

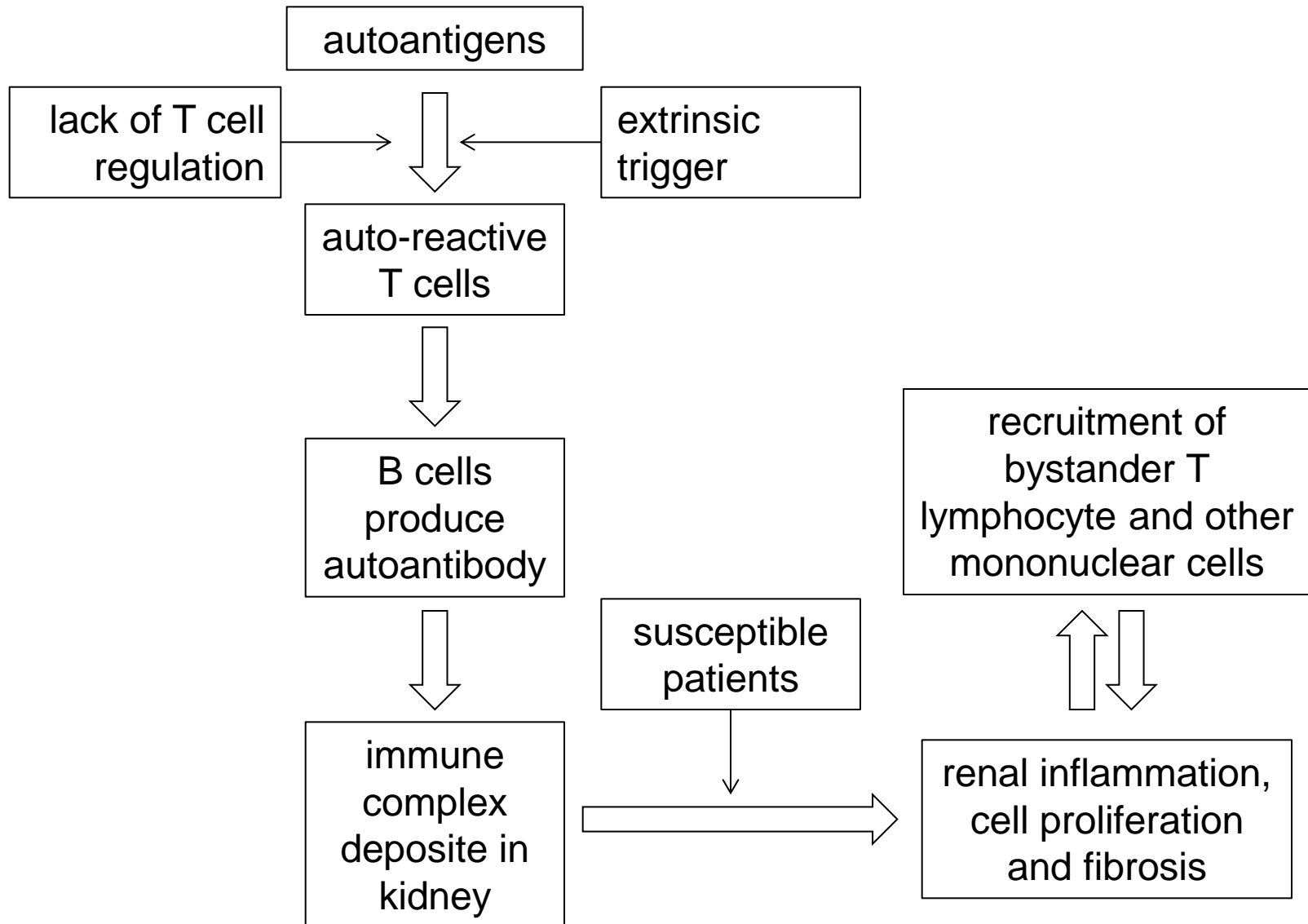
# Urinary mRNA and Lupus Disease Flare

Dr. CC Szeto

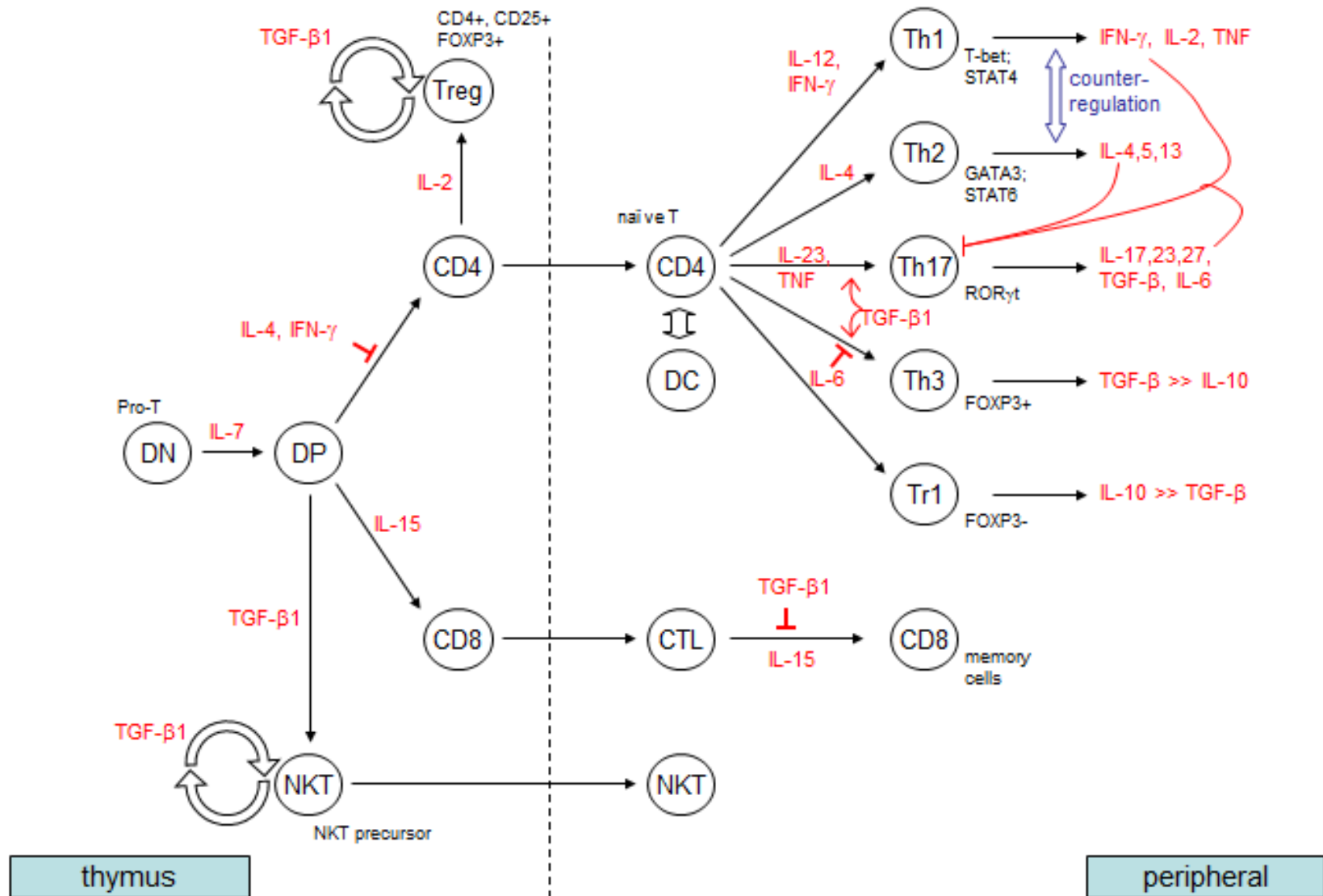
Department of Medicine & Therapeutics

The Chinese University of Hong Kong

# Hypothetical model

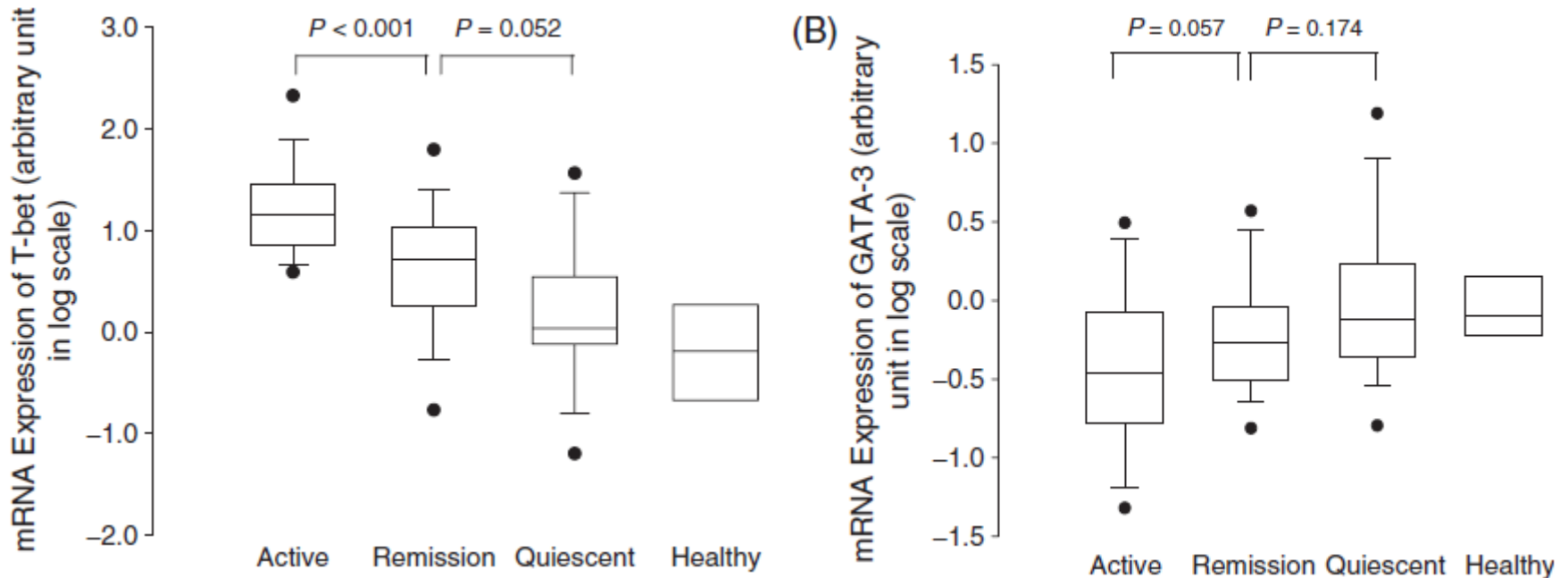


