Helping to Manage Juvenile Idiopathic Arthritis

User Report

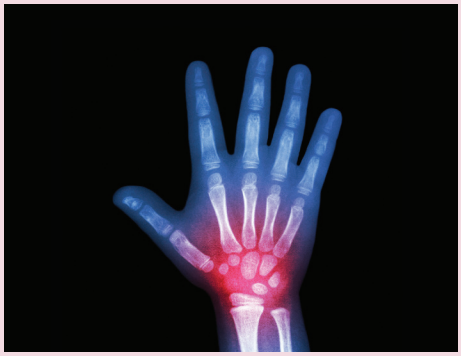
By Elizabeth Ralph, Clinical Scientist and Section Lead for Serology, Immunology Laboratory, Great Ormond Street Hospital.

"Juvenile idiopathic arthritis (JIA) is an autoimmune condition that causes joint inflammation and affects about 1 in 1000 children under the age of 16. Early treatment of inflammation is essential to minimise joint destruction.

However, prolonged medication is not desirable as the drugs used have significant side-effects. Unfortunately, the presence of symptoms indicates that the inflammatory process is already substantial. Ideally, a laboratory biomarker would identify the disease before symptoms appear, enabling anti-inflammatory medications to be administered sooner.

Research has found that myeloid related proteins (MRP) subtypes 8 and 14 function as markers of localised inflammation. In JIA, a number of studies have found that MRP8/14 is a useful and accurate marker that can detect signs of inflammation that mean treatment should be initiated. It can also predict the risk of a flare in patients that are currently on medication, to determine whether treatment can be safely stopped.

The research group of Professor Lucy Wedderburn, a Rheumatologist at the Institute of Child Health, University College London, has shown that it is possible to identify a subset of JIA patients who would respond well to treatment with the cytotoxic drug methotrexate, as they had high concentrations of MRP8/14 in their serum prior to treatment (Moncrieffe et al. Rheumatology 2013). Working with Professor Wedderburn's group, the Clinical Immunology Laboratory at Great Ormond Street Hospital, validated the BÜHLMANN serum MRP 8/14 ELISA kit for use in the clinical diagnostic lab."



Elizabeth Ralph and Fardowza Ahmed, Clinical Immunology, Great Ormond Street Hospital

"A number of criteria were established including verifying the manufacturer's data for performance characteristics such as intra- and inter-assay variability, linearity, as well as establishing independent quality control material.

Initial work carried out by Dr Simona Ursu, a post-doctoral researcher in Professor Wedderburn's group, established independent quality control material for the assay, and initial data for performance characteristics. This work was then continued by Fardowza Ahmed, Biomedical Scientist, and myself, in the Clinical Immunology lab at Great Ormond Street, over a nine month period from March to November 2015.

The assay showed good performance characteristics. The average intra-assay variability, (Table 1), was 5% which compared favourably with the manufacturer's data of 4.3%. Inter-assay variability was 11%, compared to 5.8% suggested by the manufacturer.

Although this was higher than expected, this is in line with the performance of other ELISAs carried out in the laboratory, and was deemed to be acceptable. MRP 8/14 was found to be a stable protein. A serum sample was kept at room temperature and processed over 5 consecutive days. The variability was 11% and, although slightly higher than our desired value of 10%, was accepted. The linearity of the assay was established by running the high control over 7 different dilutions and calculating the percentage recovery (Table 2).

In our lab, the percentage range was 97% to 110%; this is better than the manufacturer's data of 85% to 110%.

A recent clinical audit of the period March to December 2015 showed that 105 patient samples were analysed for MRP 8/14. In almost 60% of requests, the result of the MRP test directly influenced the clinical decision making process, demonstrating the value that this test has brought to the management of these patients. The test is now available to request by clinicians on a routine basis, with a turnaround time of 4 weeks to allow for batching of samples"

	Kit Mid QC (ng/ml)	Kit High QC (ng/ml)
Results	5076	10892
	4947	9328
	5401	9627
	4927	9508
	5035	10162
Mean (ng/ml)	5088	9903
Standard Deviation (ng/ml)	191	634
%CV	4	6

Table 1: Intra-assay variability

	In-house High QC (ng/ml)		
Dilution	**Observed**	**Expected**	**O/E (%)**
100	1102	1002	110
200	518	501	103
300	351	332	105
400	245	250	98
500	194	200	97
Mean			107
Range			97%-110%

Table 2: Assay linearity

To find out more about the serum MRP 8/14 ELISA kit, visit our website at **www.alphalabs.co.uk/mrp8-14**

Paediatric Rheumatology International Trials Organisation (PRINTO). Phagocyte-specific S100 proteins and high-sensitivity C reactive protein as biomarkers for a risk-adapted treatment to maintain remission in juvenile idiopathic arthritis: a comparative study. Ann Rheum Dis (2012): 71(12):1991-7.

Rothmund, F., Gerss, J., Ruperto, N., Däbritz, J., *et al.* Paediatric Rheumatology International Trials Organisation (PRINTO). Validation of relapse risk biomarkers for routine use in patients with juvenile idiopathic arthritis. Arthritis Care Res (Hoboken) (2013): doi: 10.1002/acr.22248

Originally published in Leading Edge - Summer 2016