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A missing immune response molecule has no ill effects on subjects

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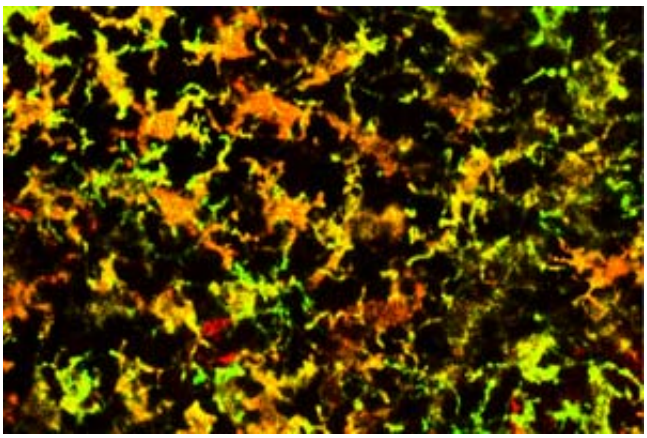

A dense network of normal CD1a (green)- and CD1c (red)-expressing Langerhans cells in human skin. Credit: A*STAR Singapore Immunology Network

A coincidence helped A*STAR researchers unravel the function of a little-understood molecule involved in the body's immune defense system.

During a clinical study involving analysis of skin biopsies, researchers from the A*STAR Singapore Immunology Network discovered an adult who completely lacked CD1a molecules.

The CD1a molecule is part of the CD1 family that plays a key role in the body's immune response to pathogens, particularly bacteria, by

delivering pathogenic molecules to the T-cells that orchestrate an immune response.

However, says lead researcher Katja Fink from A*STAR, the specific role of CD1a has been unclear. Alongside its role in immune response there was some evidence CD1a helped maintain the barrier function of the skin.

"Immune inadequacies due to CD1a defects have not been previously described," Fink says. "It has proved difficult to dissect the specific role of CD1a in immune regulation because mice, as model systems to study molecular functions, do not express CD1a."

The discovery of an adult without CD1a presented a golden opportunity to study the biological significance of CD1a expression.

Subsequent testing of the CD1a-deficient adult's family members—both the parents and all four siblings—revealed one sibling also had the same condition. Both CD1a-deficient individuals presented as healthy.

After uncovering the CD1a deficiency using microscopic analysis of blood and skin samples, the team used DNA sequencing of the CD1a molecule and genome of the family to determine its cause. Fink says the CD1a deficiency resulted from the combination of two genetic mutations: one inherited from each parent.

"This coincidence resulted in the inability of cells to produce CD1a," she says, adding the condition is "extremely rare and we did not find it in all the publicly available human genomic databases".

Importantly, the lack of CD1a expression did not produce any apparent skin abnormalities, or impair the systemic immune in either individual.

Fink says their study, in collaboration with the Dengue Research Group at the Oxford University Clinical Research Unit in Vietnam, is the first to suggest CD1a deficiency has no apparent consequences for health.

"This absence does not cause obvious problems, and we think that other CD1 molecule members can take over the role of CD1a," Fink says.

The discovery will inform future immunological research, Fink says. "We know that for anti-microbial immune responses we have to consider the role of several CD1 family members and not only focus on CD1a since different CD1 molecules might do the same job."

More information: Daniela Cerny et al. Complete human CD1a deficiency on Langerhans cells due to a rare point mutation in the coding sequence, *Journal of Allergy and Clinical Immunology* (2016). DOI: 10.1016/j.jaci.2016.05.028

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