proliferation and more importantly less divisions compared with
WT animals. FACS analysis of WT and Flt3L−/− mice synovium at
the acute phase of CIA showed that CD11b+ DC are present and
increased in articular animals compared with immunised but not
arthritic animals. CD103+ DC are only present in WT animals, and
increased in animals with a high clinical score.

Conclusions Our data shows that antigen presentation in Flt3L−/−
mice is impaired. As CD103+ DC are important in presenting and
cross-presenting antigens our data reveals an important role for
CD103+ DC in both induction and maintenance of CIA. Specifically
targeting CD103+ DC could provide a novel antirheumatic strategy.

A8.6 IDENTIFICATION OF NEW POTENTIAL THERAPEUTIC
TARGETS FOR THE TREATMENT OF RHEUMATOID ARTHRITIS: ENTPD1 (CD39) AND SNT1 (CD73)

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Background and Objectives Adenosine and ATP are known to
have important immunomodulatory properties. Extracellular ATP
has multiple roles in inflammation and can act as a damage-
associated molecular pattern (DAMP) that can activate the immune
system. Conversely, adenosine is primarily anti-inflammatory and
can inhibit the production of pro-inflammatory molecules by
immune cells. The modulation of ATP and adenosine levels are an
essential part of the induction and resolution of an inflammatory
response. ENTPD1 (CD39) is a membrane-bound ectonucleoside
triphosphate diphosphohydrolase enzyme that converts ATP and
ADP to AMP SNT1 (CD73) is a 5′-nucleotidase that dephospho-
rylates AMP to form adenosine. We investigated the role of
genes in the adenosine pathway in patients with rheumatoid arthri-
tis (RA) and determined whether expression of CD39 and CD73
would have an effect in an in vitro inflammation model.

Materials and Methods Gene expression analysis using 45k
cDNA microarrays (Stanford Functional Genomics Facility) was
performed on total RNA extracted from RA synovial tissues
obtained by arthroscopy. Adenosine pathway gene expression was
compared between high-inflammation versus low-inflammation tis-

A8.5 IDENTIFICATION AND VALIDATION OF A PROTEIN
COMBINATION INCLUDING S100A9 ABLE TO PREDICT
THE RESPONSE TO THE MTX/ETANERCEPT ASSOCIATION
IN RHEUMATOID ARTHRITIS PATIENTS

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Background The number of biologic agents in Rheumatoid Arthri-
tis (RA) is continuously increasing. However, clinicians observe that
around 30 to 40% of treated patients fail to respond to TNFα block-
ing agents. One way to optimise the drug prescription is to identify
predictive markers of drug responsiveness.

Objectives To identify a combination of serum proteins whose
expression profile would predict the RA patients responses to the
association of methotrexate (MTX) and etanercept (ETA) by mass
spectrometry-based quantification methods and ELISA.

Methods A “cohort discovery phase” of 23 patients with active
RA was treated by a subcutaneous injection of the clinical efficacy
of these drugs was evaluated with the DAS28 score after 6 months
of treatment according to the EULAR response criteria. For
proteomic analysis, a serum sample was collected in patients prior
to treatment exposure. A “label free” approach on the whole pro-
tome was performed by mass spectrometry (ThermoFisher). Differen-
tial analysis between responder and non responder samples was
performed with LCMS ProGenesis® (Non-
linear Dynamics). To validate these results a relative quantification
of selected protein was performed on the second “cohort validation
phase” by ELISA. The proteome of peripheral blood mononuclear
 cells (PBMC) from a second cohort of seven patients with similar
characteristics has also been studied by the same label free
approach.

Results The label free approach revealed 12 differentially expressed
serum proteins according to patient response. This combination of
proteins was used to build a Random Forest statistical model to pre-
dict the patient’s status. This model was validated by a blind test on
a panel of seven patients. Moreover, these results have shown the
protein S100A9 overexpression in both the serum and the PBMCs
from responder’s patients and this expression was confirmed by
ELISA.

Conclusions The label free approach has identified a combination of
predictive markers of response to MTX treatment/ETA. Thus,
using sera samples collected in patients prior to treatment exposure,
it is possible to predict response to treatment with a small error.

These proteins represent interesting candidate biomarkers of
response that must be validated in a larger population. Already iden-
tified as a diagnostic and prognostic biomarker of RA, the S100A9
protein has been identified as a predictive biomarker of response
both in serum and in PBMCs.