# Lymphocyte subsets



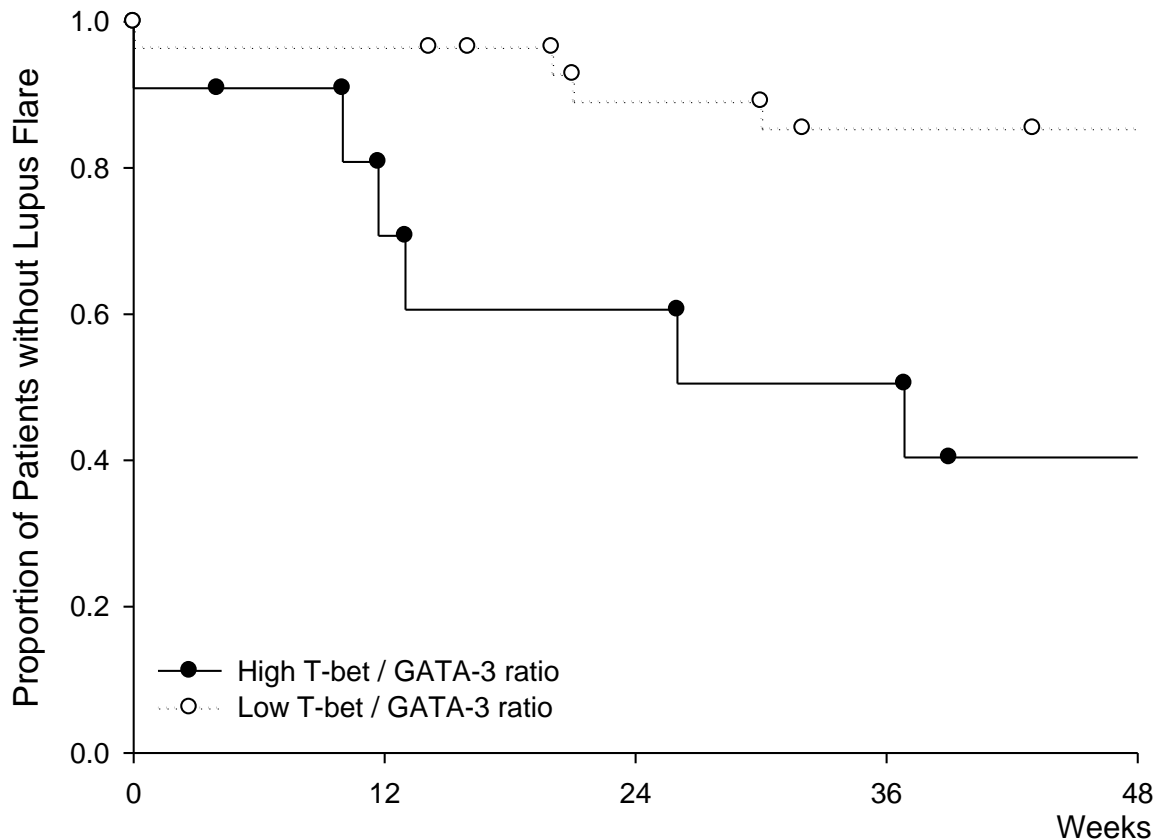
# Th1 / Th2 imbalance

- 100 patients and 10 controls



Conclusions: Patients with active lupus nephritis have increased T-bet and depressed GATA-3 expression in urinary sediment and kidney, indicating a predominant Th1 lymphocyte activation.

