How lung tissue forms immune cell hubs in times of need

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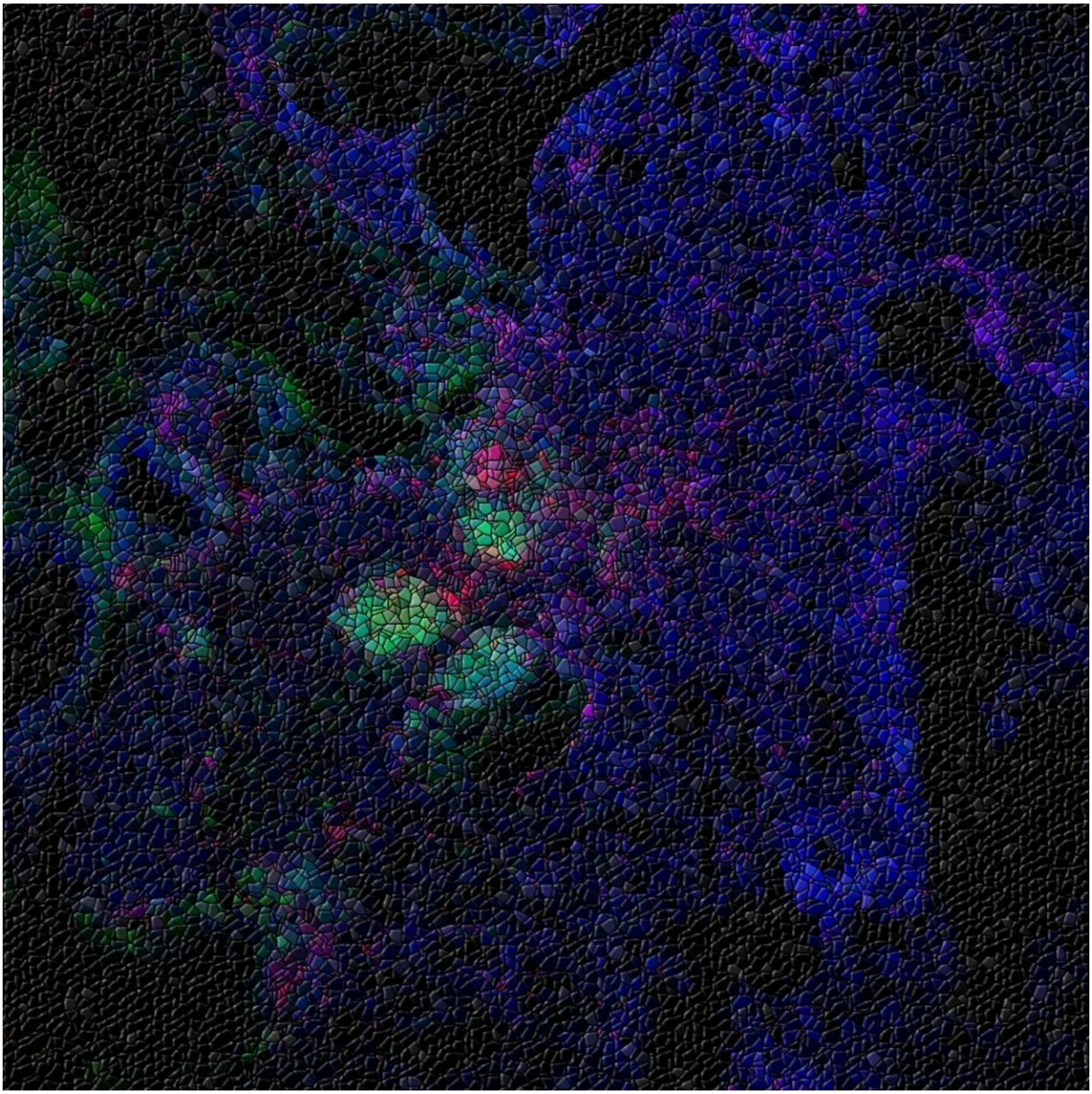

Mouse lung (blue) 14 days after influenza A infection with ectopic lymphoid structures identified by the presence of high numbers of B cells (in green) and T cells (in pink). The mosaic effect is a digital modification. Credit: Dr Alice Denton, Babraham Institute

Immunology researchers at the Babraham Institute have discovered how lung tissue in mice is remodelled in response to infection with influenza in order to support an immune system response. A key result of this tissue remodelling is the production of antibodies with the ability to provide protection against a wider range of related viruses. If the research findings can be applied to the development of the seasonal influenza vaccination, the result would be more robust protection against multiple influenza strains, not just the strain for which the vaccine is optimised against based on global epidemiology predictions. The research is published in the *Journal of Experimental Medicine* today.

"In the same way that crisis centres are created on the ground in the midst of a humanitarian effort, the immune system can commandeer non-immune-related tissues to create something that resembles an immune cell hub where white blood cells collaborate to generate a co-ordinated response to an invading pathogen." explains Dr. Alice Denton, BBSRC Future Leader Fellow at the Babraham Institute.

These transient microenvironments, called germinal centres, are vital for effective immune responses and the generation of our immune 'memory' which provides protection against subsequent infections. Despite their importance in health and disease, how germinal centres are formed in the lungs after infection is unknown.

The researchers found that germinal centre formation in the lungs is initiated via cascade of events, whereby a chemical message (type I

interferon) produced by lung cells in response to infection triggers the production of a chemical attractant—a 'come here' flag to the immune system. In response to this signal, B cells (the immune cells that produce antibodies) are recruited to the lungs and initiate the formation of germinal centres. These lung-based germinal centres produce a different repertoire of B cells; ones that produce more broadly reactive antibodies providing cross-protection across different influenza strains.

These findings indicate that understanding the compounds which stimulate a type I interferon response may be useful as vaccine additions to drive cross-protective antibody production in the lungs.

"One important function of germinal centres when responding to infection is that they support the creation of cross-reactive antibodies that can confer wider protection," says Dr. Michelle Linterman, research group leader at the Babraham Institute. "Being able to exploit this would be extremely beneficial in the case of the annual influenza vaccination where the vaccination is developed against the likely prevalent strain. In the case of vaccinating against one type of influenza virus, wider protection against other types of influenza strains would reduce infections and thereby improve health."

The research findings are also relevant to understanding immune responses that occur in non-lymphoid tissues and are known to be associated with autoimmune disease, infection, Chronic Obstructive Pulmonary Disease and cancer.

"Understanding how these ectopic immune structures form may enable the development of new therapeutics to specifically target these responses," concludes Dr. Denton. "In autoimmune disease, this has the potential to reduce the detrimental immune responses that are targeted against the body's own tissue."

More information: Denton et al. Type I interferon induces CXCL13 to support ectopic germinal center formation. *Journal of Experimental Medicine* , DOI: 10.1084/jem.20181216 , jem.rupress.org/content/early/… 9/02/04/jem.20181216

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