Policing cells demand ID to tell friend from foe

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University of Pennsylvania scientists studying macrophages, the biological cells that spring from white blood cells to eat and destroy foreign or dying cells, have discovered how these “policemen” differentiate between friend and foe. The paper appears as the cover article in the March 10 edition of the *Journal of Cell Biology*.

The knowledge suggests new ways science may be able to turn off rogue macrophages that are the root cause of the many inflammatory diseases ranging from atherosclerosis to arthritis and that provide the mechanism for tissue and organ rejection after transplant.

There is also evidence that some types of cancer cells over-express the molecular protein that macrophages recognize as friendly — like a fake ID — which allows the cancer to avoid being perceived as foreign. In addition, the molecules involved in the recognition mechanism appear somewhat variable from person to person, with possible links to success or failure in transplantation of stem cells.

Researchers studied these main “policing cells” in the body, macrophages, from the Greek for “eating cells,” and how they choose to attack and engulf foreign cells and particles but recognize and refuse to eat their own kind.

“Like a police dog, a macrophage responds to a signal that means ‘let go,’ Dennis Discher, professor of chemical and biomolecular engineering at Penn, said. “It’s what makes your body more of a 'dog eat cat' kind of

world rather than a 'dog eat dog' world."

Discher and his team observed macrophages in culture using "friendly" human blood cells and "foreign" sheep blood cells as well as plastic particles. In all cases, the macrophage binds to a target, often identified by a cloak of common IgG antibodies (the community watch), and "frisks" the target with a cell extension. This protein extension becomes a muscle-like headlock with foreign targets, wrapping around the target and pulling it in. Self-cells have a molecular protein on their surface that is specifically recognized by the macrophage to switch off the headlock, thus stopping engulfment and allowing self cells to coexist and move on.

The team found that both actin and non-muscle myosin were involved in the attack of foreign sheep cells due to recognition of the foreign protein CD47. Human red blood cells activated only actin, in a meet-and-greet maneuver. Macrophages, therefore, use a form of identification, much like police ask for a driver's license at a traffic stop; however, not every cell tailed by antibodies is a danger to the body, so macrophages check for that marker, the protein CD47. If the latter is missing or even of the wrong species, the target is devoured.

Additional experiments also showed that protein CD47 affects its receptor, SIRP-alpha, which in turn inactivates the myosin by preventing the addition of a phosphate group to the brawny molecule. By shutting down a pulling protein needed to complete phagocytosis, CD47 prevents cells that belong from being eaten.

Source: University of Pennsylvania