# Does it predict subsequent flare?

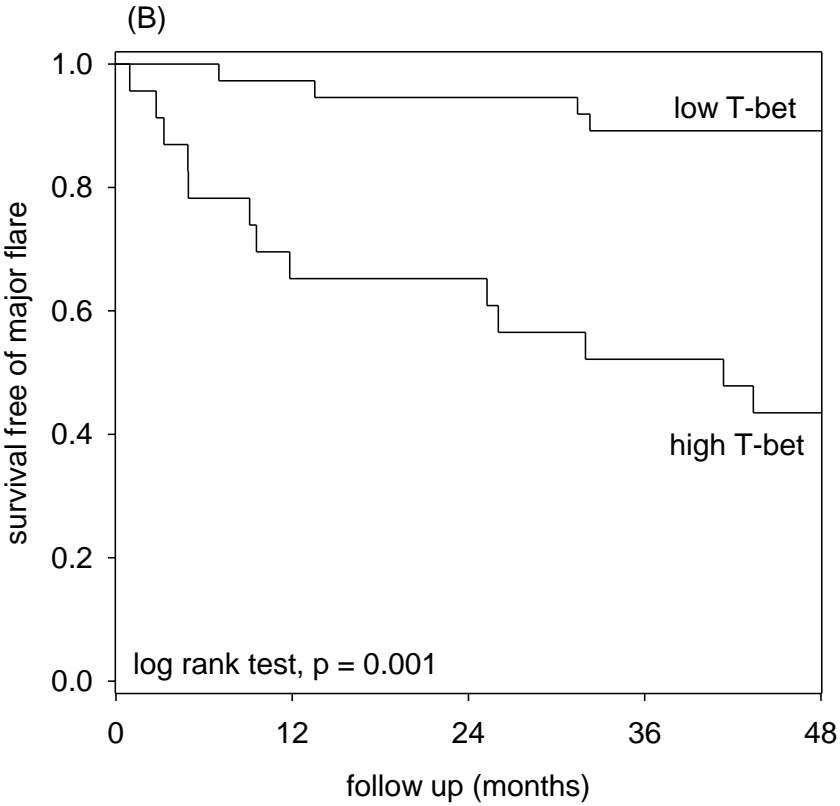
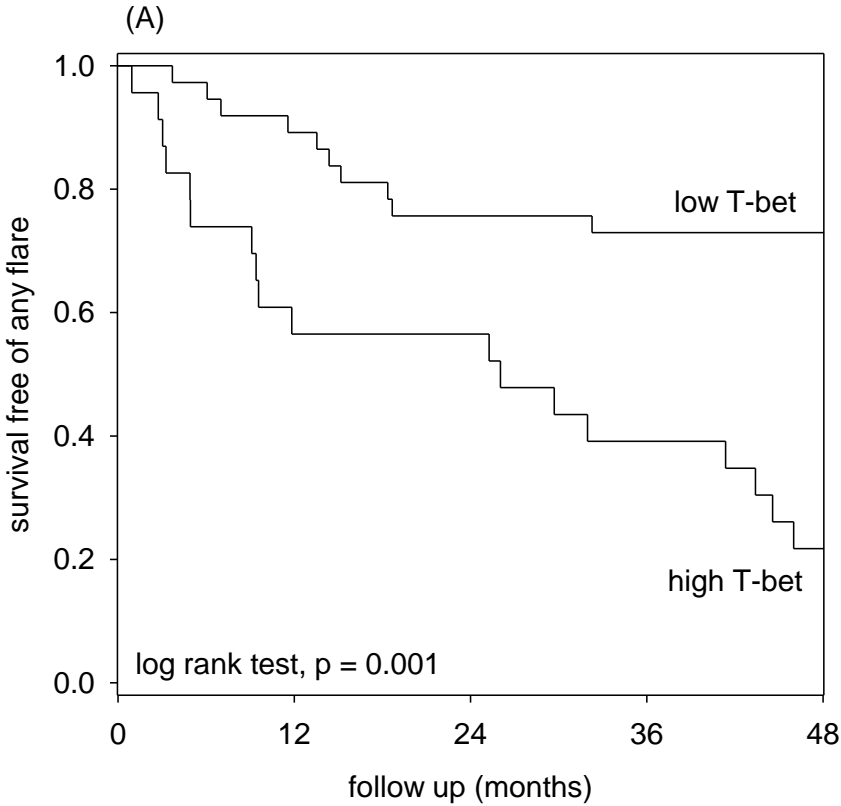


Conclusions: Patients with clinically quiescent lupus but increased T-bet to GATA-3 expression ratio in urinary sediment have a higher chance of disease flare, probably because of underlying Th1 lymphocyte activation.

