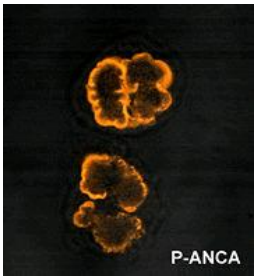
Antineutrophil cytoplasmic autoantibody (ANCA)

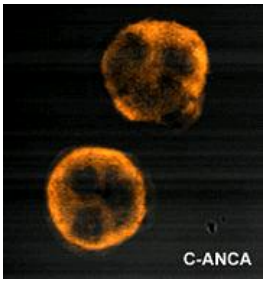
Comes in 2 distinct flavours, p-ANCA and c-ANCA.

"P" stands for perinuclear and "C" stands for cytoplasmic. Thanks to Wikipedia for the below pictures:

P is for PERINUCLEAR.

C is for CLASSICAL but may as well stand for "cytoplasmic"





The names are arbitrary; the pattern you see is staining on ethanol-fixed neutrophils. For some reason the staining process gathers the immunofluorescence antibody targets in these areas. The technique of immunofluorescence is basically all about staining the sample with antibodies targeted at the thing youre interested in, and then staining it again with fluorescing antibodies which are targeted at the first antibody.

So what the hell are these targets, then? The initial stain antibody has to bind to something.

For p-ANCA the target seems to be **MYELOPEROXIDASE**.which is a neutrophil granule protein, which generates free radicals.

For c-ANCA there are several targets, of which the commonest is **PROTEINASE 3.**

ASSOCIATONS:

These weird conditions are all grouped under the blanket term "ANCA-associated systemic vasculitides", or ASA. They are all faintly related.

p-ANCA is usually associated with

- **microscopic polyangiitis**
- **Churg-Strauss** (though only about 50% of the patients are ANCA-positive)
- **crescentic glomerulonephritis** which is actually the renal form of microscopic polyangiitis.

c-ANCA is usually associated with Wegener's granulomatosis.

Pathogenesis of ANCA- associated vasculitides:

WARNING: conjecture!
The below-presented mechanism may not represent the opinion of the scientific community at large, and may embarrass you when quoted to senior consultants.

Infection, somewhere… → **Pro-inflammatory cytokines are released, quite legitimately, as a part of the larger inflammatory response.**

Neutrophils are "PRIMED", i.e. express those CD11b adnehsion molecules on their surface.

A major portion of this priming business is the ANCA antigens, proteinase 3 and myeloperoxidase, getting traslocated to the cell surface out of the lysosomes they are usually stored in.

Induction of adhesion molecules on the endothelial surface, eg. selectin, VCAM, ICAM-1

The neutrophils now have antigens on their surface. The ANCA antibodies bind to these targets; and the Fc portions of the antibodies bind to the FC receptors. This serves to trigger neutrophil adhesion to vessel walls.

The now-activated neutrophils, coated with antibody, diapedese into the vessel walls. The normal mayhem ensues.

ANCA is floating around in the bloodstream… for whatever reason. There is still no good theory as to why we develop these antibodies. There is an association with a functional polymorphism of the PTPN22 gene, which encodes tyrosine phosphatase (which becomes increased in rheumatoid arthritis, SLE, type 1 diabetes and Hashimoto's thyroiditis.). Exposure to silica or cocaine seems to predispose to Wegeners. Smoking is protective against the ANCA vasculitides. **Treatment with propylthiouracil causes ANCA vasculitis in 50% of cases, and continues after treatment is ceased.** In short, nobody knows.