Kansas State University Research Foundation
TECHNOLOGY LICENSING PROFILE

CANCER DIAGNOSTIC ASSAYS:

Fluorescence Assays for Proteases

INVENTORS: Stephan H. Bossmann, Deryl L. Troyer, Matthew T. Basel

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Description: Researchers at Kansas State University have developed a new biomarker cancer detection platform that has shown the ability to detect solid tumors in stage I and II with high specificity using human patient blood samples. Serine, cysteine, and aspartic proteases are markers for the ability of many cancers to grow and to form metastases. Several serine, cysteine and aspartic proteases are over-expressed by numerous cancer cell lines. Elevated expression levels of urokinase and several other components of the plasminogen activation system are found to be correlated with tumor malignancy.

This diagnostic assay is comprised of protease-sensitive cleavage sequences for up to 30 proteases, which are used as linkers between two fluorophores (nanoparticles and/or organic or inorganic dyes). Depending on the nanoparticles and dyes used, optical (fluorescence), magnetic (MRI), and x-ray imaging of the tumor location and extension, together with quantitative determination of the proteases' activities, can be performed. This assay method is useful for the quantitative determination of any enzyme in blood and tissue that can cleave a specific linker between two fluorophores.

Advantages: Advantages of this IP over previous methods:

- Assays can be performed in vivo & in vitro
- Eliminates the need for invasive biopsies
- More rapid diagnostic
- Easier to use
- Less costly
- Cancer can be detected in earlier stages than using conventional technologies (e.g. classic MRI or mammograms, PSA test etc.)

Applications: This innovative technology can be used for:

- New proprietary & differentiated cancer detection platform
- Quantitative determination of the protease-activities of all cancers that over-express one or several proteases (protease signature).
- Coupling of optical (fluorescence), magnetic (MRI), and x-ray imaging of the tumor location & extension with a quantitative determination of the urokinase activity.

2005 Research Park Circle, Manhattan, KS 66502
785.532.1366
caronda@ksu.edu

Caronda Moore
Licensing Associate

Patent Status:

- US Patent Number 8,969,027, with additional divisional applications pending
- EPO Patent Number 2,260,108, validated in France, Germany and UK
- Australian Patent Number 2009221976
- Pending Applications in Canada, Mexico and India

Technology Development Status

Preliminary Proof-of-Concept Research: Initially, 32 separate participants in various stages of breast or non-small cell lung cancer were tested. Data was collected from 20 people with breast cancer -- ranging in age from 36 to 81 years old -- and 12 people with lung cancer -- ranging in age from 27 to 63 years old. Twelve people without cancer were also tested as a control group. This group ranged in age from 26 to 62 years old.

Blood samples from each participant were tested three times. Analysis of the data showed a 95 percent success rate in detecting cancer in participants, including those with breast cancer in stages II and III and those with lung cancer in stages I and II.

Advanced Proof-of-Concept Research: The studies above were followed by trials with larger patient cohorts (> 250 cancer patients and 200 healthy human subjects). Analysis of the data indicated that breast and lung cancer could be detected in stage I with 98 percent success rate. Thyroid cancer was detectable with 95 percent success in stage I as well. The recent trials, performed at Kunming Medical University, China, clearly indicate that this detection method is ideal for early cancer recognition. It can also be used to follow the progress of cancer treatment, and to detect the recurrence of cancer earlier than with other methods. The detection of other solid tumors (prostate, ovarian, pancreatic) is currently being tested.

The test is adapted to plate reader technology and requires 25 microliters of blood serum per enzyme. A result can be obtained within 30 min.

Specificity Data: Protease measurements of more than 10,000 patients at The First Hospital of Kunming Medical University have shown that Bladder Cancer, Breast Cancer, Cervical Cancer, Colorectal Cancer, Endometrial Cancer, Fibroid Cancer, Gall-Bladder Cancer, Hepatoma, Non-small Cell Lung Cancer, Ovarian Cancer, Pancreatic Cancer, and Prostate Cancer feature unique protease signatures, which permit their identification by means of blood serum testing in stages I and II.

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