Anti-DNA Activity in Systemic Lupus Erythematosus

Hughes GR, Cohen SA, Christian C.

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For me, the true excitement of laboratory research came with our initial studies of the DNA-binding test – at the end of each day setting up the assay incubations, the results rolling out on the printer were striking in their clarity: DNA binding of normal serum 0%, 10%, 5%, 15% ….DNA binding our lupus patients’ sera 90%, 85%, 100%, 95%.

In serial clinical studies, we found that fluctuations in DNA binding broadly (though not slavishly) mirrored disease activity, and concluded that “since the serological phenomena may antidate clinical exacerbations of SLE …they can provide guides in management…” [7].

In 1967, four groups reported the finding of antibodies directed against DNA in the serum of lupus patients [1-4]. Two years later, a young post-doc fellow, Ted Pincus, working with Peter Schur, Norman Talal, John Decker and Charles Christian, described a sensitive radioimmunoassay for the detection of anti-DNA antibodies – a process based on a method previously described by R.S. Farr [5]. This assay, subsequently published in the New England Medical Journal [6], looked very promising as a clinical tool, and Dr. Christian asked two of his new fellows, Selwyn Cohen and myself, helped and guided by Rob Lightfoot, to set it up and look into its clinical potential.

Both of us were new recruits to the lab: our learning curves were steep – even the making up of buffer solutions required serious concentration. And improvisation played a prominent role. For example, to photograph our ouchterlony plates we cut circular holes in the base of upturned polystyrene ice buckets in order to get a good light source from below.

For me, and I’m sure for my other clinical fellow colleagues, the experience gained from working with Chuck Christian, and rubbing shoulders with some of the great of American rheumatology, were to leave a lifelong impression.

References

Pancreatic cancer immunotherapy

Pancreatic ductal adenocarcinoma (PDA) is a particularly deadly form of cancer for which few therapies have shown efficacy. The tumor microenvironment in PDA is largely immunosuppressive, blocking antitumor immunity. Beatty et al. treated a small cohort of PDA patients with gemcitabine chemotherapy plus a monoclonal antibody that activates CD40, a protein known to promote T cell immunity. Because this combination showed efficacy in a small number of patients, the same treatment was analyzed in a mouse model of PDA. A subset of CD40 antibody-treated mice also showed tumor regressions. However, the antitumor effects depended not on T cells, but on macrophages. Macrophages that had infiltrated the tumors after antibody treatment were also tumoricidal in vitro. Thus, activation of macrophages by CD40 may promote antitumor immunity in PDA.

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Eitan Israeli

“It is easier to fight for one’s principles than to live up to them”

Alfred Adler (1870-1931), Austrian physician and psychotherapist and founder of the school of individual (differential) psychology, which advocated a holistic approach to the study of character. This signaled his break from Freud and the Psychoanalytic Society of Vienna that they had co-founded. Adler’s theories had a huge influence on 20th century psychotherapy