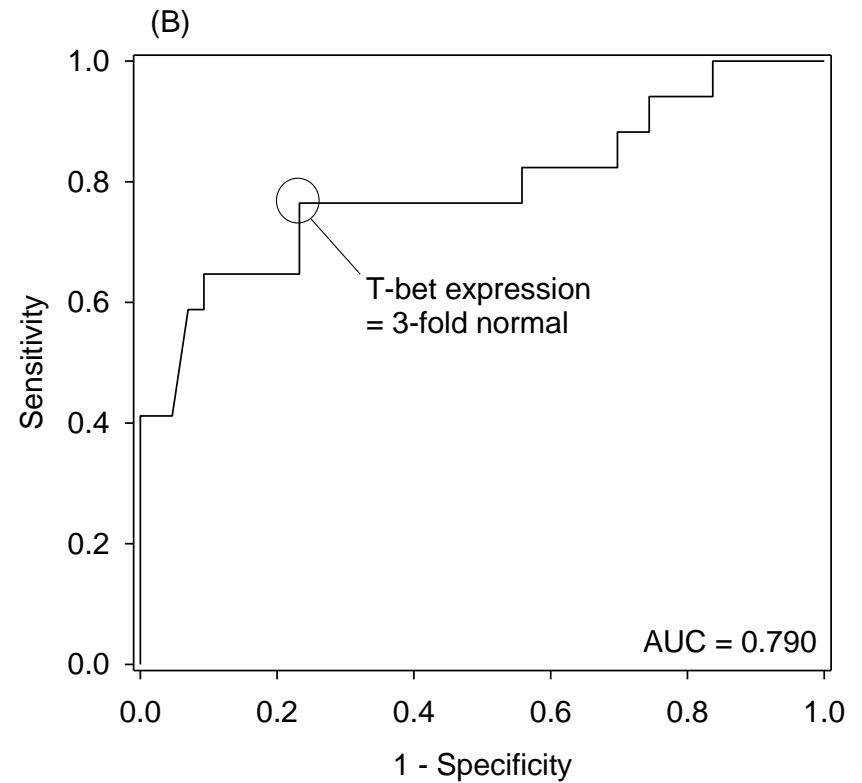
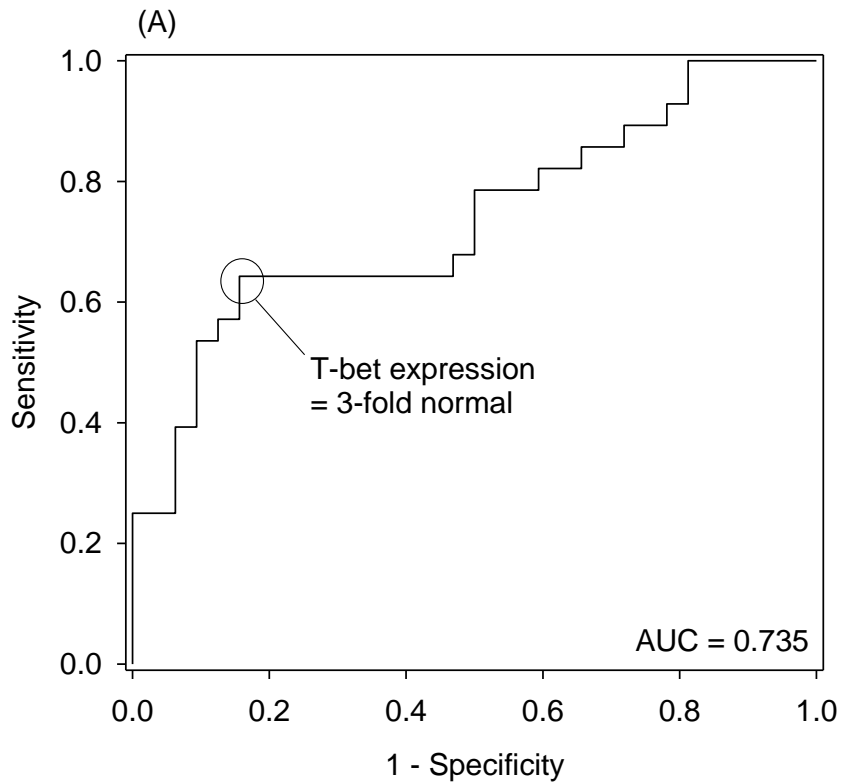
# Validation study

- 60 quiescent SLE patients
- urinary mRNA expression of T-bet and GATA-3 quantified by the RT-QPCR
- patients were followed for 4 years for disease flare

