CONNECTIVE TISSUE DISEASES

Disease severity directly affected by diet in a mouse model of SLE

Systemic lupus erythematosus (SLE) aetiology, although incompletely understood, is known to have a genetic element and to be influenced by hormones and environmental factors, such as diet. Research from Bruce Richardson and colleagues, published in *Arthritis & Rheumatism*, now shows that modification of dietary transmethylation micronutrients can directly affect disease severity in mice that are genetically predisposed to develop lupus.

“...lupus-prone mice ... fed the diet enriched in transmethylation micronutrients were protected against disease...”

Epigenetic research has established that environmental factors can influence gene expression by blocking T cell DNA methylation, which results in expression of genes that are normally silent. DNA

methylation patterns are determined by levels of DNA methyltransferase 1 (DNMT1), which are regulated by ERK signalling, as well as by dietary availability of methyl donors. Previous work by Richardson and co-workers showed that DNMT1 levels are low in T cells from patients with active SLE.

“We hypothesized that low DNMT1 levels could synergize with a diet poor in transmethylation micronutrients and might make lupus flare,” explains Richardson. “We used a transgenic lupus mouse model in which T-cell *Dnmt1* levels could be selectively decreased in T cells when doxycycline is added to their drinking water.”

Lupus-prone (C57BL/6xSJL) mice and lupus-resistant (C57BL/6) mice into which this doxycycline-inducible T-cell Erk defect had been bred were fed diets either enriched or poor in methyl donors, with or without doxycycline in their drinking water. Doxycycline-treated

lupus-prone mice with restricted methyl donor intake developed haematuria and glomerulonephritis, whereas those fed the diet enriched in transmethylation micronutrients were protected against disease. Lupus-resistant mice treated with doxycycline and fed the diet poor in methyl donors developed milder symptoms than those seen in the lupus-prone mice on the same diet.

Richardson concludes, “the implications are that a diet poor in transmethylation micronutrients can influence disease severity in people genetically predisposed to lupus, and that environmental agents causing oxidative stress can synergize with a poor diet to increase flare severity”.

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Original article Strickland, F.M. *et al.* Diet influences expression of autoimmune associated genes and disease severity by epigenetic mechanisms in a transgenic lupus model. *Arthritis Rheum.* doi:10.1002/art.37967