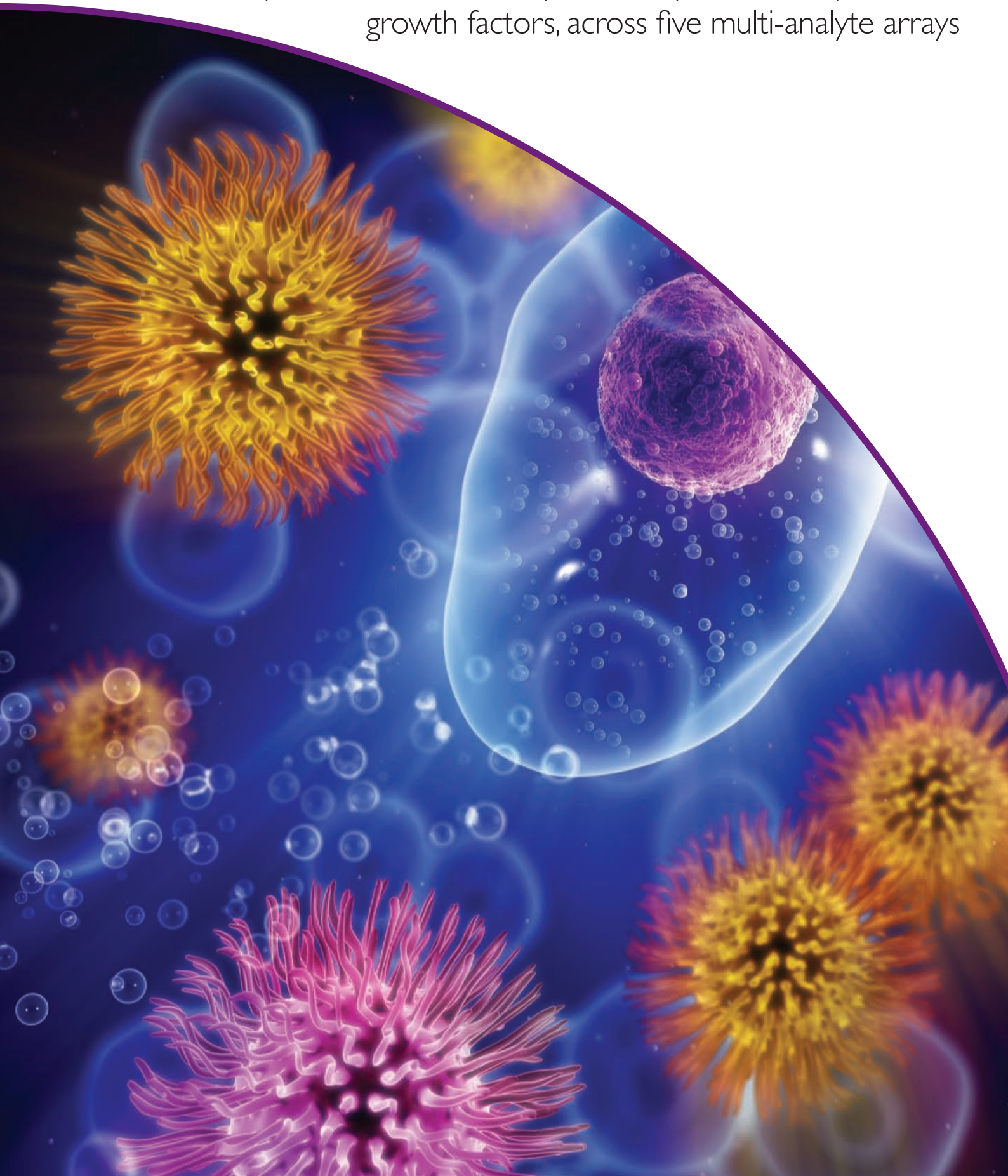
RANDOX

Cytokine Research

Offers a comprehensive menu of cytokines, cytokine receptors and growth factors, across five multi-analyte arrays