# T-bet level is important



# Cut-off value



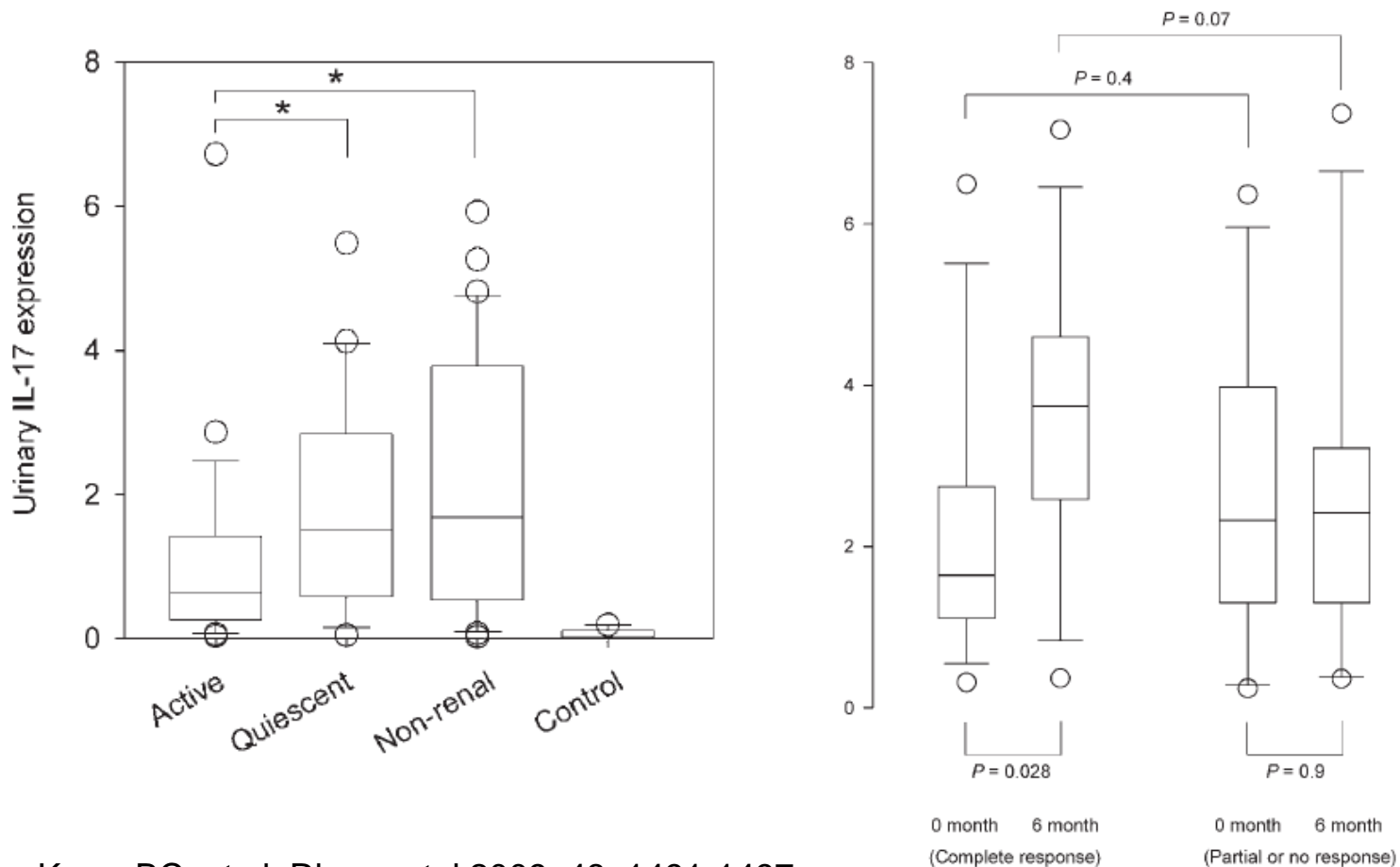


## Conclusion of this part

- high urinary T-bet mRNA level was an independent predictor of lupus flare
- possibilities
  - short term immune system (Th1) activity ?
  - baseline tendency of Th1 activation ?

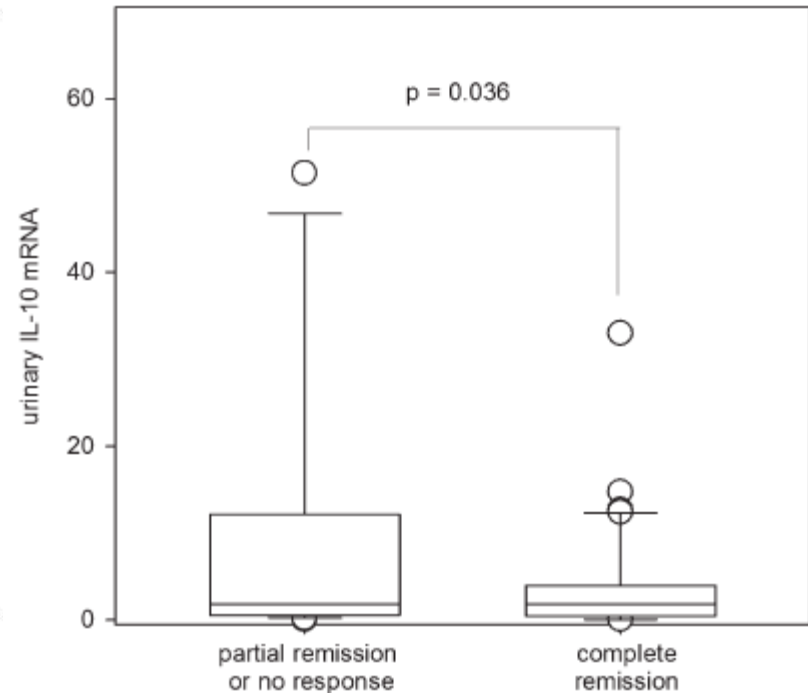
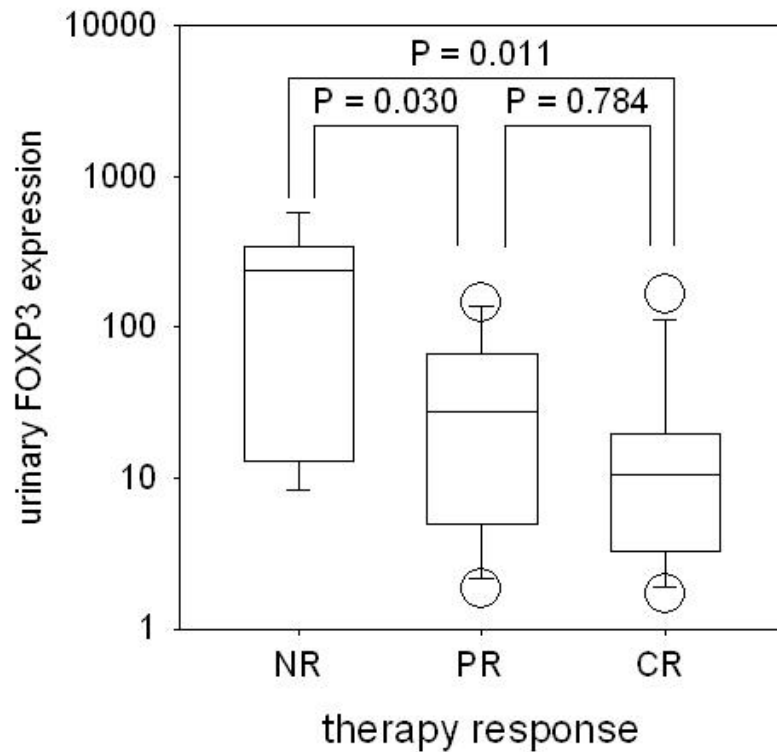
# Other lymphocyte subsets

- 78 patients with SLE nephritis with various disease activity
- urinary mRNA levels of Th17-related cytokines



