Bound to identify intruders

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The first lines of defense in our immune systems are specialized mobile units that check the identity of cells to determine whether they are 'self' or 'foreign.' A team of scientists, led by Prof. Israel Pecht of the Weizmann Institute's Immunology Department, has now revealed in fine detail how the body's 'reconnaissance unit' continuously screens and inspects identity.

These new findings may lead to deeper insights into the workings of the immune system, its function in health and malfunction in disease, as well as yielding new directions in pharmaceutical and medical research.

White blood cells called T cells employ specialized receptors called TCRs (T cell receptors) for cell identification. TCRs bind to molecules present on all our body's cells that act as 'self-I.D. cards.' Small fragments of bodily components bound to grooves in these molecules provide additional confirmation that the cell is ours and intruder-free. T cell receptors, when they examine the these complexes (antigens), are able to spot foreign bits, even when one amino acid in the antigen is out of order, and can pick just one infected cell out of thousands of healthy ones, even when they harbor a previously unknown virus.

How does this interaction take place" Pecht, together with colleagues in Germany and France, has now provided the first step-by-step understanding of the process. Using a method that resolves these biological events at millisecond (a thousandth of a second) intervals, they were able to show how TCR binding progresses through time. Their findings recently appeared in the *Proceedings of the National Academy*

of Sciences.

The team found that binding of the TCR to the antigen takes place in two separate stages, confirming the widely-held theory that the process is an 'induced fit': The original physical contact between the two molecules initiates the second step, in which conformational changes occur in the receptor as it molds itself to fit the antigen shape.

This research, says Pecht, may go a long way toward explaining a seeming paradox of long standing: How T cells can be highly specific – able to precisely identify a particular protein structure – and yet able to bind to a very wide variety of protein molecules. Additional studies based on this research may clarify the process further – shedding light on the causes of autoimmune diseases and infections such as HIV that evade the immune system, as well as advancing the search for new drugs and treatments for a variety of diseases.

Source: Weizmann Institute of Science