CRITICAL NATIONAL NEED IDEA

Critical National Need Idea Title: Sensitive detection of protein biomarkers

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This paper responds to the request of white paper from Technology Innovation Program (TIP) of National Institute of Standards and Technology. I will focus on the challenges and the demand of sensitive detection of protein biomarkers.

The former director (Elias Zerhouni) of National Institute of Health (NIH) laid down the Roadmap of the research directions of NIH (http://nihroadmap.nih.gov), biomarker detection was one of the focuses in the plan of the Roadmap. Numerous academic institutes and pharmaceutical companies took advantage of the completed Human Genome Map and discover a number of DNA or RNA biomarkers for cancer classification and detection. Although DNA is the blue print of life, proteins are the functional units of life. The area of proteomics in general or the discovery of the novel protein biomarkers is still far lagging behind genomic biomarkers discovery studies.

The estimated total number of human gene was 20,000 to 25,000. Assuming one DNA gene locus generates 5 spliced RNA variants, there will be 100,000 to 125,000 different RNA species. If each RNA variants generates one protein product, and each protein molecule undergo 5 different posttranslational modifications, there should be at least 500,000 different species of protein molecules in any tissue expressed at any time. Each modification alters the property of the protein molecule. However, the total number of plasma protein was less than 1000 using most advanced mass spectrometry approach (Omenn et al 2005 Proteomics 5:3226). Such a low percentage of protein discovered from known DNA gene number was due to the complexity of the samples and the analytical methods. Mass spectrometry, being the most sensitive protein analytical method, needs at least 1 million molecules for minimal signal detection. Immunassay, although may go down to 10,000 molecules lower limit of detection, yet it requires specific antibodies for each antigen of interested. Without a prior knowledge of the identity of proteins in a samples, immunoassay will not be feasible. All these disadvantages of proteomics approach cause a difficulty in cancer diagnostics (Hanash et al 2008 Nature 452: 571).

I hereby propose to the TIP to start an initiative that sensitive detection of protein biomarkers should be a critical national need. The program should fund research studies on improvement of protein marker detection down to single molecule level. The benefit to the national will be including but not limited to the follows:

1) Imaging individual metastasized cancer cell before the cell develop into secondary tumors will save lots of lives who died of metastatic cancers each year.

2) Military personnel get into the field in foreign countries can be monitored in real time in single molecule level can prevent any exposure of biological weapons before clinical symptoms develop.

3) In vivo analysis of real time interaction of multiple protein molecules in a cell can lead to substantial novel drug discovery.

4) Numerous infectious diseases (especially viral infections) can be prevented if early detection is available.