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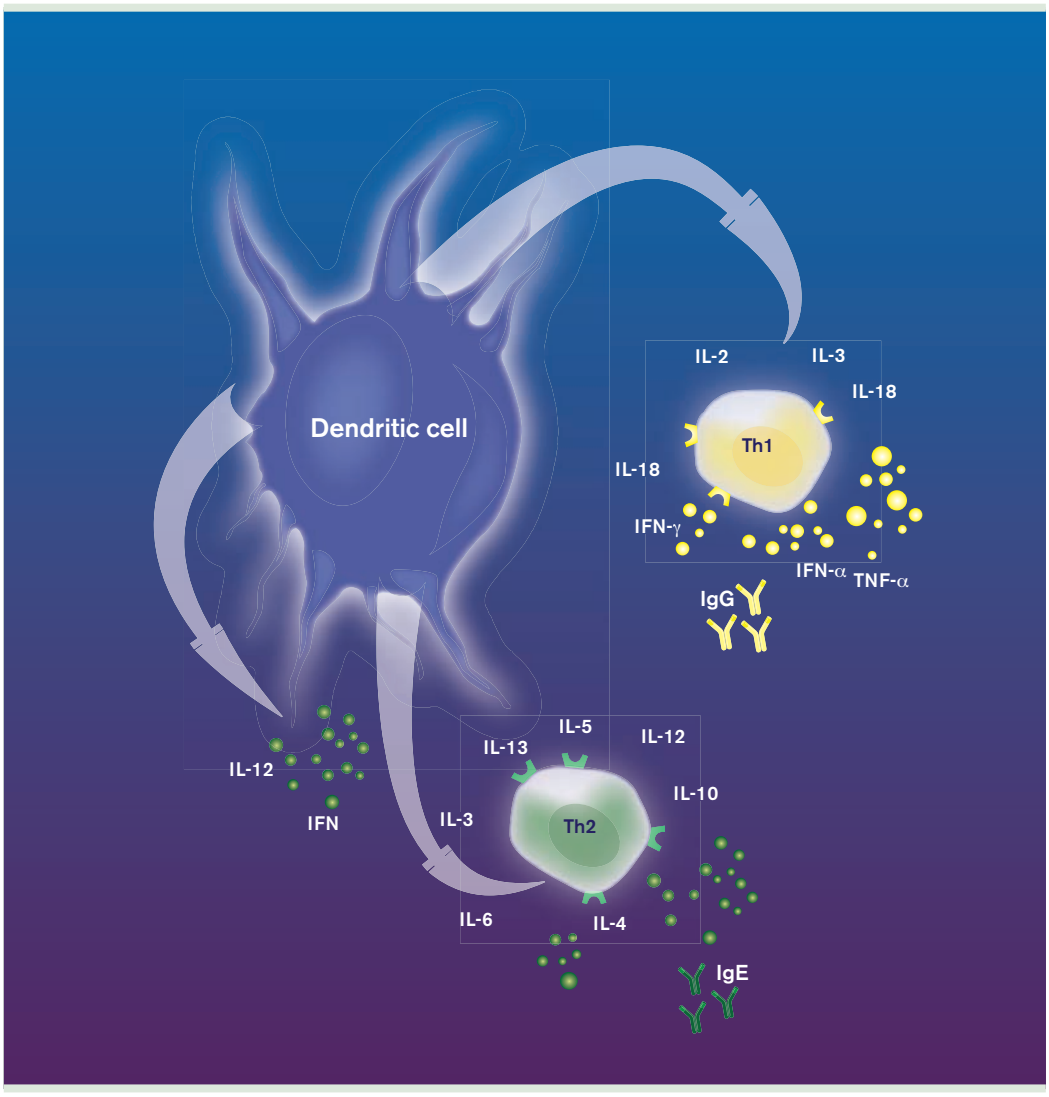

Cytokines are innate small regulatory proteins involved in immune response and are produced by various cell types including B-cells, T-cells, macrophages, neutrophils, basophils, eosinophils and endothelial cells. Cytokines function as intercellular chemical messengers. They act as external controlling elements in hematopoiesis and also mediate and control immune and inflammatory responses. They have been implicated in pathological conditions, such as cancer, cardiovascular diseases, allergic response and play a significant role in surgery recovery, including transplants.

