

This Week's Citation Classic®

Tripp M R. Hemagglutinin in the blood of the oyster, *Crassostrea virginica*.
J. Invertebr. Pathol. 8:478-84, 1966.
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A protein in the blood of normal oysters agglutinates red blood cells of several vertebrate species. It enhances phagocytosis of red cells by oyster hemocytes and may affect disposal of foreign substances in oyster tissues. (The *SCI*® indicates that this paper has been cited in more than 120 publications, making it the most-cited paper published in this journal.)

How Do Invertebrates Recognize Foreignness?

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Many invertebrate animals are important to human affairs because of their roles as dietary items, crop pests, and vectors of infectious agents. Only since 1950 have we begun to understand the details of how they interact with the latter.

In 1950, Leslie A. Stauber, a Rutgers University faculty member steeped in that institution's tradition of oyster biology, published the first experimental study of the oyster's response to foreign material in its tissues.¹ Shortly after that, Sung Y. Feng and I began our doctoral research under Stauber's tutelage. We extended his findings to show that microbes and other biological particles are removed by oyster phagocytes² and that these reactions are modulated by environmental conditions.³ As this picture of cellular defense mechanisms began to develop in the late-1950s, the oysters of Delaware Bay were devastated by an epidemic disease named "MSX."⁴ This economic catastrophe aroused new interest in invertebrate "immunology," and important studies of basic molluscan biology were initiated.

When I joined the University of Delaware faculty in 1960, I tried for several years, without notable success, to establish oyster cell cultures. In search of a more productive research problem, I turned to questions about invertebrate cellular recognition mechanisms using the oyster as my experimental subject. A crude preliminary *in vitro* experiment involved adding human red blood cells to oyster hemolymph (blood). The dramatic agglutination reaction that resulted immediately suggested that a humoral factor with antibody-like properties was present in oyster blood and might affect the interaction of biological particles and oyster phagocytes. The obvious experiments were quickly performed and they showed that a soluble substance (lectin) reacted with certain red blood cells and enhanced phagocytosis by oyster cells. The manuscript was submitted to the *Journal of Invertebrate Pathology* and accepted by the editor, Tom Cheng, a strong proponent of comparative immunology.

Agglutinins in the blood of invertebrates had been known for several years,⁵ but their function was unknown. My contribution showed that invertebrate lectins might serve as recognition molecules that could enhance the effectiveness of cellular defense mechanisms. Fortunately, several people entering the field of invertebrate immunity at that time brought with them new concepts and experimental approaches. During the intervening years, several laboratories contributed increasingly sophisticated research that has advanced understanding of phagocyte-lectin interaction.⁶ Detailed models of invertebrate recognition mechanisms are still evolving as comparative immunology of invertebrates moves toward the mainstream of immunobiology.

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2. Tripp M R. Mechanisms of removal of injected microorganisms from the American oyster, *Crassostrea virginica*. *Biol. Bull.* 119:210-23, 1960.
3. Feng S Y & Feng J S. The effect of temperature on cellular reactions of *Crassostrea virginica* to the injection of avian erythrocytes. *J. Invertebr. Pathol.* 23:22-37, 1974.
4. Haskin H H, Stauber L A & Mackin J G. *Minchinia nelsoni* n. sp. (Haplosporidia: Haplosporidiidae): causative agent of the Delaware Bay epizootic. *Science* 153:1414-6, 1966. (Cited 60 times.)
5. Tyler A. Natural hemagglutinins in the body fluids and seminal fluids of various invertebrates. *Biol. Bull.* 90:213-9, 1946. (Cited 65 times.)
6. Yang R & Yoshino T P. Immunorecognition of the freshwater bivalve, *Corbicula fluminea* II. Isolation and characterization of a plasma opsonin with hemagglutinating activity. *Develop. Comp. Immunol.* 14:397-404, 1990.