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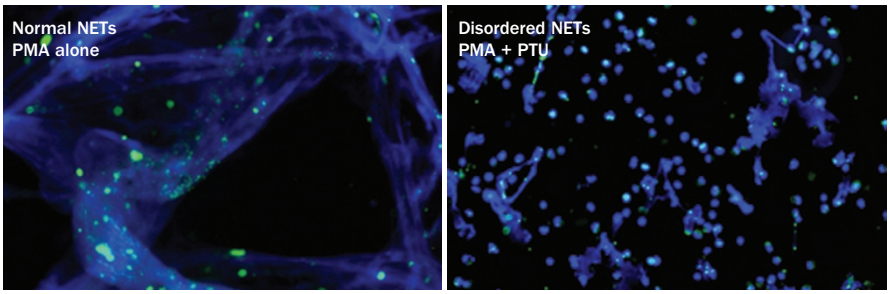
AUTOIMMUNITY

Disordered NETs implicated in pathogenesis of MPO-ANCA-associated vasculitis

Disordered neutrophil extracellular traps (NETs) produced as a result of propylthiouracil (PTU) treatment promote autoantibody production and trigger vasculitis in rat models, shows new research in *Arthritis & Rheumatism*.

The antithyroid drug PTU has been implicated in drug-mediated autoimmunity, in particular with MPO-AAV (vasculitis associated with myeloperoxidase–antineutrophil cytoplasmic antibodies [MPO–ANCA]). Given that NETs have been found in patients with MPO-AAV, Akihiro Ishizu and colleagues hypothesized that dysregulation of NETs could trigger the disease.

NETs were induced *in vitro* from human neutrophils by the application of phorbol myristate acetate (PMA), alone or with PTU. NETs induced with PTU had markedly altered morphology and were resistant to DNase I degradation—unlike 'normal' NETs (PMA alone), which were completely degraded by DNase I.



Treatment of neutrophils with PMA induces normal NET formation (chromatin, blue; myeloperoxidase, green), but induction with PMA plus PTU leads to disordered NETs (compact chromatin fibres). Abbreviations: NETs, neutrophil extracellular traps; PMA, phorbol myristate acetate; PTU, propylthiouracil. Courtesy of A. Ishizu.

Importantly, immunization of rats with abnormal NETs led to MPO–ANCA production alongside vasculitis in the lung (pulmonary capillaritis), as did oral PTU and intraperitoneal PMA administered to rats.

Abnormal NETs that persist in the body could be an important stimuli in autoimmunity. "Undetermined environmental factors could induce disordered NET formation and trigger MPO-AAV in a similar manner to PTU," says Ishizu, who plans further work to identify these factors and develop more suitable MPO-AAV animal models.

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Original article Nakazawa, D. *et al.* Abnormal confirmation and impaired degradation of NETs induced by propylthiouracil: implication of disordered NETs in MPO-ANCA-associated vasculitis. *Arthritis Rheum.* doi:10.1002/art.34619