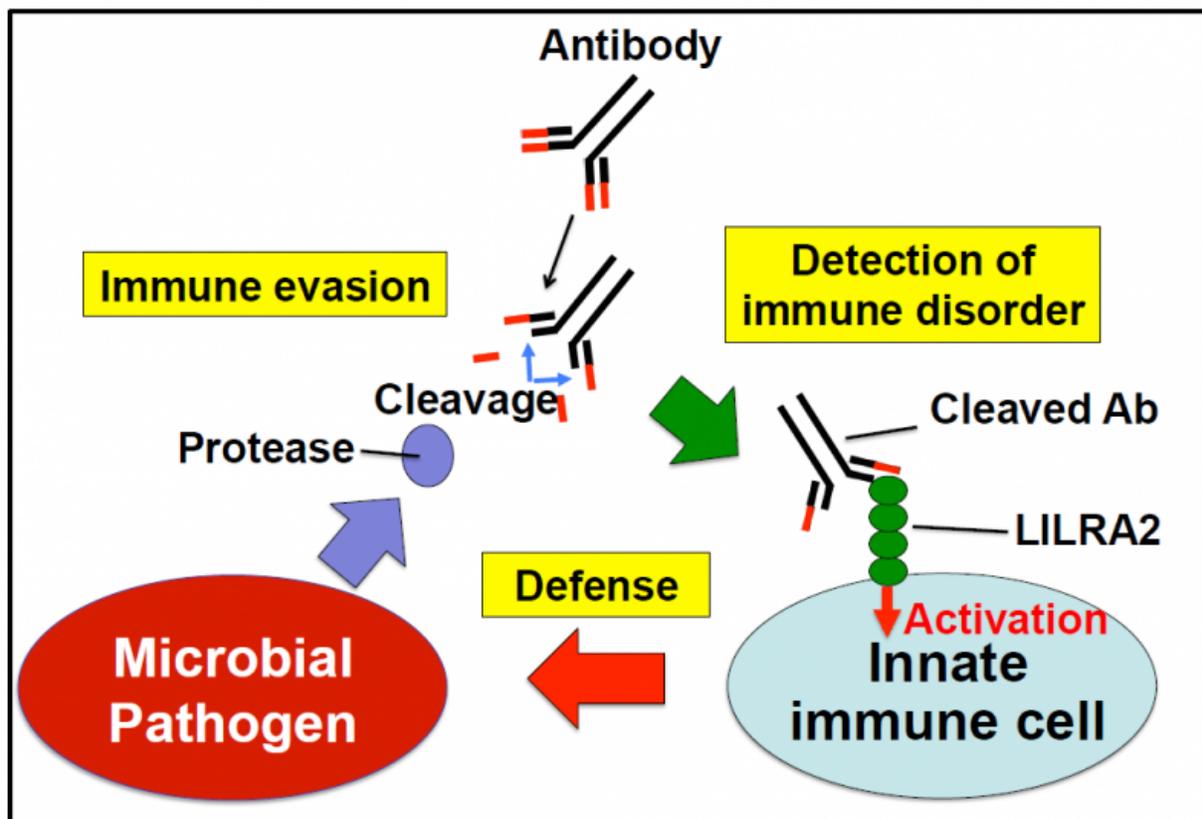


Discovery of a new defense system against microbial pathogens

July 12 2016



New concept for host defense system against microbial pathogen: Antibodies play an important role in host defense against microbial pathogens. However, microbial pathogens seem to have acquired a protease that destroys antibodies in order to evade host immune system. On the other hand, the host immune system appears to have acquired an immune activating receptor, LILRA2, that specifically recognizes microbially cleaved antibodies. Credit: Osaka University

For the first time in the world, a group of researchers discovered a human immune receptor, which detects the invasion of pathogenic microorganisms. They thereby succeeded in identifying a so far unknown host defense mechanism. These results will contribute to future developments in the treatment and prevention of infectious diseases.

Infectious diseases are a serious concern for societies around the world and continue to be a major cause of death. They are caused by pathogenic microorganisms that fight back against the host's [biological defense](#) system by producing a variety of proteins. However, the various mechanisms of this biological defense system are yet to be fully understood. Assistant Professor Kouyuki Hirayasu and Professor Hisashi Arase as well as their research group at the Immunology Frontier Research Center/Research Institute for Microbial Diseases of Osaka University, Japan now made the discovery that certain types of microorganisms evade the immune system by producing protein-splitting enzymes (protease), which cleave and thereby disable the antibodies that trigger immune responses in the host. They further found a so far unknown receptor within the host that recognizes the cleaved antibodies and fight the immune evasion mechanisms of pathogenic microorganisms.

The research team came upon these receptors (LILRA2) when they analyzed human cell strains infected with Mycoplasma, which are extremely small bacteria possessing no cell walls. As with Mycoplasma, other pathogenic microorganisms such as Legionella (parasitic bacteria within cells causing pneumonia), pneumococcus and Haemophilus influenzae (both bacteria causing pneumonia and [middle ear infection](#)) as well as Candida (a type of fungus normally resident in areas such as the mouth or vagina; may cause infections when the body's immune function drops) also produce protease that cleaves antibodies. In the case of Legionella, which infect and multiply within immune cells, findings show that their growth is inhibited when LILRA2 recognize the cleaved

antibodies. Similarly, LILRA2-expressing cells were activated in other places infected with bacteria as well, such as tympanitis (middle ear infection), inflammatory atheroma (type of skin boil), and cellulitis (bacterial skin infection).

The discovery that LILRA2 immune receptors work as a biological [defense system](#) against [pathogenic microorganisms](#) is expected to contribute to the development of new treatments and prevention of [infectious diseases](#) via the development of drugs that control LILRA2 functions and vaccines.

More information: Kouyuki Hirayasu et al. Microbially cleaved immunoglobulins are sensed by the innate immune receptor LILRA2, *Nature Microbiology* (2016). [DOI: 10.1038/nmicrobiol.2016.54](https://doi.org/10.1038/nmicrobiol.2016.54)

Provided by Osaka University

Citation: Discovery of a new defense system against microbial pathogens (2016, July 12) retrieved 19 September 2024 from <https://medicalxpress.com/news/2016-07-discovery-defense-microbial-pathogens.html>

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