

BIO/TECHNOLOGY CONFERENCE

THE REAL PROBLEMS WITH PROTEIN DESIGN

NEW ORLEANS—The protein design session at this year's *Bio/Technology* conference made clear the serious gap between theory and data in relating amino acid sequence to protein folding, conformation, and activity. As a result, except in a very limited number of cases, predictability does not yet exist. To truly tap the potential of protein engineering will require bridging this gap.

Jonathan King (MIT, Cambridge, MA), Lila Gierasch (University of Delaware, Newark), and Rainier Jaenicke (University of Regensburg, F.R.G.) focused on the dynamic properties of polypeptide chains in achieving their final conformation. Gierasch, making ingenious use of classical physical chemical techniques, has analyzed the actual behavior of synthetic signal peptides at aqueous membrane interfaces. The take-home lesson from her work is that these sequences do not encode the static property of maintaining a particular conformation. Rather, they confer the ability to switch between a subset of conformations in different environments.

King emphasized the need to identify the residue-residue interactions critical in determining folding pathways. These residues, his work shows, are often different from those specifying catalytic sites. Two interesting practical lessons emerged from his experiments. One is that protein aggregation and the formation of inclusion bodies can occur as off-pathway dead-ends in the native folding pathway. The second is that this can often be prevented by simply lowering the temperature a few degrees.

Jaenicke, one of the few people who has succeeded in refolding oligomeric proteins, showed that oligomer formation and refolding are generally competing pathways. Thus, success is largely a matter of whether the rate limiting step is refolding, chain association, or later conformational changes—again an area in which theory falls far short of data.

In the case of modifying the properties of a native protein by judicious amino acid substitutions, results have been somewhat more encouraging—particularly for proteins whose crystal structures are known. But even here

surprises are not uncommon. Charles Craik (University of California, San Francisco) likened some of his results to replacing a round tire with a square one and discovering the car now runs backwards. His group has been studying the very well characterized enzyme trypsin, which catalyzes the hydrolysis of lysine or arginine amides and esters. The proposed catalytic mechanism involves a triad of residues—His⁵⁷, Asp¹⁰², and Ser¹⁹⁵. When Craik replaced Asp¹⁰² by an asparagine, the mutant enzyme had less than 0.01 percent activity at pH 7.0.

However, at pH 10 the mutant trypsin gave significant catalysis. The crystal structures of the two molecules are nearly identical, except that His⁵⁷ occurs in two conformations in the mutant. Thus Asp¹⁰² is required both for catalytic activity at physiological pH, and also to correctly position His⁵⁷. Perhaps one reason catalysis is so difficult to model accurately is that it involves multiple states of the enzyme, and substitutions may affect these states differently.

—Harvey Bialy

Bio/Technology, The National University of Singapore, & The Science Council of Singapore

are pleased to present an extraordinary scientific meeting

THE MOLECULAR BIOLOGY OF HUMAN DISEASE: AN ASIAN PERSPECTIVE

October 5-7, 1987—Singapore

● MONDAY, OCT. 5

KEYNOTE ADDRESS

Sydney Brenner

What Molecular Biology Means for the Medical Sciences

VACCINE DEVELOPMENT TODAY AND TOMORROW

Hepatitis, the First Success

Pablo Valenzuela

Chiron

The Design of Subunit Vaccines for Production in Yeast Cells

Arthur Levinson

Genentech

The Design and Production of Subunit Vaccines in Mammalian Cells

Malaria, the Goal is in Sight

Victor Nussenzweig

New York University Medical Center

How Close are We to a Sporozoite Vaccine, and How Effective is it Likely to be?

AIDS, the Challenge on the Horizon

Flossie Wong-Staal

U.S. National Institutes of Health

The Molecular Biology of Human Immunodeficiency Virus

Myron Essex

Harvard University School of Public Health

The Natural Biology of AIDS: Lessons for a Potential Vaccine

● TUESDAY, OCT. 6

BIOLOGICAL RESPONSE MODIFIERS: PROMISE AND REALITY

George Poste

Smith, Kline & French Research Laboratories

The Challenges and Opportunities of Biological Response Modifier Therapy

Bart Sefton

Salk Institute

The Role of Receptor Signaling in Cellular Responses to Growth Factors

Kendall Smith

Dartmouth Medical School

The Structure-Activity Relationships Between Interleukin-2 and its Receptor

Y.H. Tan

Institute of Molecular and Cellular Biology, National University of Singapore

Intracellular Signaling in the Interferon System

Ken-ichi Arai

DNAX Institute of Molecular and Cellular Biology

The Molecular Biology of T-Cell-Derived Lymphokines

David Goeddel

Genentech

Will Tumor Necrosis Factor and Related Molecules Become Effective Cancer Therapeutics?

● WEDNESDAY, OCT. 7

ACCESSING THE HUMAN GENOME

Leroy Hood

California Institute of Technology

How Far are We from Sequencing the Human Genome, and What Will We Learn in the Process?

Anthony Monaco

The Boston Children's Hospital

The Isolation and Characterization of the Duchenne Muscular Dystrophy Gene, and its Implications for Treatment

Henry Erlich

Cetus

The Application of DNA Probe Technologies to the Identification of Genetic Disorders

Jan Breslow

The Rockefeller University

The Characterization of Human Apolipoprotein Genes, and Their Contribution to Atherosclerosis

Marcello Siniscalco

Memorial Sloan-Kettering Cancer Center

Chromosome Fragility, Genetic Recombination, and Human Disease

Richard Mulligan

The Whitehead Institute

Gene Replacement Technologies

CALL FOR PAPERS

The Editors of *Bio/Technology* are eager for poster presentations on topics relevant to this conference. Interested scientists are asked to submit a 250-word abstract to Research Editor, *Bio/Technology*, 65 Bleecker St., New York, NY 10012, USA. The deadline for submitting posters is 1 September 1987.

TRAVEL ARRANGEMENTS

To obtain air tickets from North America and Europe at special conference rates, please contact Aaron Krumbert at Consolidated Tours, 250 W. 57th Street, New York, NY 10019, USA. Or phone toll-free at 800/228-0877.

Sponsor's liability: Should this conference be cancelled or postponed for any reason, the sponsor's liability is limited to the return of the registration fee.

Cancellation policy: All cancellations must be received in writing. Cancellations received before 5 September to the day of the conference will be subject to a service charge of U.S. \$25. No refunds will be made after that date. Registrants who are unable to attend may, if they choose, send a substitute.

THE REGISTRATION FEE IS U.S. \$395

REGISTRATION

The registration fee is U.S. \$395. Registrants are entitled to attend all three days of conference sessions and all conference social functions, and will receive a book of abstracts and a list of other meeting attendees. Full payment or a valid purchase order must be received from each registrant before the conference.

Checks and international money orders should be payable to The Bio/Technology Singapore Conference. To register, or to obtain more information, please contact

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