proteasome inhibitor, was recently approved in the US and Canada for use in combination with lenalidomide and dexa-
methasone in patients with multiple myeloma who have
received at least 1 prior therapy. The Keyhole limpet hemo-
cyran (KLH) model of T cell-dependent antigen response was
used to determine if ixazomib depletes plasma cells resulting
in a reduction of antibodies.

Methods Briefly, rats were immunised with KLH and Titer-
Max adjuvant then treated with ixazomib twice weekly until
study termination.

Results Treatment with ixazomib significantly inhibited anti-
KLH antibodies by 34% (p<0.05) versus vehicle. Additionally,
KLH plasma cells quantified by ELISpot were decreased 78%
(p<0.01) in the spleen and 53% (p<0.01) in the bone mar-
crow compared to control. To gain some understanding of the
selectivity of plasma cell depletion total White Blood Cells,
Red Blood Cells (RBC) Platelets, Neutrophils, and total Lym-
phocytes were quantified with small a reduction only seen in
RBCs and platelets.

Conclusions Ixazomib depleted plasma cells resulting in
reduced antibodies suggesting further preclinical studies are
warranted in diseases with pathogenic antibodies such as SLE,
RA, SSc and solid organ transplant rejection.

50 EXPRESSION OF LY6C/6G DEFINES A NOVEL AIRE-
DEPENDENT SUBSET OF MEDULLARY THYMIC
EPITHELIAL CELLS WITH TOLEROGENIC FUNCTION
J Morimoto, Y Nishikawa, H Nishijima, M Matsumoto*. Division of Molecular Immunology,
Institute for Enzyme Research, Tokushima University
10.1136/lupus-2017-000215.50

Medullary thymic epithelial cells (mTECs) are a heterogeneous
population in terms of the spectrum of tissue-restricted Ags
(TRA)s expressed from each cell for ensuring the elimination
of autoreactive T-cells. Additionally, mTECs comprise cells at
different developmental stages and/or in various activation
conditions. Because of these heterogeneities, it is unclear
whether mTECs are composed of any particular subsets pos-
sessing unique properties for their developmental pathway and/or immunological function. Here, we report a distinct
mTEC subset characterised by expression of Ly6 family pro-
tein prior to and concomitant with Aire expression during its
differentiation. Ly6C/6G+ mTECs, constituting 5%–15% of
mature mTECs, were preferentially localised at the cortico-
medullary junction, and expressed high levels of TRAs and
thymocyte-attracting chemokines. Remarkably, Ly6C/6G+ mTECs were absent in Aire-deficient mice, suggesting that this
subset requires Aire and/or Aire+ mTECs for its production.
Uniquely, Ly6C/6G+ mTECs lack a post-Aire stage because of
a tendency to die after Aire had been expressed. With a
TCR-transgenic model in mice, we found that in vivo deple-
tion of Ly6C/6G+ mTECs frequently induced organ-specific
autoimmunity. We suggest that Ly6C/6G+ mTECs serve as an
important source of TRAs for efficient cross-presentation dur-
ing establishment of self-tolerance.

51 INCREASED APOPTOSIS AND ABERRANT APOPTOSIS
SIGNALLING PATHWAYS OF NATURAL CD4+CD25
+FOXP3+ REGULATORY T CELLS IN PATIENTS WITH
SYSTEMIC LUPUS ERYTHEMATOSUS
1L Na*, 1F Hao. 1Southwest Hospital Third Military Medical University, Dermatology,
Chongqing, China
10.1136/lupus-2017-000215.51

Background and aims Systemic Lupus Erythematosus(SLE) is a
prototype of autoimmune disease.Decreased cell numbers and
suppressive defects of naturally occurring CD4+CD25+FOX-
P3+regulatory T cells(Tregs) play an important role in the
breakdown of SLE immune tolerance.We have previously
observed significantly increased apoptosis of peripheral blood
CD4+ T cells in SLE patients.Our objective here was to detect
the apoptosis of Tregs in SLE patients to see if it could con-
tribute to reduced suppressive activity of Tregs,and further elu-
cidate the genes and signalling pathways which trigger the
apoptosis in these cells.

Methods The cell number and apoptosis rates of Tregs was
respectively evaluated in SLE patients and normal controls
(NCs) by FACS.The suppressive activity of Tregs was measured
by coculture with CD4+CD25+CD127dim/-T cells,The rela-
tionship of abnormal Tregs apoptosis with clinical parameters
was analysed by correlation analysis.Gene expression profiles
of unstimulated Tregs from active SLE patients and NCs were
generated by microarray analysis.Differential genes expression
were verified by real-time-PCR.