A new study unravels key signals that regulate protective and sometimes pathological inflammation of the skin. The research, published online on January 26th in the journal *Immunity* by Cell Press, identifies a "gatekeeper" that, when lost, can cause inflammatory skin disease in the absence of injury or infection. The findings may eventually lead to new treatment strategies for the more than 10% of people in the western world that suffer from inflammatory skin diseases.

Although the skin typically remains in a "quiet" state, injury or invading pathogens cause skin cells to sound the alarm and mobilize an impressive immune response called inflammation. Inflammation of the skin is a powerful and appropriate response to infection or injury, but overzealous or unwarranted inflammation of the skin is harmful. Therefore, it is important to understand how skin cells regulate the function of immune cells.

"We knew that skin cells called keratinocytes direct the local immune response, yet the signaling networks in the skin that control the immune response were poorly defined," explains senior study author, Dr. Rama Khokha, from the Ontario Cancer Institute. "In our study we investigated whether an enzyme called ADAM17 is involved in crosstalk between the skin and the immune system. ADAM17 sheds proteins from the cell surface and has been implicated in immune cell function and development."

Aditya Murphy of the Khokha lab inactivated the gene for ADAM17 in the skin of adult mice and observed spontaneous production of inflammatory proteins by keratinocytes, culminating in skin inflammation and immune cell proliferation in the mice lacking the gene for ADAM17.

"Our study provides the first demonstration of the physiological requirement of ADAM17 in Notch signaling and demonstrates that loss of this gatekeeper triggers an immune response, even in the absence of injury or infection," concludes Dr. Khokha. "A better understanding of the mechanisms that regulate communication between immune and non-immune cells will be of significant value in the treatment of diseases affecting the skin and other barrier tissues."

Provided by Cell Press