UC SANTA BARBARA

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Important Genome Sequencing Spearheaded at UCSB; Development Culminates 12 Years of Research

A tiny predatory protozoan has yielded the secrets of its genome in a project spearheaded by a veteran research scientist at the University of California, Santa Barbara. The results are published in the September 2006 issue of the prestigious peer-reviewed journal, the Public Library of Science Biology. This is an open access journal, so the article can be read or downloaded free-of-charge by anyone in the world with Internet access (see accompanying link). One unique aspect of the UCSB component of this study was the participation of numerous undergraduate students who have since gone on to graduate school or medical programs, or have obtained jobs in biotech companies.

The newly published genome sequence reveals that thousands of genes are shared by the protozoan and humans, thus confirming Tetrahymena as an important model organism for biomedical research. Many significant scientific discoveries, with important applications to human biology and medicine, have already been made with this organism. These include:

- the discovery of catalytic RNAs (a Nobel Prize winning discovery)
- dynein (the first known cell nano-scale motor)
- the structure of telomeres (specialized sequences at the ends of chromosomes)
- the machinery that maintains telomeres (whose regulation protects us from cancer and is relevant to aging)
- the role of modifications of chromatin (the complex of proteins and DNA that make up chromosomes) in gene expression.

The publication of this project caps over a decade of work by the research group of Eduardo Orias, professor in UCSB's Molecular, Cellular, and Developmental Biology Department, whose group has mapped hundreds of genetic and physical landmarks in the Tetrahymena genome. This work provided critical foundation for the genome project. Once the genome sequence became available, the maps provided the most direct verification of the high degree of accuracy and completeness of the genome sequence, as described in the article.

Orias, who organized this challenging research effort, joined the faculty of UCSB's Department of Biological Sciences in July 1959 and taught genetics. He became research professor emeritus in 1994, at which time he began his research in genomics and started mapping the Tetrahymena genome. Orias has worked with Tetrahymena for over 50 years and continues to play a key role in its development as a model organism, that is, a species used to investigate fundamental biological processes shared by all organisms.

"The published genome sequence represents a valuable scientific resource for fundamental, biomedical and biotech research," said Orias. "T. thermophila is a very user-friendly organism for scientific experimentation."

The number of genes is one measure of the complexity of an organism. Surprisingly, the genome sequence shows the Tetrahymena genome contains over 27,000 genes, a number remarkably similar to the number of genes found in the human genome. Some of the shared genes are known to cause hereditary disease when mutated and T. thermophila now provides an excellent model organism for the quick and relatively inexpensive investigation of their function.

Says Anthony D. Carter, Program Director of the Division of Genetics & Developmental Biology of National Institute of General Medical Sciences (NIGMS, one of the National Institutes of Health): "Publication of the Tetrahymena genome marks the culmination of a remarkable collaboration within the research community. Tetrahymena has a long and eminent history in the world of cell biology, and publication of its genome is likely to lead to further fundamental insights into how cells work."

The genome sequence was obtained and analyzed under the direction of Jonathan A. Eisen at the Institute for Genome Research (TIGR) in Rockville, MD. Six co-authors of the genome publication are from the MCD Biology Department, including Orias and project scientist Eileen P. Hamilton. The project was funded by the NIGMS and the National Science Foundation (NSF).

Research by Orias has been continuously supported by extramural grants, mainly from the National Institutes of Health and the National Science Foundation. He has held appointments as a visiting scientist at several research institutions in the U.S., Denmark, Italy and Japan. In 2003, he became the fifth recipient of the Emile

Maupas Medal for contributions to our knowledge of the genetics of the ciliated protozoa.

Orias has long been a strong supporter of undergraduate research. The systematic mapping of the Tetrahymena genome was started by one very talented and committed UC Santa Barbara undergraduate student, Jason Brickner (now an assistant professor at Northwestern), and continued by scores of other undergraduate researchers in the Orias lab. Altogether, more than 60 UCSB undergraduates have worked on the genetic and physical mapping project since 1994.

Eleven undergraduate co-authors, including three first co-authors, are included in 11 of the 26 papers published in notable peer-reviewed journals by this research group since 1994. The initials of dozens of students are immortalized in the names of more than 400 DNA polymorphisms that they discovered and mapped. These students have presented the results of their research at numerous campuswide, state and national undergraduate research colloquia, and several have won prizes for their work. The independent research experience that they gained was invaluable in finding opportunities to continue their education or obtain employment. Virtually all of the former undergraduate researchers have been accepted to prestigious graduate or medical school programs, or have obtained jobs in biotech companies. Partial support for many of the undergraduate students' research came from the UCSB Office for Undergraduate Research and Creative Activity (and its forerunners) and from the UCSB chapter of the California Alliance for Minority Participation (CAMP). In 2005, Orias was recognized with a CAMP "Certificate of Gratitude" for "mentoring CAMP students and encouraging their significant achievement in science, mathematics and engineering."

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Eduardo Orias

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