Cytokine Facts

- Similar functions can be stimulated by different cytokines
- They can act synergistically or antagonistically therefore measuring a single cytokine may miss an important facet of response progression
- Have duplicity of function when dealing with infection
- Can affect their host cell (autocrine), nearby cells (paracrine) or distant cells (endocrine)
- Commonly cascade so cytokines can more readily be studied if many are measured simultaneously
- Exert their influence through receptors in the cell membrane or within the cell

Hypersensitive Response

In some cases, the immune response over-reacts, turning cytokines against the body they are designed to protect. When the cytokine cascades fail to shut down, they can drive the host into a state of acute or chronically activated cells, which dominate an otherwise dormant immune system. Examples of the most obvious manifestations of this hypersensitivity are an unnecessary inflammatory response and fever; both of which can be life threatening if left untreated.

Cytokine Biochip Arrays

To determine multiple cytokines in a single sample at a single time point, Randox offers a comprehensive menu of 33 cytokines, cytokine receptors and growth factors, over five multi-analyte arrays. Each cytokine assay is performed on a 9 x 9mm activated biochip with spatially discrete test regions containing antibodies specific to each of the analytes. The combination of highly specific antibodies and advanced chemistries enables cytokines, cytokine receptors and growth factors to be detected simultaneously in a single sample, providing valuable information relating to each cytokine under test and possible associations between cytokines in each sample.

Key Benefits

- Multiple results from a single sample
- Validated for plasma and serum samples*
- Small sample volume - 100µl total / from 8.3µl sample per test
- Excellent analytical performance
- Biochips are ready-to-use
- Dedicated fully and semi-automated analysers available

*Human cell culture supernatants and other human biological fluid e.g. bronchoalveolar lavage, wound fluid and saliva can be assayed using the biochip, but will require end user optimisation.

Biochip Systems

Evidence

- Fully automated, floor standing
- Up to 1980 tests per hour
- Small sample volume
- Barcode scanner for sample traceability
- Bar-coded samples and reagents
- User-defined cut-off levels without recalibrating
- Extensive QC data generation
- Retrospective reporting
- Password protected software
- Automatic disposal of biochips
- Chain of custody features
- Suitable for high throughput laboratories

Evidence Investigator

- Semi-automated, bench-top
- Up to 702 tests in 70 minutes
- Small sample volume
- Barcode scanner for sample traceability
- Bar-coded samples and reagents
- User-defined cut-off levels without recalibrating
- Extensive QC data generation
- Ability to store and retrieve work lists saving time
- Retrospective reporting
- Password Protected Software
- Chain of custody features
- Suitable for medium throughput laboratories

Cytokine Biochip Arrays Available

Array	Cat. No.
Cytokine Array I and Cytokine High Sensitivity Array	
• Interleukin-1α (IL-1α) • Interleukin-1β (IL-1β) • Interleukin-2 (IL-2) • Interleukin-4 (IL-4) • Interleukin-6 (IL-6) • Interleukin-8 (IL-8) • Interleukin-10 (IL-10) • Epidermal Growth Factor (EGF) • Interferon-γ (IFN-γ) • Monocyte Chemotactic Protein-1 (MCP-1) • Tumour Necrosis Factor-α (TNF-α) • Vascular Endothelial Growth Factor (VEGF)	EV3508 - Evidence (360 biochips) EV3544 - Evidence (180 biochips) EV3513 - Evidence Investigator (54 biochips) EV3561 - Cytokine Array Calibrator Series CY5006 - Cytokine Control (Series 1) **High Sensitivity** EV3623 - Evidence Investigator (54 biochips) CY5005 - High Sensitivity Tri-Level Cytokine Control
Cytokine Array II	
• Eotaxin • Insulin-like Growth Factor 1 Free (IGF-1) • Interferon inducible protein-10 (IP-10) • Interleukin-1 receptor antagonist (IL-1 Ra) • Interleukin-12/23-p40 (IL12/IL23-p40) • Platelet Derived Growth Factor BB (PDGF-BB) • RANTES	EV3817 - Evidence Investigator (54 Biochips) CY5132 - Cytokine Control (Series II)
Cytokine Array III	
• Granulocyte Macrophage Colony Stimulating Factor (GM-CSF) • Interleukin-5 (IL-5) • Interleukin-15 (IL-15) • Macrophage Inflammatory Protein-1α (MIP-1α)	EV3680 - Evidence (180 biochips) EV3678 - Evidence Investigator (54 biochips) EV3679 - Cytokine Array III Calibrator Series CY5012 - Cytokine Control (Series III)
Cytokine Array IV	
• Matrix Metalloproteinase-9 (MMP-9) • Soluble IL-2 Receptor α (sIL-2Rα) • Soluble IL-6 Receptor (sIL-6R) • Soluble Tumour Necrosis Factor Receptor I (sTNFRI) • Soluble Tumour Necrosis Factor Receptor II (sTNFRII)	EV3659 - Evidence (180 biochips) EV3661 - Evidence Investigator (54 biochips) EV3658 - Cytokine Array IV Calibrator Series CY5011 - Cytokine Control (Series IV)
Cytokine Array V	
• Interleukin-3 (IL-3) • Interleukin-7 (IL-7) • Interleukin-12p70 (IL-12p70) • Interleukin-13 (IL-13) • Interleukin-23 (IL-23)	EV3666 - Evidence Investigator (54 biochips) CY5010 - Cytokine Control (Series V)

