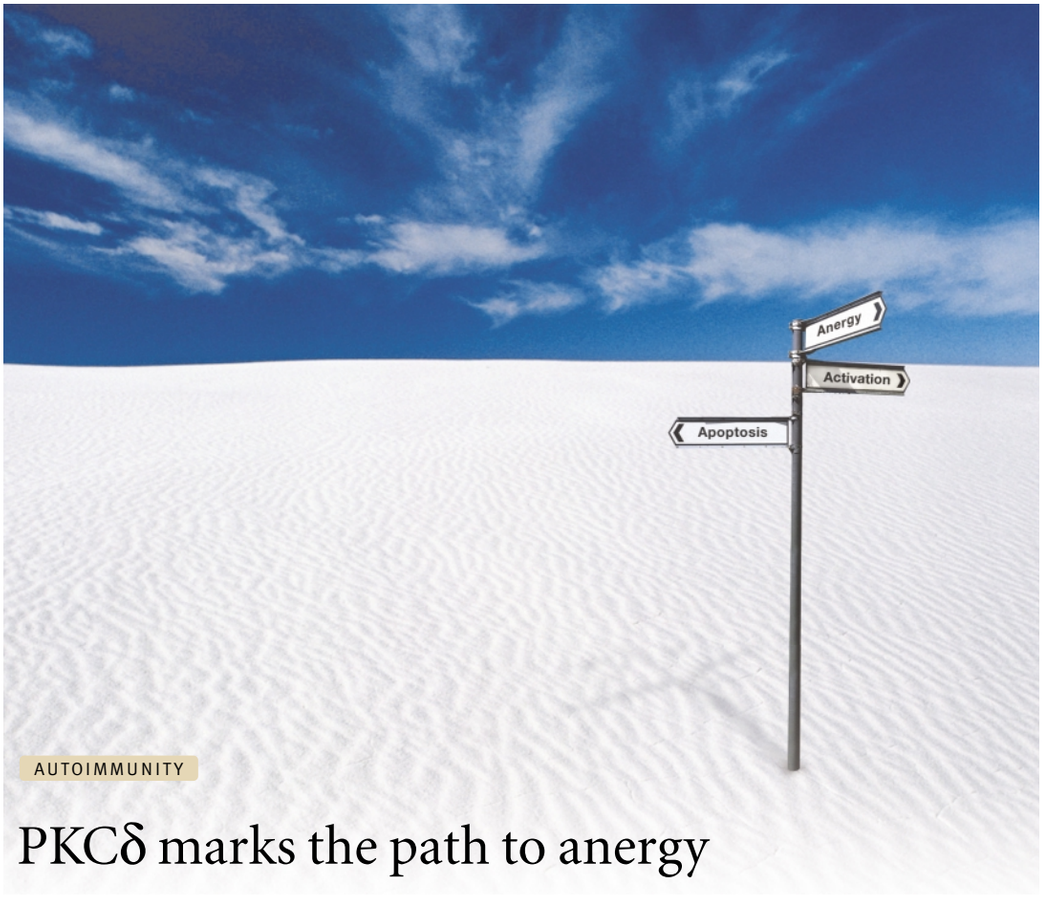
IN THE NEWS

New cure for baldness?
Sulfasalazine — an anti-inflammatory drug that is used to treat various autoimmune conditions, including psoriasis — has been in the news following reports that treating people who have bald patches with sulfasalazine can lead to hair re-growth. Research from the University of Michigan, published in the *Journal of the American Academy of Dermatology*, shows that sulfasalazine can help to stimulate hair growth in some people who have alopecia areata.

Alopecia areata affects approximately 2% of the population, and it can result in the development of bald patches or the complete loss of hair. In this study, "cosmetically acceptable regrowth" was observed in 23% of patients who were tested. The authors state that, "sulfasalazine may be considered for systemic treatment of severe alopecia areata".

