Rapid and Sensitive Diagnostic for Blood Clot Formation and Cardiovascular Disease

Tech ID: 25052 / UC Case 2011-035-0

BRIEF DESCRIPTION

This advanced, quantitative, real-time, peptide-based diagnostic technology can provide fast, safe, and highly specific diagnosis, monitoring, and imaging of thrombotic events such as pulmonary embolism, deep vein thrombosis, myocardial infarction and stroke and indirect thrombotic diseases such as cancer and diabetes.

UNMET NEED

Current standard of care for patients with chest pain and suspected acute coronary syndromes (ACS) involves considerable observation and extensive clinical reassessment of serum cardiac biomarkers. However, physicians lack a tool that can quickly and accurately stratify risk and rule out ischemic cardiac chest pain, resulting in more expensive and lengthy emergency room stays. Additionally, chronic conditions such as atherosclerosis, vasculitis, diabetes, atrial fibrillation, heart failure, obesity and metabolic syndrome increase the risk of clot formation but patients are not frequently monitored to identify the formation of clots in their early stages. Currently, there are no effective tools to quantify the size, position and rate of blood clot formation inside the body. As a result, poor diagnostic tools can result in irreversible morbidity for patients or unnecessary and expensive hospital stays and therapies. A technology is needed that can provide rapid, accurate, and safe monitoring, prognosis and diagnosis of blood clots.

Value Proposition

Thrombosis (formation of a blood clot inside a blood vessel) is the primary mechanism underlying common cardiovascular diseases such as heart attack, stroke, pulmonary embolism, and deep vein thrombosis. The present diagnostic technology may be used to detect, identify and locate disease development in patients with thrombotic disease, included suspected acute coronary syndrome. Additionally, the technology may be used to monitor patient's response to therapy or to monitor patient events and responses in clinical trials. The technology is so sensitive that it will provide a robust signal-to-noise ratio with low toxicity compared to standard contrast imaging. For example, in a live animal model of injury, the technology has been shown to deposit 10^{12} molecules of the imaging agent into a clot no larger than the head of pin in less than thirty minutes, which illustrates its tremendous sensitivity, speed and dynamic range.

TECHNOLOGY DESCRIPTION

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INVENTORS

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OTHER INFORMATION

KEYWORDS

Cancer, Thrombosis, Myocardical Infarction, Pulmonary Embolism, Stroke, Diagnostics, Imaging, Peptide, Proteolysis

CATEGORIZED AS

- **Biotechnology**
  - Proteomics
- **Imaging**
  - Medical
- **Medical**
  - Diagnostics

RELATED CASES

2011-035-0

The Craik lab at University of California, San Francisco has developed a highly sensitive real-time approach to specifically and accurately detect microscopic blood clots both in vivo and ex vivo. The invention is based on UCSF's restricted interaction peptides (RIP) platform technology of activatable and detectable membrane interacting peptides that, following activation in the presence of certain proteases, can interact with phospholipid bilayers, such as cell membranes. RIPS have a good safety profile and do not affect hepatic or renal functions. These protease-activated peptide probes can be customized to specific targets and cleaved in the presence of specific proteases, such as thrombin.

To develop a RIP probe for binding and imaging of blood clots, the Craik lab designed a peptide whose sequence is composed of Temporin L followed by the cleavage site and extended interaction sequence from protease-activated receptor-1 (PAR1) and named it PAR1–RIP. Experiments in mice demonstrated that 1) Cy5–PAR1–RIP deposits intensely at the injury site in comparison to an adjacent healthy vessel, 2) PAR1–RIP conjugated to a variety of fluorescent and NIR dyes detected and noninvasively quantified pulmonary emboli (PE) in a dose-dependent manner, 3) achieved Real-time detection and measurement of thrombus generation using PAR1–RIP formulated for NIR fluorescence or PET imaging, and 4) PAR1-RIP clears from circulation in 30 minutes.

ADVANTAGES

- **Low toxicity** enables use over longer-periods of time using multiple doses
- Sensitivity to determine **aggressiveness of procoagulant lesions**
- Specificity able to **stratify risk and rule-out thrombotic diseases**
- **Compatibility** with fluorescence, near-infrared fluorescence or radioisotope labels
- **Extremely fast** detection capabilities
- **Platform** technology can be applied to variety of indications beyond thrombosis

APPLICATIONS

- Diagnosis and assessment suspected acute coronary syndrome (ACS), pulmonary embolism, heart attack and stroke, etc) and fibrinolysis in live animals
- Diagnosis and monitoring of indirect thrombotic diseases (cancer and diabetes)
- Routine quantitative analysis of blood clot formation and dissipation

STAGE OF DEVELOPMENT

Preclinical stage

OTHER INFORMATION

Non-invasive imaging and cellular tracking of pulmonary emboli by near-infrared fluorescence and positron-emission tomography.

Nat Commun. 2015 Oct 1;6:8448.

DATA AVAILABILITY

Additional data available under CDA

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	11,712,483	08/01/2023	2011-035
United States Of America	Issued Patent	10,646,593	05/12/2020	2011-035
United States Of America	Issued Patent	9,789,209	10/17/2017	2011-035

Additional Patent Pending

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Diagnostic for Precursor Lesions of Pancreatic Cancer

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