LANGUAGE, MEANING AND THE IMMUNE SYSTEM

IRUN R. COHEN*

Department of Cell Biology, Weizmann Institute of Science, Rehovot, Israel

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The immune system has evolved to recognize and respond to invaders. These invaders, comprising infectious agents and probably some cancer cells too, communicate to the immune system with their antigens. The immune system recognizes invader antigen molecules, or actually the small parts of antigens called epitopes. Recognition of an epitope occurs when lymphocyte receptors or antibodies bind to it. The binding is degenerate: a single receptor can bind to many different epitopes, albeit with different affinities. Nevertheless, the signs of an invader include the invader's antigen epitopes. Vaccination with invader antigens is a way of alerting the immune system so that the specific invader can be efficiently rejected when the need arises.

Unfortunately, the simple vaccinations that have worked so well in the past against the simple parasites do not seem to work against the more resourceful invaders that, like human immunodeficiency virus (HIV) and many cancer cells, are able to manipulate the immune system itself. HIV is the most notorious example of an immunological manipulator: the immune system responds to the virus early in infection, but this response does not destroy the virus; it may even aid the infection. In time, the virus infection destroys the immune system; the outcome is common knowledge. Other infectious agents and tumor cells can also foil the immune response, albeit less flagrantly. To activate the immune system to reject such immunologically sophisticated invaders, we shall have to manipulate our immune systems better than they do. My point here is that epitopes alone may not transmit meaningful messages to the immune system; we have to speak its language. As in any language, meaning is muted by ambiguity.

Words are inherently ambiguous; they often have several meanings. The word "mean," for example, could relate to statistics, to intentions, to a type of inferiority, to a malicious action or habit of mind, as well as to information. Epitopes are at least as ambiguous as are words. Epitopes are *samples* of antigens; but what does the antigen signify? The antigens themselves are only *samples* of more complex entities such as viruses, bacteria, tumor cells, or normal cells. Epitopes, therefore, are only *samples* of *samples*; they can bear no intrinsic symbolism unless the system has already been primed to see them. New epitopes are akin to words that only point: words like *this*, *that*, *here*, *now*. Epitopes which the immune system remembers from past experience may acquire semantic meaning, but that is another story.

The problem posed to the immune system by ambiguity and degeneracy of recognition is not merely intellectual; the immune system, for the survival of the individual, must respond to the epitope in an appropriate way. Indeed, each type of antigen needs a different response: the self-molecule on a healthy cell should be ignored (to avoid an autoimmune disease), the same self-molecule on a tumor cell should be attacked; virulent and innocuous microbes need to activate different types of lymphocytes for effective control. In other words, each response ideally should fit the nature of the antigen. Thus, a meaningful antigenic message is a message that specifies a particular response.

Note that a functional relationship exists between response and meaning. The only way to detect objectively whether a message has transmitted *meaning* is to observe whether the message leads to a response appropriate to the content of the message. ""Duck," said the waiter" should produce a different response than ""Duck," said the boxer." Each meaning of the word *Duck* is made clear only by the entire sentence, the context in which the word *Duck* appears. The correct meaning is evident to the behavior that avoids a punch or ingests a morsel. (Obviously the appropriate response to some messages is not detected by overt behavior, but by a change in state of mind.) But why equate meaning with response; isn't it the meaning that determines the response? My point is that meaning belongs to the realm of communication — an entity that leaves no mark has no meaning — and communication is a kind

Address for correspondence: Dr. I.R. Cohen, Department of Cell biology, Weizmann Institute of Science, 76100 Rehovot, Israel.

*Incumbent of the Mauerberger Chair in Immunology and Director of the Robert Koch-Minerva Center for Research in Autoimmune Diseases.

of adaptation: the correspondence between what is sent and what is received, between what is said and what is done, between the input and the output, between the nature of the immunogenic stimulus and the immune response. Like adaptation, meaning is referential. The medium may be the message, but the response is the meaning.

To reframe the question of meaning, if epitopes are inherently ambiguous, how does the immune system interpret their meaning, that is, know how best to respond? I propose that the immune system interprets meaning using the strategy of language: it reads not single epitopes (isolated words) but strings of signals (sentences) ordered by preexisting rules (syntax). The power of language to register an unlimited variety of information derives from its combination of two complementary elements: a limited set of syntactic structures together with unlimited assemblies of large numbers of words. The assemblies of words are not predetermined, the syntactic structures are. The individual uses strings of words according to the rules of syntax and according to the semantic values of the words which are learned through association.

The language of the immune system, too, combines indeterminable variety with syntactic order in strings of signals. The antigen epitopes, which function as words, are read by an astronomical number of antibody and receptor combining sites that are generated uniquely in the lymphocytes of each individual by random genetic recombinations and mutations. Thus, the antigen receptors, like words, are essentially indeterminate and unlimited. However, the building blocks for generating the receptors and the rules for using them are largely inherited. Molecules, which have been called co-stimulatory signals, tell the immune system how to respond to epitopes; such molecules function as syntactic structures. Just as the syntactic structures of human language allow the organization of sentences that impart meaning to words, the syntactic structures of the immune system tell the system how to organize the meaning of the epitopes.

The immune syntactic structures are of two types: external and internal. External signals are made when specialized antigen-presenting cells or tissue cells interact with the invaders and then pass on the information to the lymphocytes. These cells act as intermediaries; they construct a string of signals legible to lymphocytes by processing invaders to produce epitopes along with syntactic accessory or co-stimulatory signals. The external syntactic structures communicate the context; they include major histocompatibility complex molecules, cell interaction molecules, and cytokines of all sorts.

Internal syntactic structures include the molecules by which lymphocytes interact among themselves. These internal structures relate to the networks of helper and suppressor connections between lymphocytes. Some of these connections define the internal state of the system, but the details are beyond the scope of this brief essay. So too is the subject of immunological memory. The bottom line is that the integration of epitopes and syntactic signals produces meaning — the specific immune response. The same epitope read in the context of different cytokines or cell interaction molecules has a different meaning.

HIV, tumor cells, and other invaders can be said to misinform the immune system by transmitting a string of inappropriate syntactic signals that thwart an appropriate response. New vaccines might counter this misinformation by speaking the system's proper language: a string of suitable syntactic signals along with specific epitopes. The epitopes identify the invader; the syntactic signals predicate the correct response. Such compound vaccines would have adaptive meaning; the invader will now be rejected through suitable language skills.

Thus the new immunology will emerge as a cognitive science (1,2).

References

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