Study reveals how extremely rare immune cells predict how well treatments work for recurrent hives

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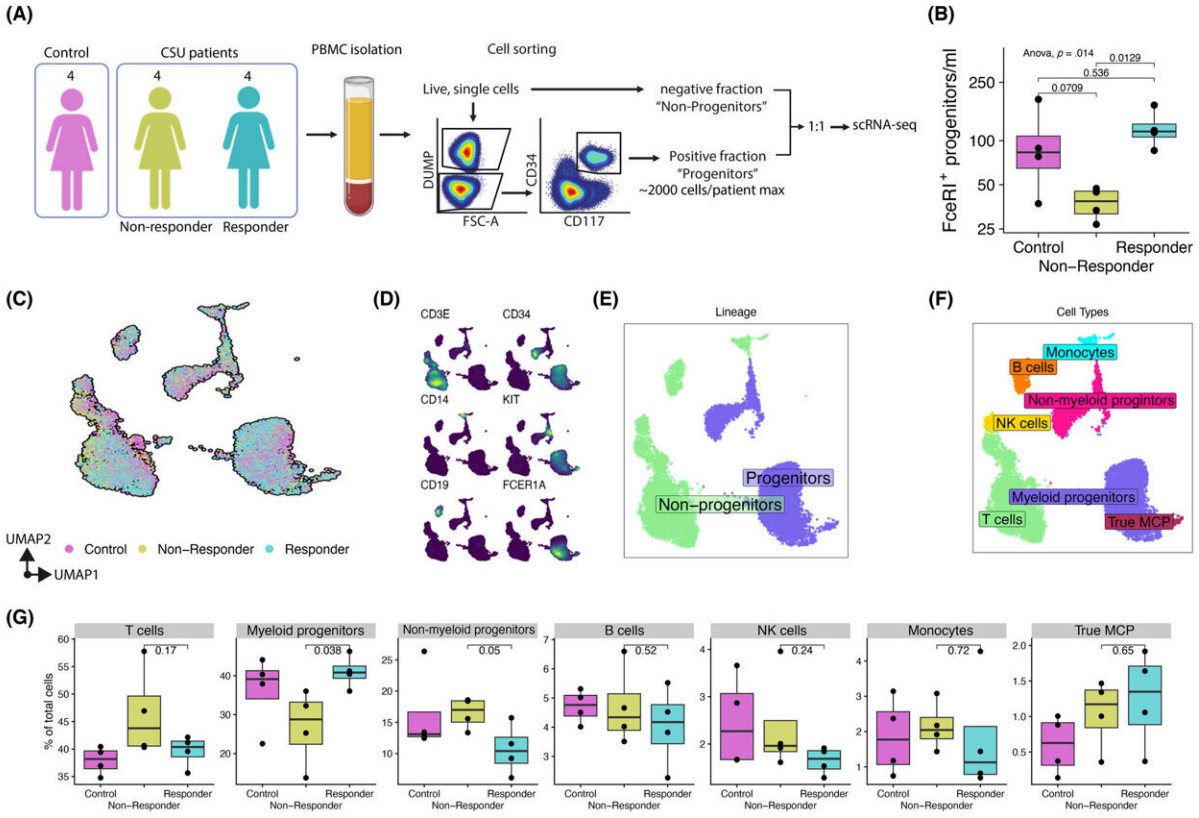

Single-cell RNA-Seq reveals that Lin−CD34+CD117+ contain both myeloid and lymphoid progenitors with a higher proportion of myeloid progenitors in CSU patients that subsequently responded to omalizumab. Credit: *Allergy* (2024).

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A study which examines the common skin condition, chronic spontaneous urticaria (CSU), characterized by recurrent hives, has been recently published by Trinity College Dublin researchers in the journal *Allergy*.

This study is the first of its kind to show a link between rare cell types and treatment response. Professor Niall Conlon, Clinical Professor, School of Medicine and Consultant Immunologist, St James's Hospital and Clinical Lead at Ireland's only UCARE center for urticaria management led the research team.

Chronic spontaneous urticaria (CSU) is a common but underreported disease, where individuals develop recurrent, unpredictable and intensely itchy hives and skin swellings with no obvious trigger. The UCARE center at St. James's Hospital sees 10-20 new patients with CSU per week. Although CSU shares some symptoms with food allergy, it is not caused by an allergy to food or medicines.

Diagnosis of CSU can be late and difficult, due to a lack of awareness about the condition. Furthermore, individuals with this disease can become distressed and experience many frustrations ranging from difficulties at work and interpersonal relationships, to problems with sleep disturbance, low mood, and anxiety.

The study explored a rare form of mast cells called myeloid progenitors in blood, in patients with the condition. The team compared these cells in people with CSU and healthy controls. Treatment response to the anti-

IgE therapy omalizumab, was also assessed. Individuals who had a fast response to omalizumab were found to have higher numbers of myeloid progenitors in their blood when compared to people who had a slow (or no) response, to omalizumab.

The study therefore points to the intriguing possibility of using these cell types to predict who might respond to treatment with anti-IgE therapies.

Dr. Barry Moran, a scientist at Trinity Biomedical Science Institute (TBSI), Trinity College who contributed to the study said, "We developed a flow assay to identify this rare cell type. We were excited to find that our findings and clinical correlates were complemented by transcriptomic data."

David McMahon from the Irish Skin Foundation said, "CSU refers to hives that come and go, without any particular or obvious trigger, and last for longer than 6 weeks. For some people affected by CSU, the quality of life impacts can be profound and far reaching."

CSU is frequently mistaken for an allergic reaction. Specific triggers such as allergic reactions to foods are often sought. Unfortunately, attempts to avoid suspected allergic triggers do not help. This can be frustrating for people who suffer with this condition.

Symptoms for many people with CSU can be completely controlled by regular treatment with antihistamines. Often, these medications need to be used at high doses. Some individuals will not respond to this simple intervention and will need referral to a specialist center such as the UCARE center in St. James's Hospital.

Individuals who do not respond to high dose antihistamines are considered for the anti-IgE biologic treatment, omalizumab. This treatment is only available in a specialist setting.

Dr. Conor Finlay, a scientist from the Trinity Translational Medicine Institute (TTMI) and one of the senior authors of the study, said, "Mast cells pack a punch, when activated by IgE antibodies they can be said to explode and release inflammatory factors into the skin—this is what causes itching and hives."

Dr. Niall Conlon, a senior author on the study and consultant immunologist, said, "For some people, treatment with omalizumab, an injectable drug that steadies mast cells, really works. However, for others this drug is less effective or takes much longer to work. It would really help us to understand better why certain people don't respond as well to omalizumab. Information on how this happens might help us direct our treatments more effectively and make patients better, quicker"

Dr. Katie Ridge, the lead author on the study, said, "Mast cells are tricky cells to study. Mature mast cells are not found in the blood. That is why we used a method to study an extremely rare immature form of mast cells in the blood, called mast cell progenitors. Our findings point to potential inflammatory signals in this disease and highlight how chronic urticaria is more than skin deep.

"Our findings have significant implications not only in relation the individuals with urticaria but potentially other allergic diseases whereby we may be able to predict treatment response using exploration of this cell type."

More information: Katie Ridge et al, Lin−CD117+CD34+FcεRI+ progenitor cells are increased in chronic spontaneous urticaria and predict clinical responsiveness to anti-IgE therapy, *Allergy* (2024). DOI: 10.1111/all.16127

Provided by Trinity College Dublin