# Regulatory T cells

- 2 studies with 98 patients with active lupus nephritis



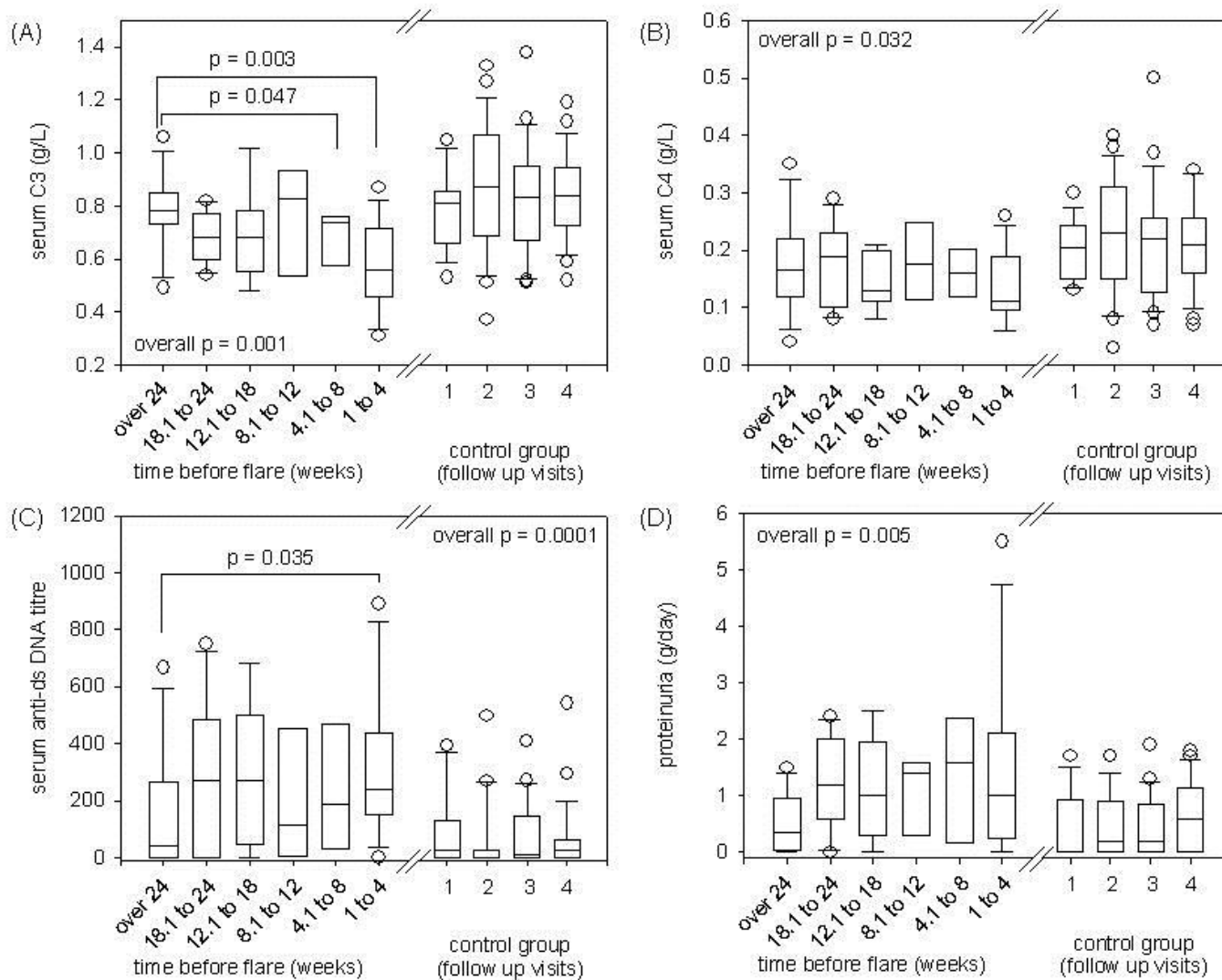
Wang G, et al. Rheumatol 2009; 48: 755-760.

Luk CC, et al. J Rheumatol 2015; 42: 1150-1155.

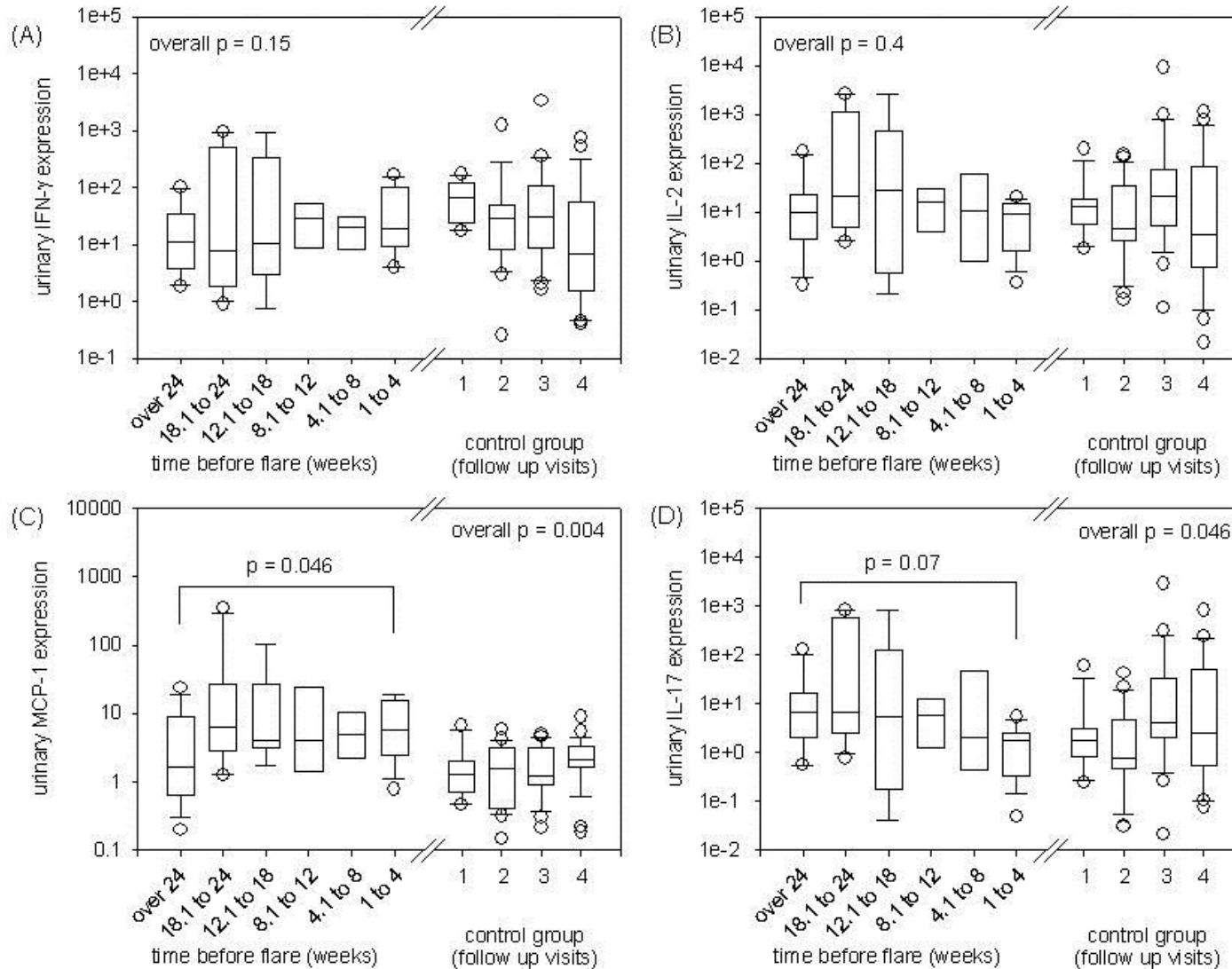
# Is monitoring of urinary mRNA useful?

