Figuring Out How Patients Develop an Anti-drug Response to a Therapeutic Monoclonal Antibody

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Functional Analysis of the Anti-adalimumab Response Using Patient-derived Monoclonal Antibodies

Adalimumab is an antibody that binds to tumor necrosis factor-α (TNFα) and stops it from activating TNF receptors. The antibody is used as a drug to treat inflammation associated with autoimmune diseases. However, adalimumab and its like can elicit anti-drug antibodies in patients. In this Paper of the Week, Theo Rispens at the Sanquin Blood Supply in The Netherlands and colleagues studied antibodies from two patients against adalimumab. By analyzing the binding regions for the antibodies against adalimumab, the investigators found that the anti-adalimumab antibodies bound to multiple epitopes on the drug that overlapped but were distinct. The authors say, “These results are important for understanding the relationship between self and non-self or idioptic determinants on therapeutic antibodies and their potential immunogenicity.”

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All monoclonal antibodies compete with anti-adalimumab 2.4 and TNF for the binding to adalimumab. A, binding of biotinylated anti-adalimumab 2.4 to adalimumab was inhibited by the addition of unlabeled monoclonal anti-adalimumab antibodies. The control monoclonal antibody cetuximab did not inhibit binding. B, in response to 1 ng of TNF, ECRF-24 cells produce IL-8 in the linear range of the titration curve. Adalimumab (30 ng) can neutralize TNF, thereby preventing IL-8 production. 0.1 µg of all antibodies (except anti-adalimumab 2.4) was sufficient to completely restore IL-8 production in the presence of adalimumab. Results represent mean and S.E. (error bars) from three experiments. ADA, anti-drug antibody; ADL, adalimumab.

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