Pyrite Shrink-Wrap Laminate As A Hydroxyl Radical Generator

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BRIEF DESCRIPTION

The invention is a diagnostic technology, as well as a research and development tool. It is a simple, easy to operate, and effective platform for the analysis of pharmaceuticals and biological species. Specifically, this platform generates hydroxyl radicals for oxidative footprinting – a technique commonly employed in protein mapping and analysis. The platform itself is inexpenisve to fabricate, scalable, and requires nothing more than an ordinary pipet to use. In addition, it is highly amenable to scale-up, multiplexing, and automation, and so it holds promise as a high-throughput method for mapping protein structure in support of product development, validation, and regulatory approval in the protein-based therapeutics industry.

FULL DESCRIPTION

Protein footprinting is a method of biochemical analysis that investigates the structure and interactions of large complex biomolecules, such as proteins and nucleic acids. This method can help identify individual residues within a folded macromolecule that are exposed to the environment by measuring their reactivity towards small but highly reactive exogenous probes. The hydroxyl radical (·OH) is an especially effective footprinting probe due to its high reactivity and small size. However, the methods currently available for generating hydroxyl radicals, which include radiolysis of water and laser photolysis of hydrogen peroxide, require a sizable investment in infrastructure.

Researchers at UCI have now developed a small, inexpensive, and easy to use platform – pyrite shrink-wrap laminate, which will lower the barrier to dissemination of oxidative protein footprinting techniques by eliminating the need for prohibitively expensive and bulky equipment (a source of ionizing radiation, a UV laser, and/or a microfluidic sample handling platform) traditionally required for the generation of hydroxyl radicals. The sole requirement for operation of this new platform is a standard laboratory pipette. In addition, high throughput experiments are possible with a multi-channel pipette or robotic sample handler.

The current invention employs Fenton chemistry supported by the mineral iron pyrite (cubic FeS2) to generate hydroxyl radicals for oxidative footprinting. The earlier reported attempts to use powdered pyrite for footprinting studies of DNA and RNA in microfluidic devices proved difficult, due to incompatibility of the powdered mineral with multiplexed microfluidic mixers. The novel mediator of Fenton chemistry now developed at UCI avoids this pitfall by using pyrite nanocrystals deposited onto a shape memory polymer (commodity shrink-wrap). Thermally shrinking such pyrite-coated films causes the stiffer nanocrystalline layer to buckle, and results in a highly textured, highly reactive, robustly integrated laminate surface of pyrite nanocrystals. Next, footprinting studies can be carried out by pipetting sample drops into the wells that are thermoformed into the pyrite-containing laminate. The iron in the shrink-warp laminate successfully catalyzes the production of hydroxyl radicals in a controlled manner via the Fenton reaction. The radicals can then be used for oxidative protein footprinting.

While •OH generation for protein footprinting can be achieved by radiolysis, photolysis, and electrochemistry, the current invention presents a simpler, lower cost, practical solution that requires less material than any other known footprinting technique. As such, it may represent a welcome analytical tool for both academic and industrial laboratories.

SUGGESTED USES

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OTHER INFORMATION

KEYWORDS

Oxidative footprinting, Protein footprinting, Nucleic acid footprinting, Protein interactions, Fenton chemistry, Pyrate, Hydroxyl radical generation, Laminate, Shrink wrap

CATEGORIZED AS

- **Biotechnology**
  - Health
  - Proteomics
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Oxidative footprinting studies of biologically relevant macromolecules, such as proteins and nucleic acids. Both academic laboratories and pharmaceutical companies involved in developing biologic therapeutics are potential users.

Manufacturers of therapeutic antibodies and biosimilar biologics need to map the solvent accessible surfaces of their molecules, as well as map the target epitopes. This technology will enable a simple and inexpensive way to accomplish these goals for development as well as regulatory analysis.

ADVANTAGES

Low cost of device manufacturing and operation

Ease of device operation

Scalable operation

Amenable to multiplexing and automation

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	9,880,173	01/30/2018	2015-327

STATE OF DEVELOPMENT

Laboratory tested and published in a peer-reviewed journal. Validation of the technology for Fab – antigen and Mab – antigen complexes is underway.

RELATED MATERIALS

» M. Leser, J. Pegan, M. El Makkaoui, J. C. Schlatterer, M. Khine, M. Law, M. Brenowitz; Protein footprinting by pyrite shrink-wrap Laminate; Lab Chip, 2015, 15, 1646. - 04/07/2015

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