C3$^{-/-}$ mice failed to induce ICOSL$^+$ B cells in tumours exposed to chemotherapy and, accordingly, had reduced sensitivity to chemotherapy. Moreover, mice with B cell-specific *Cr2* deletion showed no chemotherapy-induced ICOSL upregulation and a compromised antitumour T cell response.

In vitro studies of human cells showed that the complement–CR2 axis is also required for chemotherapy-induced ICOSL$^+$ B cell generation and revealed that chemotherapy-induced tumour cell death, including the associated exposure of phosphatidylserine, activates the complement system. In co-culture experiments, B cells exposed to chemotherapy-treated tumour cells markedly increased antitumour T cell responses in the presence of human serum, an effect that could be abrogated by blockade of ICOSL or by heating the serum to inactivate complement.

During their study, the authors noted that some of the breast cancer lines used failed to induce ICOSL$^+$ B cells after chemotherapy. Expression analysis revealed that levels of complement inhibitor CD55 were lower in cancer cell lines that could induce ICOSL$^+$ B cells than in those that could not. Accordingly, overexpression of CD55 increased tumour size in mice treated with chemotherapy, prevented the induction of ICOSL$^+$ B cells and was instead associated with infiltration of T_{reg} cells. The opposite effects were observed following *Cd55* silencing in tumour cells.

Finally, clinical importance was suggested by the observation that tumoural CD55 expression was higher in patients who did not respond to neoadjuvant chemotherapy and was associated with worse clinical outcomes. This, the authors suggest, makes CD55 an attractive therapeutic target to enhance the efficacy of immunogenic chemotherapy.

Lucy Bird

ORIGINAL ARTICLE Lu, Y. et al. Complement signals determine opposite effects of B cells in chemotherapy-induced immunity. *Cell* https://doi.org/10.1016/j.cell.2020.02.015 (2020)
RELATED ARTICLE Sharonov, G. V. et al. B cells, plasma cells and antibody repertoires in the tumour microenvironment. *Nat. Rev. Immunol.* https://doi.org/10.1038/s41577-019-0257-x (2020)

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antitumour immune responses. They report that desilylation mediated by the cancer-imaging probe phenylalanine trifluoroborate (Phe-BF_3) can be used to release active GSDMA3 from silyl-linked gold nanoparticles. As both nanoparticles and Phe-BF_3 accumulate in tumours, this enables the tumour-selective release of GSDMA3. In two mouse models of breast cancer, three rounds of treatment with the GSDMA3-conjugated nanoparticles and Phe-BF_3 resulted in massive tumour shrinkage, which was associated with an increased proportion of pyroptotic cells in the tumour and was shown to depend on increased infiltration of T cells and NK cells. Pyroptosis of less than 15% of tumour cells was sufficient to eliminate the entire mammary tumour graft. Of particular interest, one round of treatment with GSDMA3–nanoparticles and Phe-BF_3 did not prevent tumour growth but improved the response to subsequent checkpoint blockade with anti-PD1 therapy. This suggests that the inflammatory effects of gasdermin activation in the tumour environment could improve the efficacy of cancer immunotherapies by increasing lymphocyte infiltration and/or activation — in other words, turning 'cold' tumours 'hot'.

Kirsty Minton

ORIGINAL ARTICLES Zhang, Z. et al. Gasdermin E suppresses tumour growth by activating anti-tumour immunity. *Nature* **579**, 415–420 (2020) | Wang, Q. et al. A bioorthogonal system reveals antitumour immune function of pyroptosis. *Nature* **579**, 421–426 (2020)
RELATED ARTICLE Broz, P., Pelegrín, P. & Shao, F. The gasdermins, a protein family executing cell death and inflammation. *Nat. Rev. Immunol.* **20**, 143–157 (2020)

Journal Club

INTESTINAL PROTECTION WITHOUT T CELL HELP

Consider the scenario of a mouse that lacks all secondary lymphoid tissues and T cells. This mouse must co-exist with the huge biomass of microorganisms living in the gut. Can it do this? Amazingly, yes! A landmark paper by Sidonia Fagarasan and colleagues published in 2008 revealed that isolated lymphoid follicles (ILFs) in the gut can function as inductive sites for the generation of IgA-producing plasma cells in the absence of T cell help. This primordial mechanism for maintaining homeostasis with our microbiota could also explain why humans with hyper-IgM syndrome, who harbour mutations in CD40 and hence have defective B cell–T cell interactions, retain intestinal IgA responses.

At the time of this publication, my lab had been puzzling over why lymphotoxin (LT)-deficient mice have a selective deficiency in IgA. Seminal findings from Reina Mebius' group had shown that lymphoid tissue inducer (LTi) cells are a crucial source of LTαβ that, through stimulation of LTβ receptor on stromal cells, initiates the development of lymphoid tissue anlage. Fagarasan and colleagues made the next leap in our understanding by showing that LTαβ-expressing 'LTi-like' cells in the adult gut interact with gut-resident stromal cells to orchestrate T cell-independent IgA production within ILFs. Not only did this paper provide an explanation for IgA deficiency in LT-deficient mice, but it also showed that interactions within ILFs facilitate the proteolytic processing of transforming growth factor-β to its active form, which functions to promote antibody class switching to IgA.

> "among early studies that ushered in a new appreciation of 'LTi-like' cells, which we now know as innate lymphoid cells"

Fagarasan's paper was among early studies that ushered in a new appreciation of 'LTi-like' cells, which we now know as innate lymphoid cells. Indeed, Peter Lane in his commentary on this paper noted: "Just as the complexity of DC biology has emerged over the last 20 years, the next decade is likely to see the dissection of diversity in LTi subpopulations." Twelve years later that prophecy has been proved correct owing to seminal work by the Fagarasan lab and others.

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The author declares no competing interests.

ORIGINAL ARTICLE Tsuji, M. et al. Requirement for lymphoid tissue-inducer cells in isolated follicle formation and T cell-independent immunoglobulin A generation in the gut. *Immunity* **29**, 261–271 (2008)
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