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******UT Health Science Center neurologists awarded $700,000 in grants to study nerve cancer that strikes children.*

DALLAS--Neurologists at The University of Texas Health Science Center here have been awarded three major research grants totaling more than $700,000 from the National Cancer Institute for studies of a nerve-cell malignancy known as neuroblastoma, the most common solid cancer afflicting children.

Goals of the coordinated five-year research effort are to seek improved drug therapy for treating the disease and to understand more completely the biochemical functions of neuroblastoma cells, said Dr. Roger N. Rosenberg, chairman of neurology at UTHSCD's Southwestern Medical School, in announcing receipt of the awards.

Dr. Rosenberg will be chief investigator for the overall project, in collaboration with Dr. Fred Baskin who will be senior researcher.

The Southwestern medical scientists will study neuroblastoma cells grown in a laboratory environment seeking answers to a perplexing riddle so far hampering effective chemotherapy treatment of the disease--the fact that the malignant nerve cells eventually develop resistance to previously potent cancer-killing drugs.

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By delving deep into the biochemistry of nerve-cell growth and development, the research team hopes "to determine the molecular basis for that resistance," Dr. Rosenberg said.

The scientists also expect to obtain valuable information about the metabolism and biochemical functions of the nerve cell and about development of the normal brain.

Neuroblastoma cells, in the scientist's terminology, are "undifferentiated"--that is, they have no properties or work capabilities of the mature neuron. They divide uncontrollably, and appear able to revert back and forth from a mature to an embryonic state.

The Dallas studies will concentrate on studying regulatory factors in that back-and-forth process or "differentiation," Dr. Rosenberg said.

A key factor in that regulatory mechanism is known to be folic acid metabolism. Folic acid is an essential vitamin in the brain for the manufacture of essential cell nutrients.

Current anti-cancer chemicals destroy neuroblastoma cells by inhibiting certain enzymes required for production of folic acid, thus in effect cutting off the malignant cells' food supply.

Two such cancer-killing drugs will be used in the Dallas experiments. They are fluoro-deoxyuridine (FUDR), and amino-hydroxyquinazoline (AHQ), both of which disrupt folic acid development at key points along its metabolic pathway.

In existing chemotherapy, more than 99 per cent of cancerous cells are initially killed by these and other chemical compounds, Dr. Rosenberg explained. But a tiny fraction of the cells "adapt" to their new metabolic environment--becoming mutants, different but able to continue dividing, somehow resistant to the toxic drug.

"We believe the resistant cells get around the drug by making more of the enzymes that the drugs were initially inhibiting," the neurology chairman said.

Mutant or resistant cells have been found to have abnormal amounts of one essential enzyme for folic acid development--thymidylate synthetase (TS). Intricate studies will be carried out to try to determine whether the resistant cells do in fact have altered properties for making more of these enzymes.

Neuroblastoma victims invariably are young children, their median age being 3 years. Some infants are born with the disease, which appears as multiple small tumors in the peripheral or outer nervous system. Oddly, no mothers of victims have ever had the disease.

While relatively rare compared to such other malignancies as lung cancer, neuroblastoma ranks as the most common solid tumor among children.

Currently available chemotherapy has increased victims' longevity, but the overall outlook for patients under present treatment techniques is "dismal," Dr. Baskin noted. Infrequently (but more often than in other cancers), neuroblastoma goes into spontaneous remission--cells stop abnormal division and the tumors are absorbed by the host.

A long-term therapy goal is to seek ways to stimulate this process chemically using non-toxic drugs, Dr. Baskin said.

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