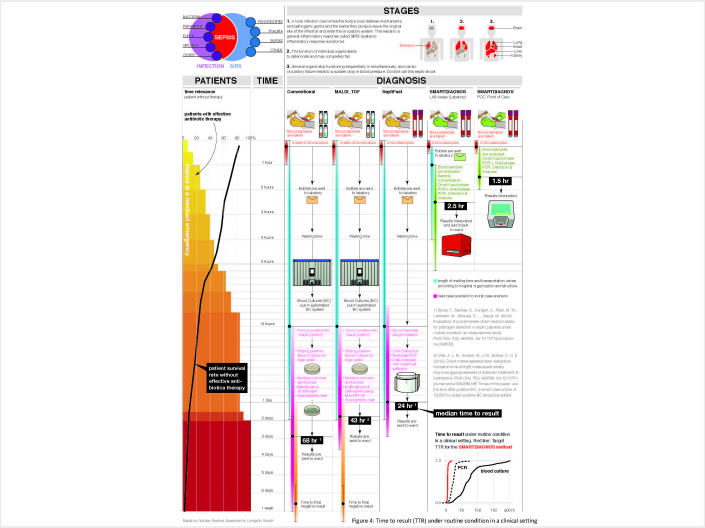
The new SMARTDIAGNOS diagnostic equipment will provide better patient stratification: The inclusion of miRNA biomarker(s) will allow better stratification of patients with sepsis from patients with ni-SIRS.

The new SMARTDIAGNOS diagnostic equipment will allow targeted AM treatment at a much earlier stage: The inclusion of 100 AM resistance genes covering 90-95% of the AMR currently seen in

sepsis will allow targeted AM treatment and adjustment of AM treatment already after 1-3 hrs / 3-5 hrs (POC system / LAB system) compared to 48-90 hrs using gold standard methods.

The expected outcomes of the project are: The SMARTDIAGNOS system will go beyond the state of the art for1) shorter time (1-3 h), 2) higher sensitivity (95%), 3) higher selectivity (99%), 4) multiplexing capability, and automation. Fast and correct detection of sepsis-related pathogens and their AMR genes will improve patient outcome, shorten intensive care stay and thus reduce health care costs.

The two systems will improve clinical decisions and drastically reduce mortality and long-term side effects by providing information for targeted AM therapy within 1-3 hrs. Fast and appropriate AM treatment will decrease morbidity and mortality of sepsis by up to 20% as well as the use of AM. Health costs will on the long term be reduced by 10,000-14,000 € per sepsis case, resulting in a 3-8 B€/year saving for EU health care systems.



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Ostatnia aktualizacja: 6 Listopada 2024

Permalink: https://cordis.europa.eu/project/id/687697/reporting/pl