THERAPY

Response to T-cell-dependent vaccine thwarted by TNF blockade

Humoral responses to a T-cell-dependent hepatitis B vaccine are severely compromised by anti-TNF therapy, reveals a study in patients with spondyloarthritis (SpA). Phenotypic analyses of circulating memory B cells, as well as a comparative lack of restriction in humoral response to a T-cell-independent vaccine, showed that B-cell maturation in germinal centres was compromised by the therapy.

“These data plead for adapted vaccination strategies...”

“We observe a strong suppression of the induction of T-cell-dependent antibodies against hepatitis B when patients receive their primary vaccination during TNF blockade,” says Dominique Baeten, a lead author of the new study. Coupled with evidence of suppressed somatic hypermutation, he continues, the

findings indicate that “TNF blockade can interfere with T-cell-dependent germinal centre responses.”

Previous studies indicated that patients with SpA or rheumatoid arthritis (RA) treated with anti-TNF agents do not develop IgG antibodies against T-cell-dependent nuclear antigens. Furthermore, TNF blockade in rats inhibited alloimmune response to transplantation, prolonging graft survival.

“Studying the induction of autoimmune or alloimmune response in humans is very challenging,” explains Baeten; “therefore, we used a vaccination approach with which we could control the timing of induction of the response and compare T-cell-independent and T-cell-dependent responses.”

Patients with SpA treated with infliximab, etanercept, or no TNF blocker (10 in each group) were vaccinated against hepatitis B and *Streptococcus pneumoniae*—a T-cell-independent

vaccine—12 weeks after the start of therapy. The authors chose to study patients with SpA as they lack the overt B-cell alterations seen in patients with RA.

At week 26, median antibody titres against hepatitis B were 595 IU/ml in those not receiving anti-TNF therapy, but only 10 IU/ml in patients taking TNF blockers ($P = 0.005$). By comparison, the *S. pneumoniae* vaccine induced average titres of 3,300 mU/ml and 1,545 mU/ml in anti-TNF treated and untreated patients, respectively ($P = 0.01$).

“These data plead for adapted vaccination strategies for T-cell-dependent vaccines in patients receiving TNF blockers,” concludes Baeten.

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