Examples of Research Applications for Cytokine Biochip Arrays

Cytokine Biochip Arrays have been used in a number of research and clinical studies. A sample of independent publications are shown below:

Disease State	Research application	References
Coronavirus-associated severe acute respiratory syndrome (SARS)	Cytokine measurement in SARS patients at different stages.	Guo, G.H. *et al.* (2004) ***Chin. J. Lab. Med. 27***:277
Tendinopathies	Measurement of cytokine levels after local treatment with platelet rich plasma.	Banfi, G. *et al.* (2006) ***Br. J. Sports Med.* 40**:816
STANISLAS study	Biological determinants, associations and reference values. Heritability for plasma VEGF concentration. MCP-1 plasma concentrations and polymorphisms. Association of inflammatory markers with high sensitivity CRP. Association between EGF and lipid concentrations.	Berrahmoune, H. *et al.* (2006) ***Clin. Chem. 52***:504-510 Berrahmoune, H. *et al.* (2007) ***Ann. Hum. Genet. 71***:54-63 Berrahmoune, H. *et al.* (2007) ***Atherosclerosis 192***:348-353 Berrahmoune, H. *et al.* (2007) ***Clin. Chem. Lab. Med. 45***:1339-1346 Berrahmoune, H. *et al.* (2009) ***Clin. Chim.Acta. 402***:196-198
PIVUS study	Investigation if intima-media echogenecity is related to cardiovascular factors or to markers of inflammation and oxidation.	Anderson, J. et al. (2009) **Atherosclerosis. 204**: 612-618:
Alzheimer's disease & mild cognitive impairment	Alzheimer's disease and cognitive decline.	Chiappelli, M. *et al.* (2006) ***Rejuvenation Res.* 9**:485-493
Alzheimer's disease	Characterization of inflammatory molecules and relationship with cognitive decline	Corsi, M.M. et al.(2011) Biogerontology. 12: 451-454.
Down's syndrome	Altered levels of signalling molecules. Age related changes in plasma levels.	Licastro, F. *et al.* (2006) ***Int. J. Immunopathol. Pharmacol.* 19**: 181-185 Dogliotti, G. et al. (2010) ***Immunity and Ageing. 7***: 2
HIV	Immunological and virological discordance.	Sachdeva, N. *et al.* (2007) ***Scand. J. Immunol.* 65**:549 - 554 Sachdeva, N. *et al.* (2008) **J. Immunol. 181**:2887 - 2897
Renal failure	Simultaneous determination of cytokines in patients on haemodialysis.	Sertic, J. *et al.* (2007) ***Clin. Chem. Lab. Med.* 45**:1347-1352 Badiou, S. *et al.* (2008) ***Clin. J. Am. Soc. Nephrol.* 3**:423-430
Acute coronary syndromes	Risk stratification for heart failure and death. Cytokine profiling in women with ACS. Determination of upstream markers for early identification of patients at risk for myocardial necrosis and adverse outcomes. Long-term risk stratification of heart failure and death.	Kavsak, P.A. *et al.* (2007) ***Clin. Chem. 53***:2112-2118 Kavsak, P.A. *et al.* (2008) ***Clin. Biochem. 41***:607-610 Kavsak, P.A. *et al.* (2008) ***Clin. Chim. Acta 387***:133-138 Kavsak, P.A. *et al.* (2010) ***Clin. Biochem. 43***:505-507