- cohort of 134 adult SLE patients
- prospectively followed for 56 weeks
- identified 19 patients with a single disease flare
- compared to 19 matched controls with no disease flare during the same period
- mRNA levels of eight pre-defined target genes in their urinary sediment before disease flare were measured

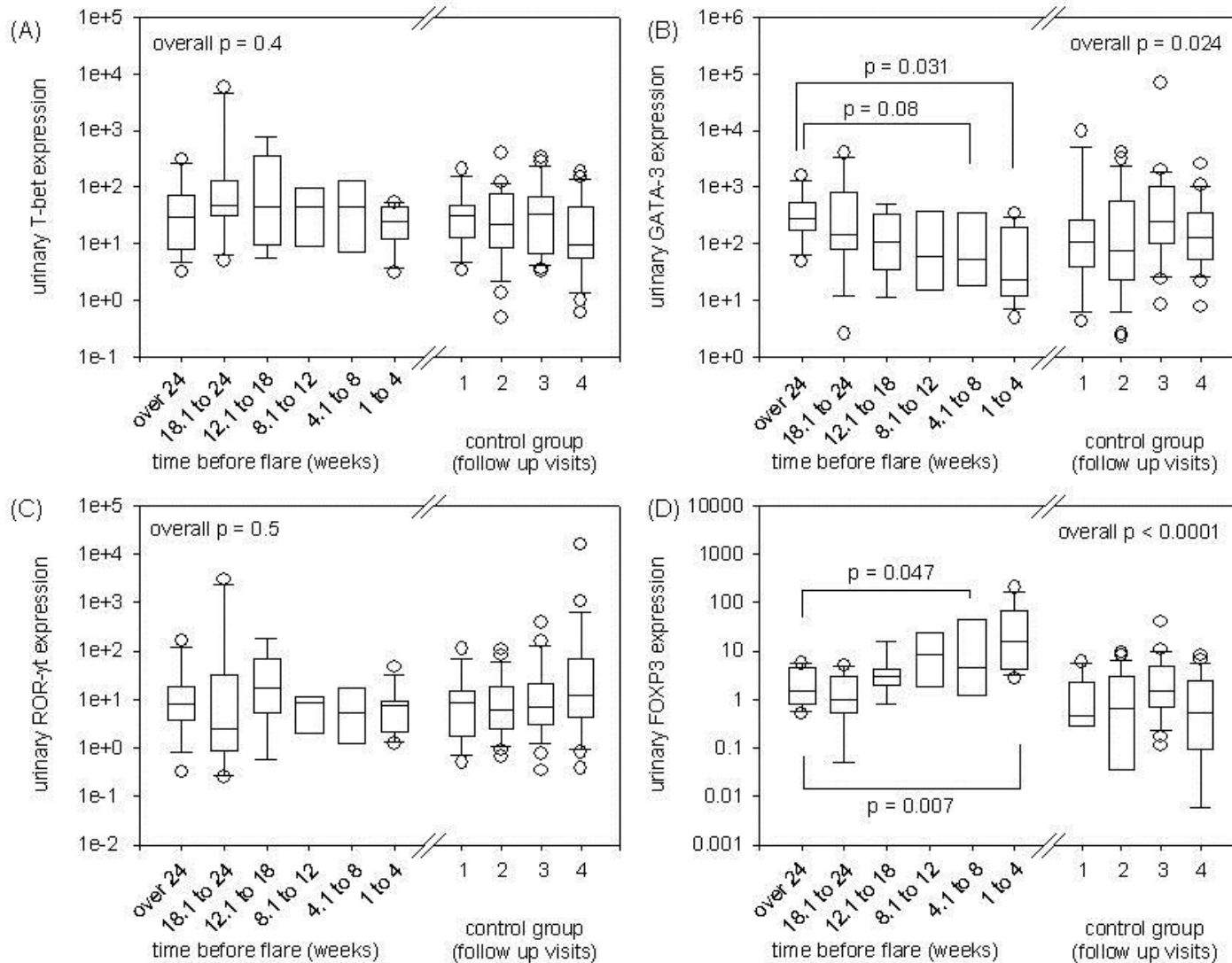
# Change in serological markers



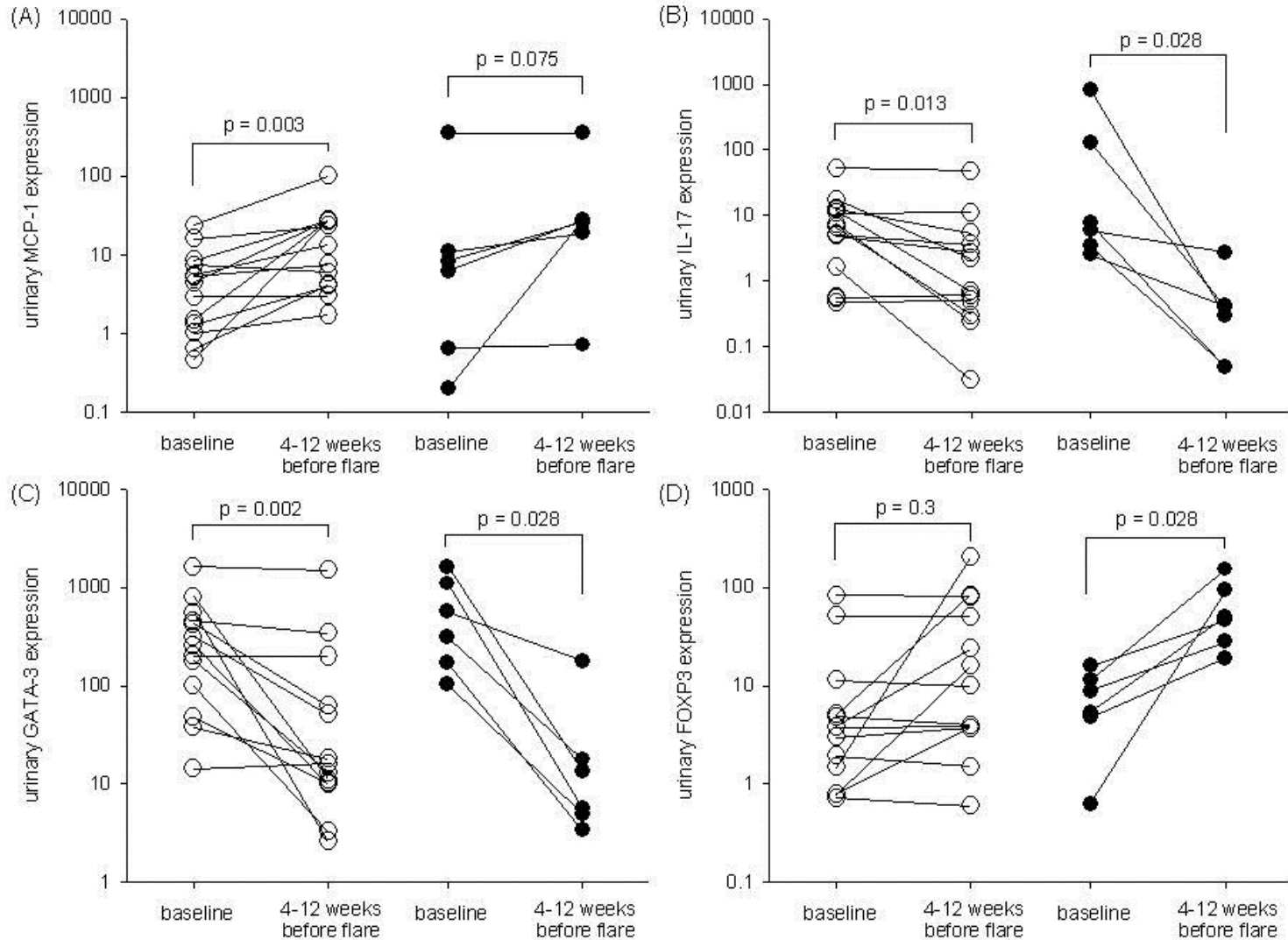
# Change in inflammatory cytokine mRNA



# Change in Th transcription factor mRNA

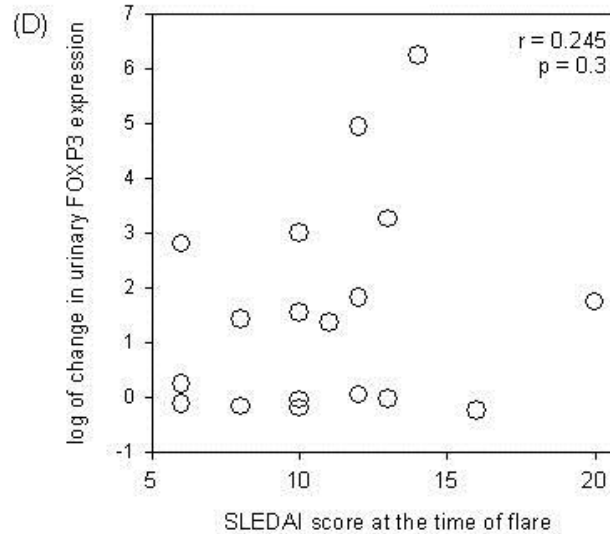
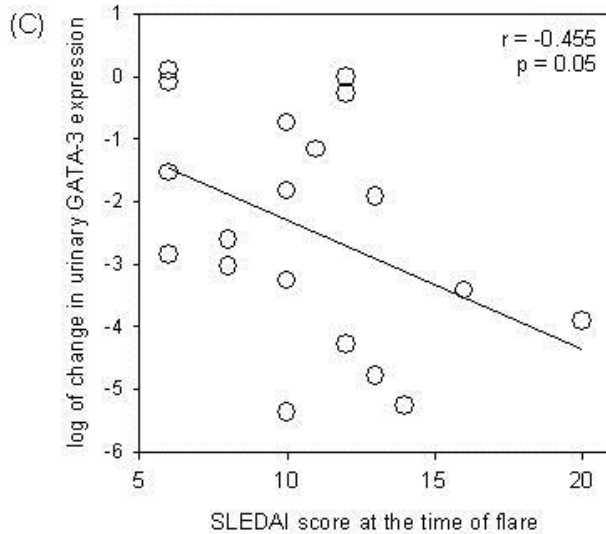
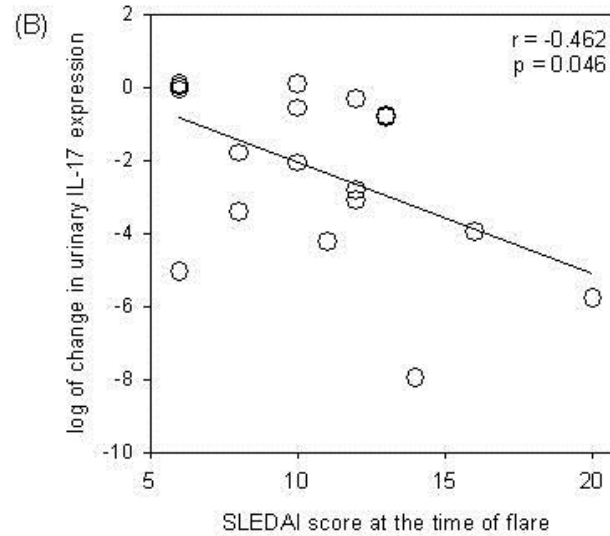
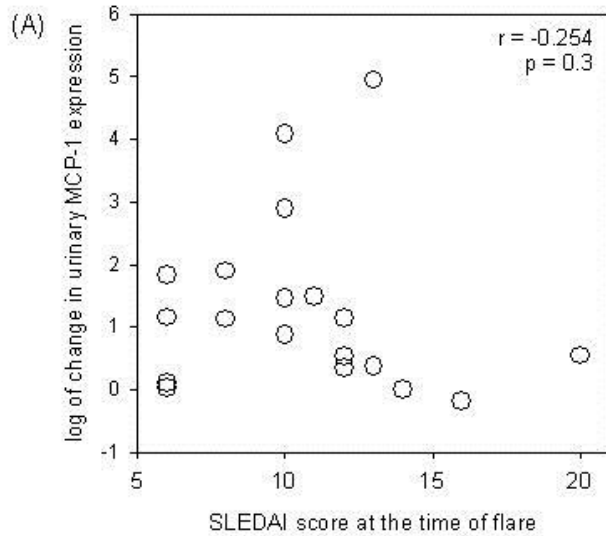


# Major vs minor flares





# Severity of flare and change in urinary mRNA



# Summary

- baseline urinary T-bet mRNA level in quiescent SLE patient is an independent risk factor of subsequent flare
- serial monitoring of MCP-1, IL-17, GATA-3 and FOXP3 mRNA level in urinary sediment may provide an early clue for detecting disease flare

# Further research questions

- predictive accuracy and cost-effectiveness when added on to current serological monitoring
- optimal frequency of monitoring
- role of pre-emptive treatment
- prediction of refractory disease

# Acknowledgement

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- 
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