John J. Voohees from the University of Michigan told *Reuters Health* that, "When it works, it works great", but that, "in at least one half of people it doesn't work at all". Voohees went on to explain that alopecia occurs when the immune system attacks hair follicles, which causes inflammation and prevents hair growth. Sulfasalazine might help to treat alopecia by inhibiting inflammation (*Reuters Health*).



AUTOIMMUNITY

PKCδ marks the path to anergy

Gene targeting has revealed a specific and essential role for protein kinase-Cδ (PKCδ) in the induction of B-cell anergy — the state of functional inactivation that is induced in response to self-antigens. *Pkcδ*-knockout mice have been engineered independently by two groups, who report their findings back-to-back in *Nature*.

Unravelling the differences between the B-cell-signalling pathways that lead to activation, anergy or death is the key to understanding B-cell tolerance, and it might lead to new therapies for antibody-mediated autoimmune diseases. PKCδ is a member of the novel PKC family, which includes PKCδ, -ε, -θ and -η. It is emerging that the different family members have diverse roles in the immune system and are implicated in various cellular processes, such as growth, differentiation and death. PKCδ is known to be expressed highly by B cells and to be involved in B-cell receptor (BCR) signalling, but its physiological role had not been determined.

Both groups report that the spleen and lymph nodes of *Pkcδ*$^{-/-}$ mice are enlarged, owing to an expansion of the B-cell population; however, B-cell development is normal. An abundance of germinal centres in the spleen and lymph nodes of *Pkcδ*$^{-/-}$ mice indicates that peripheral B cells are out of control.

What might be driving the aberrant activation of B cells in *Pkcδ*$^{-/-}$ mice? Both groups show that there is a marked increase in the production of IgG antibodies that are specific for nuclear antigens. Moreover, histological analysis of the kidneys showed pathology that is the result of immune-complex deposition. This indicates that B-cell tolerance to self-antigens is defective in the absence of PKCδ.

Mecklenbräuer and co-workers used the classic hen-egg lysozyme (HEL) transgenic model to disect the tolerance defect. *Pkcδ*$^{-/-}$ mice were crossed with mice that were doubly transgenic for an HEL-specific BCR, and either a membrane or soluble form of HEL. As expected, HEL-specific B cells were deleted in mice that expressed membrane HEL, and this deletion was unaffected by PKCδ deficiency. However, in mice that expressed soluble HEL, *Pkcδ*$^{-/-}$ HEL-specific B cells failed to become anergic and, instead, proliferated and differentiated into antibody-producing cells.

This group then examined the responses of *Pkcδ*$^{-/-}$ mice to antigenic stimulation. They found that PKCδ-sufficient and PKCδ-deficient B cells had similar thresholds for activation *in vitro*, and the levels of proliferation and kinetics of calcium flux were comparable. The authors conclude that *Pkcδ*$^{-/-}$ B cells have a specific defect in the induction of anergy, rather than a generalized enhancement of signalling. By contrast, Miyamoto and colleagues found that the proliferation of *Pkcδ*$^{-/-}$ B cells *in vitro* in response to various mitogenic stimuli was increased, and their study implicates the increased expression of interleukin-6 — a growth-promoting cytokine — in the absence of PKCδ as a possible mechanism. This apparent discrepancy between the two studies remains to be resolved.

Jennifer Bell

References and links

ORIGINAL RESEARCH PAPER Mecklenbraüer, I., Saijo, K., Zheng, N. Y., Leitges, M. & Tarakhovsky, A. Protein kinase Cδ controls self-antigen-induced B-cell tolerance. *Nature* **416**, 860–865 (2002) | Miyamoto, A. *et al*. Increased proliferation of B cells and auto-immunity in mice lacking protein kinase Cδ. *Nature* **416**, 865–869 (2002)

WEB SITE

Alexander Tarakhovsky's lab:
http://www.rockefeller.edu/labheads/tarakhovsky/tarakhovsky.html