Aortic stenosis	To investigate the impact of leukocyte filtration of blood cardioplegia	Onorati, F. et al. (2013) **Eur. J., Cardiothorac. Surg. 43**: 81-89
Hypertension	Effect of antihypertensive drugs on adipose tissue with respect to insuline resistance.	Palming, J. *et al.* (2011) ***Horm. Metab. Res. 43***:319-324
Dysglycaemia and coronary artery disease	Effects of statins.	Settergren, M. *et al.* ***European Heart Journal 29***:1753-1760
Hereditary hemochromatosis	MCP-1 levels and correlations with HFE mutation status and iron indexes.	Lawless, M.W. *et al.* (2007) ***Tissue Antigens* 70**:294-300
Rheumatoid arthritis	Effects of anti-TNFα therapy. Response to etanercept therapy. Response to rituximab therapy.	Metsios, G.S. et al. (2007) **Rheumatology. 46**:1824-1827 Fabre, S. *et al.* (2008) ***Clin. Exp. Immunol. 153***:188-195 Fabre, S. *et al.* (2009) ***Clin. Exp. Immunol. 155***:395-402
Type 2 diabetes mellitus	Evaluation of the levels of cytokines in patients with or without diabetic retinopathy. Italian Diabetes and Exercise Study for the evaluation of efficacy of an intensive lifestyle intervention on modifiable CVD risk factors.	Lee, J-H. *et al.* (2008) ***Am. Clin. Lab. Sci. 38***:361-367 Balducci, S. *et al.* (2008) **Nutr. Metab. Cardiovasc. Dis. 18**:585-595
Type 2 diabetes and metabolic syndrome	Effect of different exercise modalities on inflammatory markers.	Balducci, S. *et al.* (2010) **Nutr. Metab. Cardiovasc. Dis. 20**:608-617
Insulin resistance & Metabolic Syndrome	Measurement of inflammatory markers.	Ingelsson, E, *et al.* (2008) ***Eur. J. Clin. Invest. 38***: 502-509
Age related macular degeneration	Bevacizumab treatment.	Roh M.I. (2009) ***Retina 29***: 523-529
Macular edema	Bevacizumab treatment.	Roh, M.I. (2009) ***Ophtalmology 116***: 80 - 86
Cataract	Effect of intraocular surgery and ketamine on aqueous and serum cytokines	Tu, K.L. (2007) **Mol.Vis. 13**: 1130-1137
Metastatic disease	Response to anti-metastatic agent.	Kavsak, P.A (2009) ***Clin. Biochem. 42***: 1162-1165
Post myocardial infarction	Association between inflammatory markers and MMPs in men and women.	Samnegård, A. *et al.* (2009) ***Atherosclerosis 202***: 550-556
Colon Cancer	Determination of levels of cytokines in serum of patients and comparison with controls.	Bünger S. *et al.* (2011) J. ***Biomol. Screen 16***: 1018-1026
Oesophageal cancer	Marker examination after neoadjuvant chemoradiation and major cancer surgery.	Byrne, M. *et al.* (2010) ***Br. J. Cancer 102***: 73-79
Barrett esophagus	Study of the proinflammatory impact of adipocytokines	Ryan, A.M. et al. (2008) **Ann. Surg. 247**: 909-915
Asymptomatic long-segment Barrett's esophagus	Antireflux surgery and medical therapy comparison.	Babar, M. *et al.* (2010) ***Am. J. Surg. 199***: 137-143
Stress	Psychological stress in women.	Asberg, M. *et al.* (2009) ***PLoS ONE, 4***: es590

Examples of Research Applications for Cytokine Biochip Arrays (continued)

