SOUTHWESTERN NEWS

Media Contact: Morgan Lyons
(214) 648-3404
or e-mail: MLyons@mednet.swmed.edu

ANSWERS ABOUT ONE DISEASE MAY YIELD CLUES TO OTHERS

DALLAS — August 25, 1995 — By cloning a gene for a rare disease, researchers at UT Southwestern Medical Center at Dallas are not only able to offer new hope to patients with Cockayne syndrome, but they also are gaining new knowledge about the genetic origins of other diseases.

Dr. Errol C. Friedberg and his colleagues reported their findings in the August 25 issue of the journal, *Cell*. Friedberg holds the Senator Betty and Dr. Andy Andujar Distinguished Chairmanship of Pathology at UT Southwestern.

Cockayne syndrome (CS) is an inherited condition that produces severe mental and physical health problems including dwarfism, mental retardation, skin diseases, deafness, and premature aging. The symptoms of CS usually appear before a child's second birthday, and most patients die in their preteen years from multiple complications associated with the disease.

Like persons with the syndrome, Cockayne cells are abnormally susceptible to ultraviolet (UV) light. Researchers have held that UV-light sensitivity is caused by a defect in one of the body's DNA repair mechanisms. "But our findings suggest that Cockayne syndrome is a function of a defect in DNA expression or transcription, not repair," Friedberg said. The researchers determined the Cockayne gene expresses a protein (known as the WD repeat protein) involved in DNA transcription.

"In recent years there's been a lot of excitement about the relationship between DNA repair and transcription," Friedberg said. "An important finding of our research is that what was previously thought to be a DNA repair-defective disease may in fact be the result of

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defects in the transcription function of the WD repeat protein, which is involved in both transcription and repair."

The findings are significant for investigators looking at the genetic basis of other diseases. Researchers have connected several diseases with either defects in DNA repair or DNA transcription. Knowing the genetic origin of a disease — where the error occurs in the DNA replication process — could help scientists develop more precise diagnostic and clinical tools to treat a disease.

In the case of Cockayne syndrome, one of the most potentially powerful benefits of cloning the gene is the ability to detect carriers more precisely. When both parents are carriers, the chances are one-in-four that they will have a child with CS. Genetic testing is the only way to identify a carrier.

Cloning the CS also creates the possibility for clinical advances in diagnosing and treating the syndrome. For example, Friedberg believes researchers will eventually be able to develop more precise diagnostic tests to determine if children have CS.

"Any time a human disease gene is cloned, it provides a lot of support and optimism for people affected by the disease," Friedberg said.

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