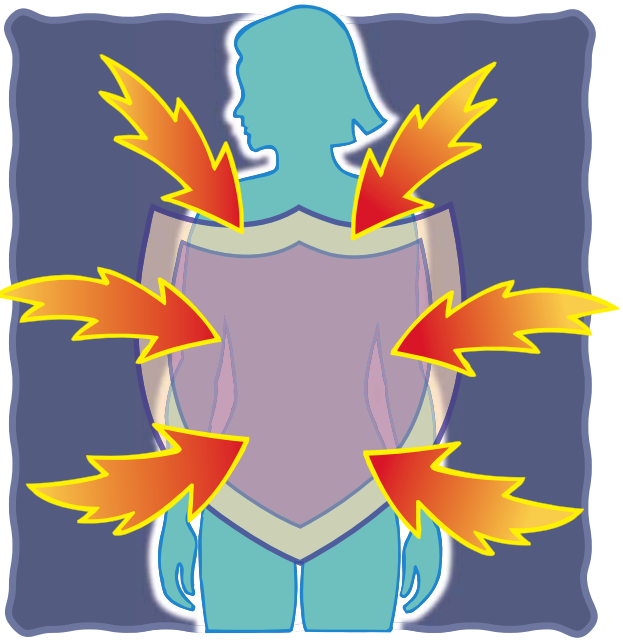
Taking aim at immune disorders

THE TECHNOLOGY Designing new drugs to treat immune disorders is no small feat. But as part of an international collaboration, Professor Christodoulos Floudas has developed a way to make peptides, short proteins that could become medicines to help control immune disorders such as cardiovascular disease, respiratory syndromes, and rheumatoid arthritis.



Floudas, the Stephen C. Macaleer '63 Professor in Engineering and Applied Science, has created the peptides using computational modeling, and predicted the way these would interact with their target by either boosting or inhibiting immune-system activity. "We have developed a novel protein-design framework, but this method is still in the discovery phase," said Floudas. Other members of the multi-disciplinary team have synthesized the peptides and tested their activity in human cells.

Floudas

Specifically, the approach focuses on the complement system, an important component of our immune system. The complement system is a link between our innate and adaptive immune systems — the innate immune system is the first line of defense against pathogens, while the adaptive immune system generates antibodies against pathogens to which we have been exposed.

Floudas and his team designed peptides targeting a specific component of the complement system, C3a, which helps the innate immune system to clear pathogens such as viruses and bacteria and to promote inflammation — our body's natural response to protect itself. But while we would never heal without acute inflammation, chronic inflammation can damage tissue in the body and lead to disorders such as rheumatoid arthritis and Crohn's disease.

THE POTENTIAL Floudas, who has been at Princeton since 2007, also is studying other components of the complement system. Several of his approaches to design proteins have been shown to work against other immune diseases, HIV, and cancer therapeutics: The peptides designed in the Floudas lab have been synthesized and tested in vitro, the first step to test the activity and effectiveness of a potential drug.

"C3a is an inhibitor of inflammation, and [for organ transplantation] we need inhibitors that control the overactivation of the complement system," said Floudas. Some of the peptides designed by Floudas to inhibit the complement system eventually could be used to prevent organ rejection, which remains relatively high among recipients of kidney, lung, and other transplants. P *By Anna Azvolinsky *09*

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