Disease State	Research application	References
Exercise	Cytokine measurement in triathlon athletes during a competitive season.	Banfi, G. *et al.* (2008) ***Clin. Chem. Lab. Med. 46***:250-252
	Effects of a short bout of resistance exercise on components of the stress and inflammatory responses in healthy young male volunteers.	Fatouros, I. *et al.* (2010) ***Stress 13***:461-468
	Investigation of changes induced by playing soccer in the systemic profiles of growth factors and cytokines involved in the inflammatory response.	De Paola, M. *et al.* (2011) ***Eur. J. Neurol. 18***:85-92
	Sex differences in immunovariables and respiratory infection in athletes engaged in endurance-based physical activity	Gleeson, M.,et al. (2011) **Exerc. Immunol. Rev. 17**: 122-135.
Elderly population studies	Investigation of proinflammatory cytokines in elderly patients with heart failure	Haugen, E. et al. (2008). **Exp. Clin. Cardiol. 13**:19-24
	Investigating the association between serum fatty acid composition and various inflammatory and endothelial function markers.	Petersson, H. *et al.* (2009) ***Atherosclerosis 203***:298-303
	Evaluation of the inter-relationship between soluble CTLA-4 and other inflammatory markers.	Sakthivel, P. *et al.* (2010) ***Scand. J. Clin. Lab. Invest. 70***:237-243
	BELFRAIL study to study the dynamic Interaction between health, frailty and disability in a multi-system approach.	Vaes, B. et al. (2010). **BMC Geriatrics. 10**:39
	Investigation of inflammatory markers in relation to left ventricular geometry and diastolic function.	Masiha, S. *et al.* (2013). **J. Hum. Hypertens. 27**:13-17
	Analysis of associations of biomarkers and combinations of biomarkers with lung function	Kuhlmann, A. *et al.* (2013). **BMC Geriatrics. 13**:82
Uveal melanoma	Expression of 12 cytokines in aqueous humour before and after combined Ruthenium-106 brachytherapy and transpupillary thermotherapy.	Lee C.S. *et al.* (2012) ***Acta Ophthalmol. 90***: e314 – e320
Coal workers 'pneumoconiosis (CWP)	Levels of IL-8 and and TNFα as CWP biomarkers were related to cross-sectional findings and 1-year progressive changes of pneumoconiosis	Lee, J.S. *et al.*(2010) **Saf. Health Work. 1**: 69-79.
Pediatric pulmonary hypertension	Evaluation of associations between hemodynamics , adverse events and protein markers	Duncan, M., *et al.* (2012) **Mediators Inflamm.** 143428
Bladder cancer (hematuria)	Biomarkers in multivariate algorithms for diagnosis	Abogunrin, F., *et al.* (2012) **Cancer. 118(10)**: 2641-2650. Duggan, B., *et al.* (2012) **Cancer. 18(22)**:5720. Reid, C.N. *et al.* (2012) **PloS One 7**: e53354 Emmert-Streib, F., *et al.* (2013) **BMC Med. 11(1)**: 12
Psoriasis vulgaris and allergic contact dermatitis	Analysis of cytokines and growth factors in serum to compare systemic inflammatory responses in these diseases	Kaur, S. et al. (2012) **Dermatology. 225**: 54-61
Cystic fibrosis and dialyzed patients	Evaluation of simultaneous analysis in chronic inflammatory diseases	Tirelli, A,S. et al. (2013) **Cytokine. 62**: 413-420
Chronic bronchitis	Evaluation of the efficacy of cefditoren and levofloxacin in inflammatory reduction, clinical recovery and microbial eradication	Blasi, F. *et al.* (2013) **Therapeutics and Clinical Risk Management. 9**: 55-64
Acute leukemia	Evaluation of serum levels of cytokines and adhesion molecules in patients with acute lymphoblastic leukemia	Horacek, J. M. *et al.* (2013) **Exp. Oncol. 35**: 229-230
	Evaluation of serum levels of cytokines and adhesion molecules in patients with acute myeloid leukemia	Horacek, J. M. *et al.* (2013) **Biomed. Pap. Med. Fac. Univ. Palacky Olomouc Czech. Repub 157**
Polycystic ovary syndrome (PCOS)	Investigation of the effects of PCOS on chronic inflammation	Phelan, N. *et al.* (2013) **Clin. Endocrinol. 78**: 107-113
In vitro studies	TCR-MHC Class II interactions between T cells and monocytes.	Van Beem, R.T. (2008) ***J. Immunol. 180***: 5141 - 5148
	Cytokine secretion by human -THP-1 macrophages.	Frisdal, E. *et al.* (2011) ***J. Biol. Chem. 286***:30926-30936
	Effect of procalcitonin in bacterial LPS and LPS-induced cytokine release in human peripheral blood mononuclear cells	Matera, G. et al. (2012) ***BMC Microbiology. 12***:68

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