Rheumatoid arthritis (RA) affects approximately 1% adults worldwide, and in USA, more than 250,000 hospitalisations each year. RA is a chronic inflammatory disease initiated and driven by cytokines (IL-1, TNF etc.) leading to substantial disability and health care expenditures. There is a recent shift towards early aggressive treatment and this issue highlights the importance of accurate diagnosis of RA early in the disease process. The pathogenic events in RA have been reported (Fig. 1). Early diagnosis and identification of representative RA patient cohorts is also critical for research aimed at developing a complete picture of the RA disease process, its treatment, and outcomes. However, given the complex nature of symptoms, the diagnosis of RA is complicated and challenging, especially in its early phases when intervention is crucial and more effective. Currently, identifying patients with RA criteria is usually based on physician report data, which may be expensive and difficult to obtain for the large patient samples. In recent years, cytokines related to joint diseases have been indicated. The role of some cytokines in chronic inflammation has been clarified with clinical results obtained with inhibitors. Studies have also shown that the same cytokines are also involved in other types of arthritis, such as ankylosing spondylitis, and in many inflammatory diseases. However, the detailed situation is far from being completely understood. Today the list of cytokines, chemokines, and other factors which may affect RA reaches more than 100, making the choice of target more difficult. With old techniques, only a few major cytokines, eg. tumour necrosis factor (TNF), interleukin (IL)-1 etc. have been identified. Although there are several useful protein-based analyses, (eg. 2-D gel Electrophoresis /mass spectrometry, Western blot, and ELISA, they are not suitable for high throughput and parallel studies in RA patients. We need the technique to detect proteins found in very low concentrations, such as cytokines, growth factors, or hormones from very small amount of biological specimens or samples from large populations, which required the testing method should be high throughput, quantitative, and highly economical in the use of specimens and reagents. Therefore, to develop a large sample of patients with RA not biased by patient inclusion in university trials or specialty clinics, we have suggested adapting the protein arrays technology.

In the last decade, the advent of high throughput cDNA microarrays provided a tremendous breakthrough by measuring the expression levels of tens of thousands of genes in a single experiment. This capacity allows the expression of entire genetic ensembles to be monitored in parallel during different stages of embryonic development, disease progress, or drug response. Most recently, proteins were utilised in the same format to detect protein-protein, enzyme-substrate and drug-protein interactions although the difficulty to develop protein arrays is much more than to develop a DNA microarray. However, protein arrays are advantageous over traditional methods and have the potential to detect simultaneously low abundance proteins, such as cytokines from limited volume samples. With the collaboration with The Department of Biomedical Engineering at Duke University, we are one of the few research institutes working on protein arrays. Some advances on human and mouse cytokine detection protein array have been made during the past few years which can detect and profile more than 100, making the choice of target more difficult. With old techniques, only a few major cytokines, eg. tumour necrosis factor (TNF), interleukin (IL)-1 etc. have been identified. Although there are several useful protein-based analyses, (eg. 2-D gel Electrophoresis /mass spectrometry, Western blot, and ELISA, they are not suitable for high throughput and parallel studies in RA patients. We need the technique to detect proteins found in very low concentrations, such as cytokines, growth factors, or hormones from very small amount of biological specimens or samples from large populations, which required the testing method should be high throughput, quantitative, and highly economical in the use of specimens and reagents. Therefore, to develop a large sample of patients with RA not biased by patient inclusion in university trials or specialty clinics, we have suggested adapting the protein arrays technology.

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In summary:

- Our primary goal is to develop cytokine protein detection arrays for the temporal profiling of cytokines etc. for RA or other inflammatory diseases.
- It is desirable that this array should be compatible with commercially available fluorescence scanners and automated arrayers originally designed for cDNA microarray analysis.

- The low-level proteins (10 pg/mL cytokines), reproducibility and high throughpaht should make protein arrays a possible tool for RA prognosis and diagnosis.

Key References: