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UCSB Researchers Discover New Biotechnology to Identify and Engineer Substrates for Proteases

Proteases play key roles in most diseases, but their substrates are unknown.

This technology should help solve the puzzles of cancer, Alzheimer?s, atherosclerosis and infectious diseases.

Santa Barbara, California ? May 1, 2006 ? Researchers at UC Santa Barbara have developed a new biot echnology that enables scientists to identify and engineer protease substrates, giving them the means of crafting pharmaceuticals to outsmart disease. Their work, authored by Patrick Daugherty, an assistant professor of Chemical Engineering, and Kevin Boulware, a PhD candidate, are published online today in the Proceedings of the National Academy of Sciences.

Proteases (or peptidases) are encoded by about two percent of genes in the human genome and play key roles in nearly all diseases. They act as ?molecular scissors? by attaching to specific sequences contained within other prot eins, called substrates, and cutting them in specific locations. For example, proteases are responsible for digesting food, for determining the proper time for cells to die, and for removing damaged proteins from the body.

But the substrates for most proteases are unknown, and this has limited researchers? ability to facilitate or th wart protease action. By identifying substrates, scientists gain the ability to regulate protein function, creating the capacity to speed up, slow down or eliminate particular protease actions. Daugherty?s approach also makes it easier to measure protease action and thus develop pharmaceuticals that control protease activity.

Daugherty and Boulware developed a general combinatorial approach to identify optimal substrates of proteases, using quantitative kinetic screening of cellular libraries of peptide substrates (CLiPS). The results suggest that CLiPS will be broadly useful for characterizing proteases and developing optimal substrates for therapeutic applications.

Of the roughly 1,000 proteases in the human genome, only about ten percent of the targets have been identified, but Daugherty believes that scientists will identify nearly all of them in the next five to ten years. ?This te chnology will give us a scalable tool that will allow us to effectively tackle this challenge,? he says.

Released by Barbara Bronson Gray

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