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METABOLOMICS OF RHEUMATOID ARTHRITIS USING MASS SPECTROMETRY TECHNIQUES

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Rheumatoid arthritis (RA) is an autoimmune disease that causes chronic inflammation of the synovial lining of the joints. It affects females more frequently than males and is typically diagnosed between the ages of 40-60 years with symptoms developing gradually. If untreated, RA can lead to permanent joint damage and an increased risk of premature mortality. Synthetic DMARDS (sDMARDs) such as methotrexate (MTX), biological DMARDS (bDMARDs) such as TNF-α antagonists (e.g., etanercept, adalimumab, or infliximab), and antibodies that deplete B cells (e.g., Rituximab) are widely used in inhibiting synovial inflammation and retarding bone erosion. It has been estimated that 30-40% of patients have poor or no response to these treatments. Metabolomics is a rapidly developing approach in biomarker research which involves the measurement of the set of final products and by products of metabolic pathways using NMR and mass spectrometry methods. Since RA disrupts metabolite (products) pathological processes, metabolomics can measure the alterations in these metabolite profiles long before overt signs and symptoms of the disease appears. Metabolomics should provide a more accurate representation of the RA phenotype than that accounted for by genetic, epigenetic, gastrointestinal microbiome and environmental factors. Many metabolomics studies have been published identifying potential RA biomarkers for use in diagnosis, prognosis or prediction of drug treatment. Here, we discuss the advantages and disadvantages of metabolomics RA biomarker research using mass spectrometry techniques.

Biography

Gary W Caldwell received his PhD in Physical/Organic Chemistry from Indiana University in 1982 under the direction of Dr. John E Bartmess using Ion Cyclotron Resonance Spectrometry to study gas-phase ion chemistry. Following his PhD, he performed Postdoctoral Research with Dr. Paul Kebarle at the University of Alberta in Canada using High-Pressure Mass Spectrometry to study gas-phase ion chemistry. He joined Janssen Pharmaceutical Research and Development, a subsidiary of Johnson & Johnson in 1985. During his 32-year career with Janssen Pharmaceutical R&D, he has managed a variety of functions within the drug discovery units. These functions include the NMR, GC/MS & LC/MS/MS spectroscopy group, the medicinal chemistry intermediates group, the large-scale separation group, the drug discovery in-vivo/in-vitro PK/ADME groups and the compound management group. His research interests primarily involve the use of advanced spectrometric and chromatographic techniques to chemically and biologically characterize new drug targets and drug entities. Presently, he is working on establishing targeted and untargeted metabolomic methods to understand "on" and "off" target effects to improve drug efficacy and reduce drug toxicity. He is the author of over 150 publications, two patents, over 50 poster presentations, and has given over 40 invited talks at universities, companies, and conferences. He is the Co-editor of ***Frontier in Drug Design & Discovery*** (volumes 1-4), and Editor of ***Optimization in Drug Discovery: In-vitro Methods*** (volumes 1-2).

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